Studies of pathophysiology and psychosocial functioning in adolescents with anorectal anomalies

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Studies of pathophysiology and psychosocial functioning in adolescents with anorectal anomalies

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A thesis submitted in fulfilment
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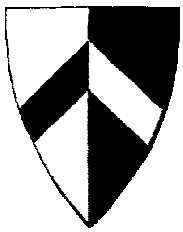

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I hereby certify that the work embodied in this thesis is the result of original research and has not been submitted for a higher degree to another University or institution.

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Abstract

Introduction: Anorectal anomalies (ARA) are a range of congenital conditions ranging from a slight malposition of the anus to complex anomalies of the hindgut and urogenital organ. Despite advanced surgical and treatment modalities, voluntary bowel control is poor following surgical care with high rates of faecal incontinence (FI), and also constipation after all grades of reconstructive surgery. The main aim was to determine the impact that FI and constipation has on psychosocial functioning in the context of ARA in comparison to patients with idiopathic constipation (IC) and healthy controls. We also investigated the pathophysiological mechanisms that might contribute to poor bowel function in patients with ARA.

Methods: Study comprised 52 patients (19 females; range 11-43 years) with ARA, 46 (13 females; range 11-31 years) IC and 51 healthy controls (26 females; range 11-42 years). Constipation and FI were evaluated using KESS and Vaizey scores respectively (a higher score indicating greater symptom severity). Psychometric tests included: Gastrointestinal Quality of Life Index, Children's Depression Inventory/Beck Depression Inventory, General Health Questionnaire-28, State-Trait Anxiety Inventory/Children, Pennebaker Inventory of Limbic Languidness, Big Five Inventory, Level of Hopefulness, Cognitive Emotion Regulation Questionnaire and Weinberger Attitude Inventory. Physiological investigations were undertaken in 32 adults, presenting with a history of previous surgery for ARA and urge FI. Physiological assessment included: anal manometry; rectal sensation (balloon distension); pudendal nerve function (motor latencies); endo-anal ultrasound; colonic transit and proctography.

Results: Significantly higher KESS scores were found in patients with IC (<0.0001) compared to ARA and healthy controls and significantly higher Vaizey scores found in - 3

patients with ARA (<0.0001) and IC (0.0002) compared to healthy controls. Poorer GIQOL scores were found in patients with IC compared to healthy controls ($p<0.001$) and ARA compared to healthy controls ($p<0.01$). There was a significant relationship between poor quality of life and high KESS scores in ARA and IC ($p = 0.003$) and high Vaizey Incontinence scores ($p = 0.02$). Patients with ARA did not have higher psychiatric morbidity in comparison to IC and healthy controls. Personality traits and level of hopefulness appeared the same across the three groups. IC significantly put less emphasis on their general physical health ($p<0.0001$) in comparison to ARA and healthy controls. ARA significantly used more 'positive reappraisal' and 'putting into perspective' as their main coping mechanism compared to healthy controls. Anorectal physiology was abnormal in all subjects with ARA, involving multiple mechanisms. Anal resting tone and squeeze increments were attenuated in 23/32 and 17/32 patients respectively. Both anal sphincters were deficient on endosonography in the majority of patients with ARA. Evidence of pudendal neuropathy in 11/13 (85%) patients studied. Rectal sensation and emptying was abnormal in 17/22 (77%) and 9/14 patients (64%) respectively. Eight out of 17 patients had delayed colonic transit (47%).

Conclusions: Symptoms of FI and constipation are major determinants for poor quality of life in patients with ARA. Contrary to our expectations, they share similar bowel and psychosocial functioning to patients with IC. Adolescents with ARA and IC had minimal psychiatric morbidity, yet experience condition-specific psychosocial problems affecting their daily life. The chronic nature of the patient's problem appeared to have stimulated psychologically protective factors such as positive coping strategies. While the structural integrity of the anal sphincters is the major factor contributing to continence, this study confirms that extra-sphincteric mechanisms, particularly rectal sensory function, may be equally important.

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Dedication

To my brother

Giannis Athanasakos

who initiated my journey into medical research and

who has never lost faith in me.

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Firstly I would like to thank those closest to me in my life. I wouldn't be in this position today without the love and the support from my parents. I would like to thank them both for their endless love and sacrifices they have made towards my education and dreams. My deepest acknowledgment goes to my beautiful brother Gianni – he is the reason for me entering the medical sciences in the first place. Living with him for the past two years has only brought us closer together and despite being the youngest, he has made me a stronger person with his words of wisdom. He has proven that a child with Hirschsprung's disease can live a fulfilling life despite the challenges it may bring and I wish that all his dreams come true in the future.

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Most time spent was at the Wingate Institute of Neurogastroenterology where my office was placed. Special thanks to Professor David Evans and Professor David Wingate who accepted me to be part of the institute in the first place which always had a rich family network. I would like to take the opportunity to thank Dr David Burleigh for our endless chats, advice he gave me and most of all supporting me at all times. I would also like to thank our secretaries at the Wingate Institute, Sam Mills, Nici Kingston and Lyn Buckley for their secretarial assistance, working under stressful moments, and being such wonderful friends – the day wouldn't be the same without them. I particularly am grateful to Sam Mills whose sense of humour got me through the day and who will always be a dear friend to me. I want to thank Ron Ling for being such a lovely person to me and who is an absolute gentleman. Special thanks to Tony Price, Jacqueline Lee, Jeannette Wilson and Dan Holly from The

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Publications

Publications

Athanasakos EP, Ward HC, Williams NS, Scott SM. (2008). Importance of extrasphincteric mechanisms in the pathophysiology of faecal incontinence in adults with a history of anorectal anomaly. *British Journal of Surgery* 95 (11): 1394-400.

Keshtgar AS, **Athanasakos E**, Clayden GS, Ward HC. (2008). Evaluation of outcome of anorectal anomaly in childhood: the role of anorectal manometry and endosonography. *Pediatric Surgery International* 24 (8): 885-92.

Athanasakos E, Starling J, Ross F, Nunn K, Cass, D**.** (2006). An example of psychological adjustment in chronic illness: Hirschsprung's disease. *Pediatric Surgery International,* 22 (4): 319-25

Abstracts

Presented as oral and/or poster at national and international conferences

Athanasakos EP, Kemal K, Malliwal R, Ward HC, Knowles CH, Scott SM, Williams NS. (2009) Determinants of psychosocial morbidity in patients with congenital anorectal anomalies**.**

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Athanasakos EP, Kemal K, Malliwal R, Knowles CH, Scott SM, Williams NS, Aziz Q, Ward HC. (2009). Clinical outcomes & psychosocial functioning in patients with anorectal anomalies & idiopathic constipation with an Antegrade Continence Enema (ACE).
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Athanasakos EP, Kemal K, Malliwal R, Ward HC, Knowles CH, Scott SM, Williams NS. (2009) Back to basics – anatomical and surgical review of anorectal anomalies.
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Boyle DJ, Gill KA, Ward HC, **Athanasakos EP**, Scott MS, Lunniss PJ, Williams NS. (2008). Novel surgical treatment in a patient with combined rectal evacuatory dysfunction and faecal incontinence associated with previous anorectal malformation.
***Presented* at:** *Paediatric Colorectal Club, Salamanca (oral)*

Athanasakos E, Ward HC, Williams NS, Scott MS. (2006). Pathophysiology of faecal incontinence in adults with previous surgery for anorectal anomaly: The importance of extra-sphincteric mechanisms.
Presented at: *Paediatric Colorectal Club, Helsiniki, Finland (oral), The 2006 Annual Meeting of the Association of Coloproctology of Great Britain and Ireland (poster).*

Patient Seminar

Patients with anorectal anomalies and idiopathic constipation involved in this research project were invited to a patient support seminar in order to inform them about our findings (2009).

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List of Abbreviations

ARA	Anorectal anomalies
IC	Idiopathic constipation
IAS	Internal anal sphincter
EAS	External anal sphincter
FI	Faecal Incontinence
VACTERL	(vertebral, anorectal, cardiac, tracheo-oesophageal, renal and limb
PSARP	Posterior sagittal anorectoplasty
ACE	Antegrade Continence Enema
GIPU	Gastrointestinal Physiology Unit
GIQOL	Gastrointestinal Quality of Life Index
CDI	Children's Depression Inventory
BDI	Beck Depression Inventory
GHQ-28	General Health Questionnaire
STAIC	State-Trait Anxiety Inventory for Children
STAI	State-Trait Anxiety Inventory for Adult
PILL	Pennebaker Inventory of Limbic Languidness
BFI	Big Five Inventory
BFI-TTC	Big Five Inventory-Transition to College
H.O.P.E.S	Hunter Opinions Personal Expectations Scale
GPH	Global personal hopefulness
CERQ	Cognitive Emotion Regulation Questionnaire
WAI	Weinberger Adjustment Inventory

df	degrees of freedom
χ^2	Chi-squared
CI	Confidence interval
r^2	R-squared

CHAPTER 1

INTRODUCTION

1.0 INTRODUCTION

"A properly functioning rectum is an unappreciated gift of the greatest price" (Potts, 1959). One is unable to embark on the task of writing about congenital anorectal anomalies (ARA) without being overwhelmed by the complexity of these conditions – the continuous debate about the pathological anatomy, nomenclature of different forms and the ideal surgical technique to use. In addition, this chapter will investigate the ongoing bowel difficulties that patients with ARA live with after reconstructive surgery.

1.1 THE RECTUM AND ANAL CANAL

Normal faecal continence is maintained by a complex integrated functional unit – including the rectum, anal canal and pelvic floor musculature (Fleshman, 1993, Rao, 2004a, Rao, 2006). Other factors involved in the maintenance of continence include normal stool frequency and consistency, and rectal compliance (Rasmussen, 1994, Deutekom et al., 2007). A summary of the normal human anatomy will be firstly reviewed prior to discussing the pathophysiology of ARA.

1.1.1 Developmental importance of the anorectum in humans

There are a number of developmental stages involved in the structure of the normal anatomy of the lower end of the anus, rectum and genitourinary tract. The primitive gut develops during the fourth week of gestation when the embryo folds and incorporates the dorsal part of the yolk sac into the embryo (Moore K, 2003). A lining of the primitive gut called the

endoderm gives rise to most of the epithelium and glands of the digestive system, biliary passages and parenchyma of liver and pancreas. The epithelium of the cranial (mouth) and caudal (anal pit) ends of the digestive tract originate from the proximal and distal ectoderm known as the stomodeum and proctodeum respectively (Figure 1.1 D)**.** The primitive gut is divided into three parts: foregut, midgut and hindgut. Considerable emphasis will be placed on the hindgut, since this is the area of anatomical interest for this thesis.

The hindgut endoderm includes the left one third to one half of the transverse colon; the descending colon and sigmoid colon; the rectum and the superior part of the anal canal; and the epithelium of the urinary bladder and most of the urethra (Moore K, 2003, Moore, 1999). The hindgut continues into the caudal part of the embryo where it develops a large chamber, called the 'cloaca' (Latin: *a sewer*) (Rao, 2004a, Moore K, 2003). Once the hindgut is distinguished in the embryo, a fingerlike diverticulum (Moore K, 2003, Healey JE, 1990) called the 'allantois' (a tubular extension of the cloaca that receives urinary wastes from the foetus), appears from the hindgut and continues into the yolk stalk. Fusion of the yolk stalk and body stalk produces the umbilical stalk or umbilical cord (Figure 1.1 A).

By the fourth week of development, the cloaca and the cloacal membrane are present (Figure 1.1). The cloacal membrane differentiates the internal from the external parts of the cloaca (Fonkalsrud Eric W, 2004). This membrane is composed of endoderm (inner layer) of the cloaca and ectoderm (outer layer) of the proctoderm or anal pit (Moore K, 2003, Healey JE, 1990). The proctodeum (anal pit) is an invagination of surface (epidermal) ectoderm that forms in the hindgut and develops into the anus (Figure 1.1 D). The cloacal membrane ruptures making the hindgut continuous with the outside of the embryo through the anus. At

its cephalic part, the cloaca accepts laterally the mesonephric ducts which ascend to the vas deferens in the male, and the metanephric ducts develop into the ureters in both sexes (Healey JE, 1990).

During the fourth and sixth weeks of foetal development, a band of mesenchymal cells called the urorectal septum grows caudally, until it forms a complete partition that separates the cloaca into the dorsal (posterior) anal canal and ventral (anterior) urogenital sinus that retains connection to the allantois (Fleshman, 1993, Moore K, 2003, Moore, 1999) (Figure 1.1 A). Forklike extensions are formed, as the septum grows towards the cloaca, producing infoldings of the lateral walls of the cloaca. These folds eventually fuse, dividing the cloaca into two parts (Figure 1.1 D_1 and $F_{1)}$: (i) the rectum and cranial part of the anal canal dorsally; (ii) and the urogenital sinus ventrally. The urogenital sinus mainly gives rise to the urinary bladder and urethra. In the adult, the area of fusion of the urorectal septum with the cloacal membrane is defined by the perineal body, tendinous centre of the perineum (Moore K, 2003). This is the landmark of the perineum where many muscles meet. Additionally, the urorectal septum divides the cloacal sphincter into: anterior part which develops into the superficial transverse perineal, bulbospongiosus, ischiocavernous muscles and posterior part by becoming the external anal sphincter (Moore K, 2003), the pudendal nerve supplying all these muscles.

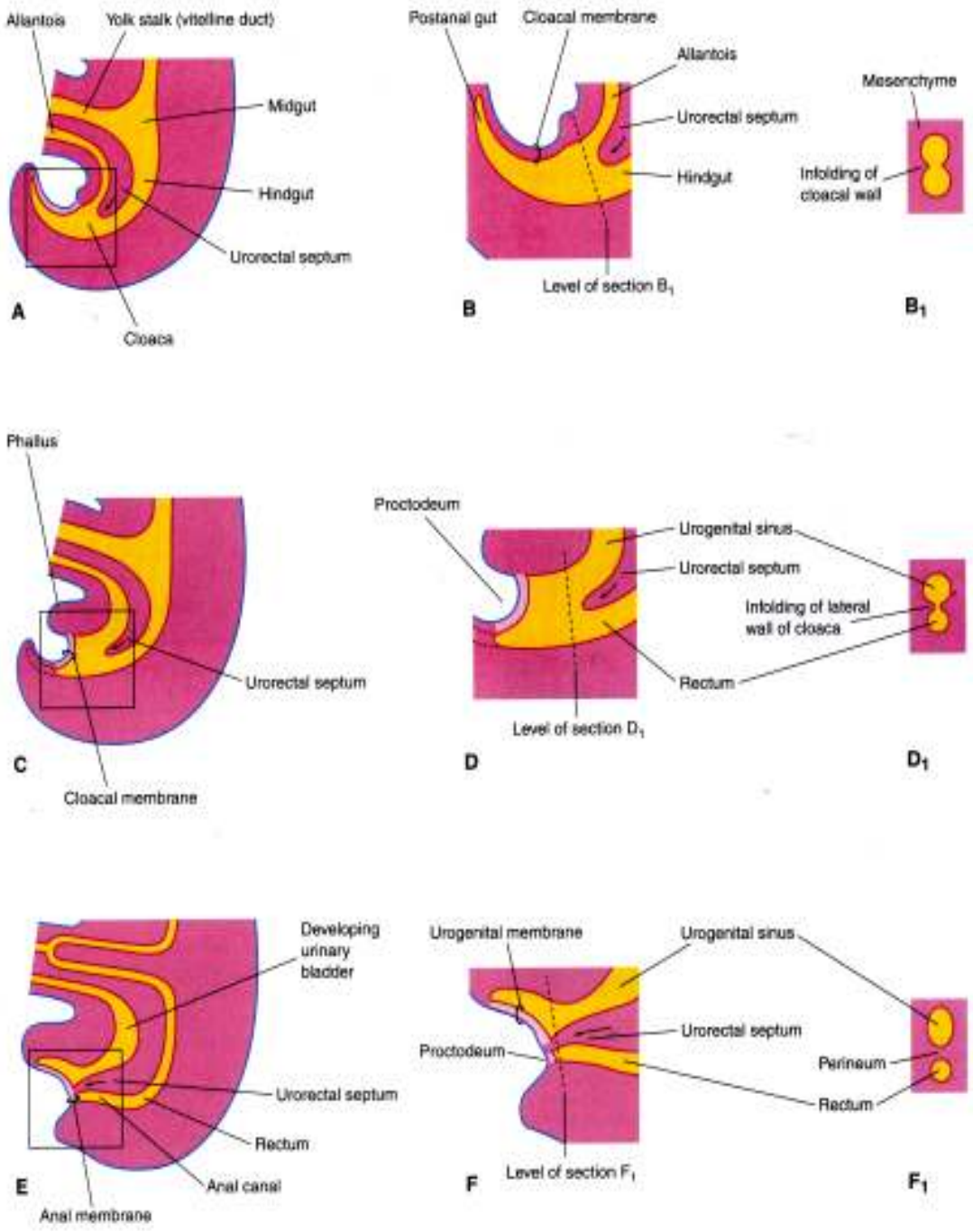


Figure 1.1: Stages in the partitioning of the cloaca into the rectum and urogenital sinus by the urorectal septum. A, C and E view from the left side at 4, 6 and 7 weeks respectively. B, D and F enlargements of the cloaca region. B_1, D_1 and F_1, transverse sections of the cloaca at the levels shown in B, D and F respectively (Moore K, 2003).

Finally, when the separation of the cloaca is complete (seventh week), the cloacal membrane bursts, resulting in separate openings for the anal canal behind and the urogenital ostium in front (Moore K, 2003, Healey JE, 1990). Between the tenth to twelfth weeks of gestation, there is continued elongation of the urethra and anal canals, but the external genitalia are not yet developed. It is by the fourteenth to sixteenth of gestation, that male and female differentiation is established (Fonkalsrud Eric W, 2004). The following account will later focus on how most ARA seen, result from abnormal partitioning of the cloaca by the urorectal septum into the rectum and anal canal posteriorly and the urinary bladder and urethra anteriorly (Moore K, 2003).

1.1.2 Normal anatomy of the anorectum in humans

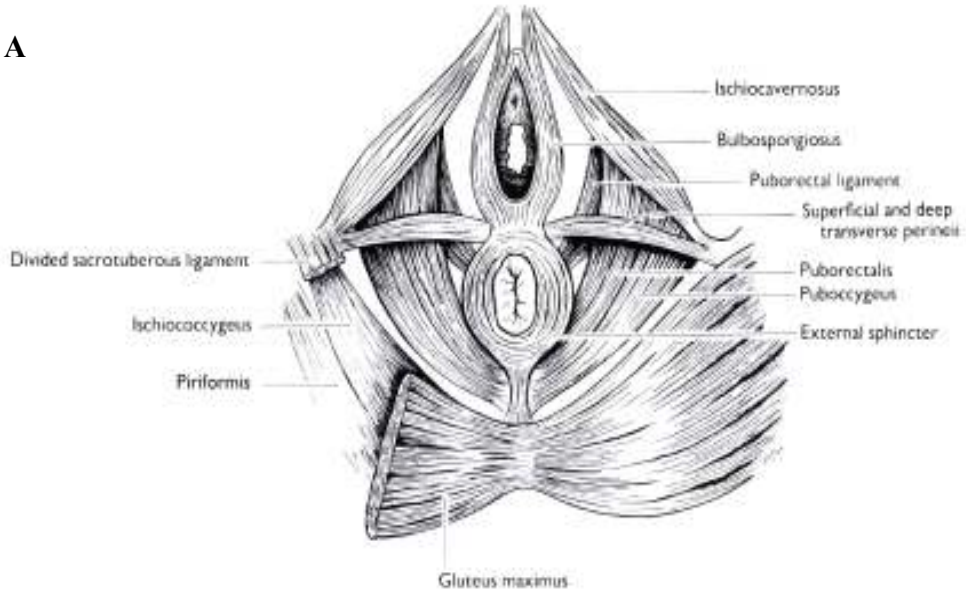
There is no doubt, that that there is no area of greater confusion than in the understanding of the musculature of the anorectal region, both in the normal and in ARA. Thus the following account will attempt to provide a detailed description of these structures.

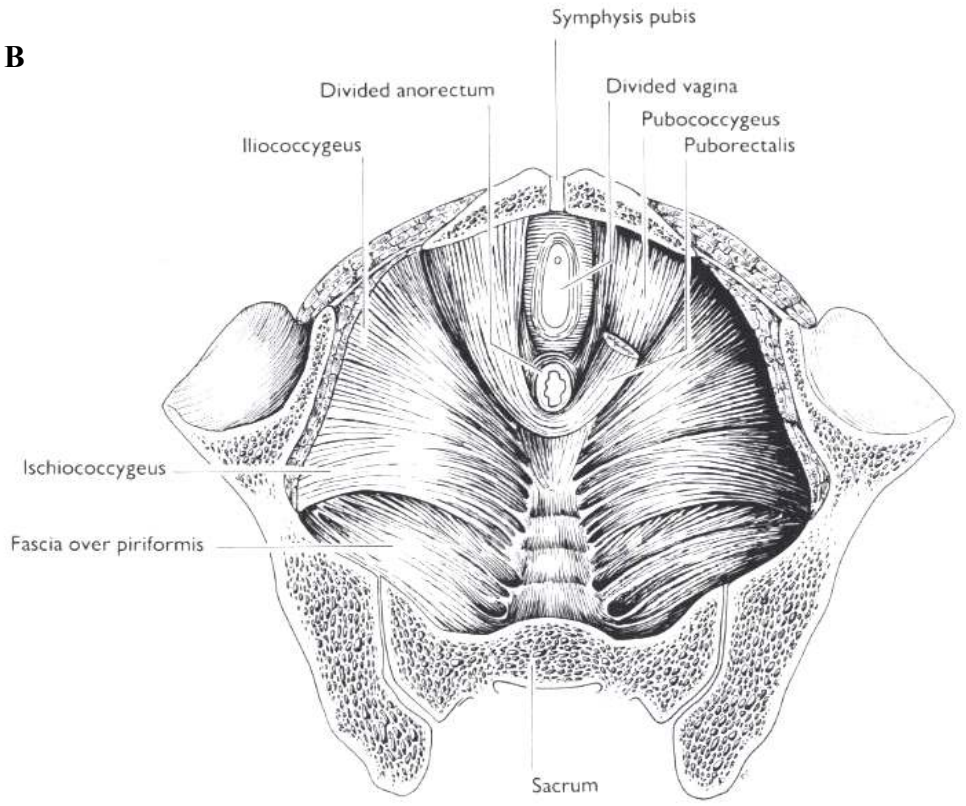
The terminal segment of the gastrointestinal tract extends from the third sacral segment to the anus and is divided into: the rectum and the anal canal (Healey JE, 1990). Surgeons generally define the anal canal as the part that starts at the anorectal junction (i.e. the point passing through the levator ani muscles) and terminates at the anal verge (Keighley, 1993, Gordon PH, 2007). Anatomists however, acknowledge the anal canal as the part of the intestinal tract that extends from the dentate line to the anal verge.

1.1.2.1 Pelvic floor muscles

Anatomists have traditionally described the levator ani as a broad muscular sheet attached anteriorly to the pubic bone (Standring, 2004). The levator ani makes up most of the pelvic floor, which is divided into parts named according to their attachments and the pelvic structures to which they are related. These include: ischiococcygeus, iliococcygeus and pubococcygeus (Figure 1.2 A, B). Pubococcygeus is further subdivided to the pelvic structures to which they relate, i.e. pubourethralis and puborectalis in the male, pubovaginalis and puborectalis in the female (Standring, 2004). The pubococcygeus makes up the main part of the levator ani, which arises from the anterior half of the obtruator fascia and back of the pubis (Gordon PH, 2007, Moore, 1999). The main role of pubococcygeus is to act as a lateral compressor of the visceral canals which cross the pelvic floor (Standring, 2004). Fibres from ischiococcygeus (Figure 1.2 A, B) attach to the sacrum and coccyx with its remaining parts joining to the midline. The posterior part of the levator ani is the iliococcygeus, which arises from the ischial spine (Moore, 1999, Standring, 2004). The ventromedial segment is termed the pubovisceralis muscle as it holds the urethra, vagina, and anorectum within its sling like fibres. It is drawn caudally by the viscera passing through it to which it is attached. The pubovisceralis is part of the levator, separated from it by its function, closing the urogenital and anorectal hiatuses by contraction. Further division of this muscle, a segment composed of fibres passing, but intimately in contact with, the anorectum in the shape of a U-loop is named the puborectalis (Figure 1.2 A, B). The puborectalis plays an important role in maintaining the angle between the anal canal and rectum (Bailey H, 2004). There is a close relationship between the puborectalis portion of the levator ani and the external anal sphincter (EAS) (Bailey H, 2004). The puborectalis muscle passes directly backward from the back of the pubic symphysis and the

Figure 1.2: Anatomy of the pelvic floor muscles. (A) A pelvic view of the levator ani to show its various components, particularly the ischiococcygeus and iliococygeus, the pubococcygeus and puborectalis, (B) The levator ani viewed fro the perineum (Gordon PH, 2007).





superior fascia of the urogenital diaphragm, runs backward alongside the anorectal junction continuing with its fellow muscle (i.e. pubococcygeus), straight behind the rectum, where they form a 'U-shaped loop' that slings the rectum to the pubis (Rasmussen, 1994, Gordon PH, 2007, Standring, 2004). It is the puborectalis part which supports the EAS and assists in creating the anorectal angle. Neighbouring muscles such as iliococcygeus and to lesser extent, the ischiococcygeus, help puborectalis in maintaining anorectal and urinary continence (Standring, 2004).

1.1.2.2 Sphincteric Mechanisms

The anal canal can be divided endosonographically into three sections (Davies, 2006). The:

1. high anal canal: a level midway between the inferior border of the puborectalis and complete formation of the external sphincter ring anteriorly.
2. middle anal canal: completion of the external ring anteriorly in combination with maximal internal sphincter thickness.
3. low anal canal: immediately caudal to the termination of the internal sphincter, it comprises the superficial external sphincter.

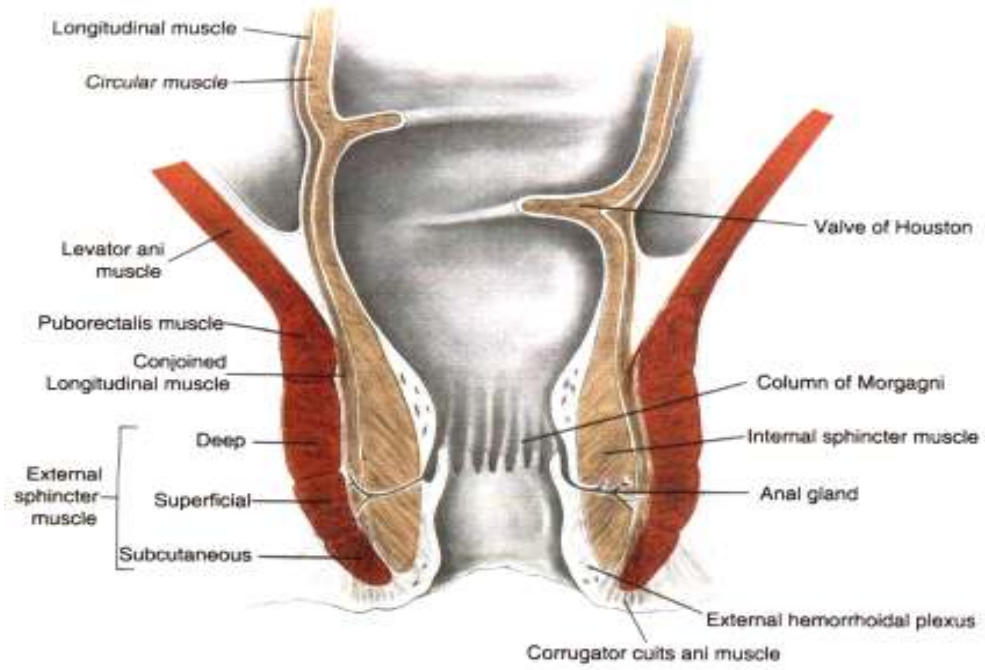
The walls of the anal canal are formed by an important sphincter complex consisting of two overlapping muscular tubes including of the internal anal sphincter (IAS) and the external anal sphincter (EAS) (Figure 1.3) (Sangwan and Solla, 1998, Rasmussen, 1994, Deutekom et al., 2007, Keighley, 1993, Rao, 2004a, Moore, 1999, Healey JE, 1990, Nivatvongs Santhat, 1997, Smith, 1987, Lamah and Kumar, 1999, Ellis, 2002). The IAS is an involuntary and thickened muscle (0.2-0.5 cm thick) which is a downward continuation of the inner circular muscle coat of the rectum (Figure 1.3) (Bailey H, 2004, Ellis, 2002, Rao, 2004b) surrounding the entire anal canal, reaching from the anorectal ring to 1 to 1.5 cm

below the dentate line (Rao, 2004a, Rao, 2004b, Sangwan and Solla, 1998). As shown above, the anal canal can be divided into three sections where the IAS is found to surround the upper two, with two-thirds of its length above the anal valve line (pectinate line). Its lower border is identified by the intersphincteric groove on the skin, thus defining the upper limit of the low canal zone (Davies, 2006). The EAS is a voluntary muscle which encircles the IAS, extending further downwards, curving medially to take up a position just below and lateral to the lower edge of the IAS, close to the skin of the anal orifice (Gordon PH, 2007, Ellis, 2002). The EAS is thicker than the IAS (i.e. 0.6 cm to 1.0 cm thick) (Keighley, 1993, Lunniss and Phillips, 1992) and a rather complex structure from skin up to levator ani, divided into strata of which are circular, some disposed anteroposteriorly, anchored anteriorly at the perineal body, and posteriorly to the skin or coccyx (Burleigh, 1983). It is at this level that a palpable groove is found called the intersphincteric groove or plane which is a surgically significant to allow surgeons access for operations on the sphincter muscles (Gordon PH, 2007, Rao, 2004a, Rao, 2004b, Sangwan and Solla, 1998). Despite the fact that both sphincters are separate, they are integrated in function (Rao, 2004a, Bailey H, 2004). At the level of the anorectal ring, fibres of the levator ani and puborectalis are joined by the longitudinal muscle coat of the rectum, which is known as the conjoint longitudinal muscle (Figure 1.3) (Gordon PH, 2007, Lunniss and Phillips, 1992).

The pectinate (dentate) line is found approximately at the midpoint of the anal canal, 2cm from the anal verge (Healey JE, 1990, Nivatvongs Santhat, 1997). This line is covered with squamous epithelium below and stratified epithelium above the line (Healey JE, 1990, Nivatvongs Santhat, 1997). Located about 1.5 cm proximal to the pectinate line is the anorectal line, which may signify the true embryological separation between the rectum and anal canal (Healey JE, 1990, Nivatvongs Santhat, 1997). The main relations of the anal canal

include posteriorly the fibrous tissue between the coccyx (anococcygeal body/raphe); laterally to ischiorectal fossae containing fat; and anteriorly to the perineal body separating it from the bulb of the urethra in the male or the lower vagina in the female (Ellis, 2002).

Figure 1.3: Anatomy of the anal canal showing the anal sphincters (Gordon PH, 2007)



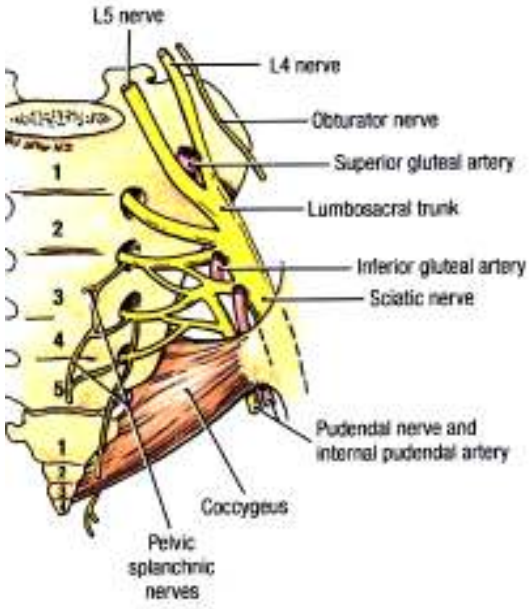
1.1.2.3 Nerve Supply of the Normal Rectum and Sphincters

The second, third and fourth sacral segments of the spinal cord are the nerve centres of the arcs that subserve the receptors and effectors of the rectum, anus, bladder, and urethra, and, together with higher centres in the brain, are responsible for continence. These centres in the spinal cord also subserve cutaneous sensation in the anal canal to the level of the valves and in the perianal region. The sympathetic supply, however, arises in the second, third and fourth lumbar segments (Figure 1.4) (Holschneider, 2006).

Branches from the anterior roots of the third and fourth sacral nerves unite to form the main nerve pathway to the ilio-pubococcygeus muscles. The pudendal nerve (Figure 1.4), which arises from the anterior division of the second, third and fourth sacral nerves clings to the lateral wall of the pelvis in the pudendal, or Alcock's canal (Holschneider, 2006). It supplies the peripheral aspects of the deep surface of the levator ani, iliococygeus, pubococcygeus and puborectalis (Roberts, 2005) through its inferior hemorrhoidal and perineal branches, which cross the ischioanal space to enter the muscle . It also supplies EAS, as well as providing sensory fibres to the anal canal perineum (Snooks and Swash, 1984). There is evidence of dual nerve supply to the muscles of continence which are provided by transcutaneous stimulation of the spinal cord and cauda equina. At the vertebral level of L1, stimulation is associated with a rapid response in the puborectalis muscle (Rao, 2004a). The IAS is visceral in origin consisting of smooth muscle innervated by the intrinsic enteric nervous system: autonomic (sympathetic, parasympathetic and nitrinergic (Burleigh, 1983, Davies, 2006). The sympathetic (L1 and L2) fibres are supplied via the hypogastric nerves which are excitatory and the parasympathetic (S2-S4) innervation through the pelvic nerves which are inhibitory (Keighley, 1993). The EAS, is supplied by the inferior rectal branch of the pudendal nerve which arises from the anterior primary rami of the second, third and fourth sacral spinal nerves (Keighley, 1993) (Figure 1.4).

The perineal branch of the fourth sacral nerve, a nerve that must be distinguished from the perineal branches of the pudendal nerve, enters the ischiorectal fossa medial to the ischial spine on the caudal and lateral aspects of the coccygeus muscle, and its branches are directed medially to the posterior fibres of the puborectalis sling and EAS (Wilson, 1967). This nerve can be of surgical risk, especially when deep lateral cuts are directed from the vicinity of the coccyx and anococcygeal body.

Figure 1.4: The sacral and coccygeal nerve plexuses (Gordon PH, 2007)



1.1.3 Normal physiology of the anorectum in humans

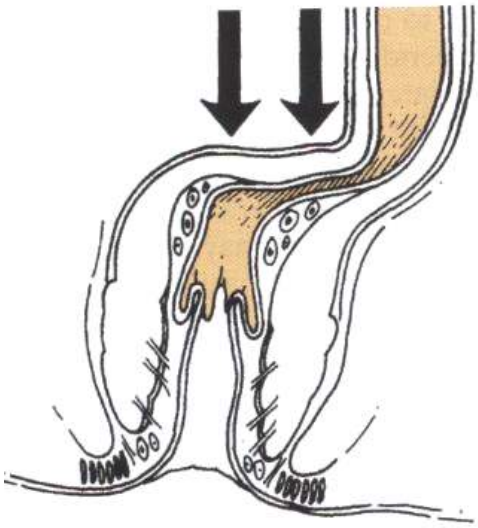
1.1.3.1 Mechanism of continence

A well-functioning, compliant rectum or neorectum is needed for the continence mechanism (Rasmussen and Christiansen, 1996). This is maintained by the structural and functional integrity of the rectum, anus and adjoining pelvic floor musculature along with the integration of somatic and visceral muscle function with sensory information under local, spinal and central control (Gordon PH, 2007, Rao et al., 2004). The continence mechanism dependent on several factors including the following: normal anal sphincter and pelvic floor function; rectal compliance, capacity and sensations; colonic transit and stool consistency and central nervous system control (Hobday et al., 2001). Neuropathways will be briefly discussed in relation to continence as formal discussion goes beyond the scope of this thesis.

Stool weight and volume does vary from individual to individual, yet it is the frequency of the passing stool that plays an important role in continence. The colonic transit time is rapid when the large bowel content is liquid because the left colon does not store fluid well (Gordon PH, 2007). To ensure normal faecal control one should ask whether the faecal contents are solid, liquid or gas, as some patients may be continent for solid stool, but not necessarily for liquid or gas. Stool can build up in the rectum for a variable time period before the urge to defecate is experienced. The ability of the rectum to retain stool is known as reservoir continence. The lateral angulations found in the sigmoid colon and the valves of Houston (Figure 1.3), provide a mechanical barrier and retard progression of stool. It is the weight of the stool that tends to accentuate these angles and thus enhance their barrier effect (Gordon PH, 2007). The high-pressure zone found in the anal canal and the anorectal angle offers a mechanical barrier to defaecation (Rasmussen, 1994, Standring, 2004) and the rectal curvatures and transverse folds as mentioned above, may also contribute to a lesser extent (Bharucha, 2004).

It is the activity of the anal sphincters and the puborectalis muscle, which are responsible for the zone of high pressure inside the anal canal (Gordon PH, 2007, Standring, 2004). Since the IAS is innervated by the autonomic nervous system, it is not subject to voluntary control. Thus, this muscle exists in a continuously tonic state and is essential for maintaining the closure of the resting pressure of the anal canal and initiates the act of defecation by reflex dilation in response to rectal distension (Gordon PH, 2007, Rao, 2004b, Standring, 2004, Rasmussen and Christiansen, 1996). The EAS contributes a small amount to anal resting pressure, but is responsible for the squeeze pressure. Without this high resting pressure in the anal canal, we would be unable as humans to prevent leakage of mucus and gas (Gordon PH, 2007, Moore, 1999, Lunniss, 2007).

Figure 1.5: Flap valve mechanism (Gordon PH, 2007)



Faecal continence is also helped by the acute anorectal angle, which is due to the continuous tonic activity of the puborectalis muscle and EAS (Gordon PH, 2007). The persistent tonic contraction of these muscles is based on a proprioceptive reflex mechanism where the receptors are situated in the striated muscles of the pelvic floor and the ganglia in the lubosacral spinal cord (Parks et al., 1962). The tonic contraction produced by the puborectalis muscle, creates what is called a 'flap valve' (Figure 1.5). It is the puborectalis muscle which creates a forward pull that maintains the angle, giving rises to a flap-like valve whereby the anterior rectal wall is pushed downwards onto the anal canal when the intra-abdominal pressure during weight lifting, straining, laughing and coughing rises, thus stopping the passage of faeces into the anal canal (Parks, 1975), although the contribution of the anorectal angle has been challenged in the literature, where it has been suggested that the puborectalis functions by sphincteric occlusion of the anal canal (Bartolo et al., 1986). Thus,

for defecation to occur, the flap valve must be opened, by lengthening the puborectalis, lowering the pelvic floor and obliterating the angle (Keighley, 1993).

Reflex responses from both anal sphincters are essential for the maintenance of anal continence. Both anal sphincters work simultaneously to create the reflex response. This occurs by a brief conscious contraction of the EAS, puborectalis and pelvic floor musculature which propels the contents in an oral direction (Sun et al., 1990), allowing the IAS to recover following relaxation in response rectal distension (RAIR). It is therefore during this sampling response, that continence will be sustained by synchronous contraction of the EAS, which permits time for impulses to reach conscious awareness (i.e. the individual can decide how to respond) (Keighley, 1993). Naturally, as the colon accommodates to its new volume, stretch receptors are no longer activated by afferent stimuli and thus the rectal pressure remain low and the urge to defecate is abated.

Extrinsic afferent neurones mediate the conscious sensation of urgency which is activated by mechanoreceptors. It is these afferents which monitor the filling state and contraction level of the rectum (Ruhl et al., 1998). The ability of the rectum to adapt to the imposed stretch is called 'rectal compliance', which allows rectal contents to be accommodated for and for defaecation to be delayed. Under normal conditions, the viscoelastic properties of the rectal wall allow it to maintain a low intraluminal pressure during filling, so that continence is not threatened.

1.1.2.2 Mechanism of defaecation

The process of defaecation is simply the act of evacuating faecal material from the rectum, yet it is a rather complex mechanism that involves both a reflex response and voluntary

performance. The reflex response is initiated due to the sudden distension of the rectal wall, resulting from mass movements of the colon wall moving the faecal bolus into the rectum (Keighley, 1993, Gordon PH, 2007, Smith, 2002). As mentioned previously, when a faecal bolus enters the rectum, the stretch receptors (which reside within the muscles of the pelvic floor) register a sensation and an urge to defecate (Keighley, 1993, Gordon PH, 2007, Smith, 2002). There are four components to the reflex response: 1) increased activity in the sigmoid colon; 2) distension of the rectum; 3) reflex contraction of the rectum; and 4) relaxation of the IAS and EAS (which are normally closed). We know that the process of defaecation is basically due to an intrinsic reflex response which is mediated by impulses in the intramural nerve plexi. It is reinforced by an autonomic reflex transmitted in the spinal cord (Figure 1.6). This involves parasympathetic nerve fibres which arise from the sacral spinal cord and innervates the terminal colon. Thus, when faeces enters the rectum, distension of the wall activates receptors which send afferent signals that spread through the myenteric plexus in order to initiate peristaltic waves in the descending and sigmoid regions of the colon and rectum (Smith, 2002). As long as faecal matter is retained in the descending and sigmoid colon, the rectum remains empty and the individual feels no urge to defecate. It is the distension of the left colon which initiates these peristaltic waves, propelling the faecal mass downward into the rectum (Gordon PH, 2007). Thus, as the wave approaches the anus, the sphincters are inhibited, and they relax. If the EAS is relaxed voluntarily when the faeces are pushed towards it, defaecation will proceed. Parasympathetic signals intensify the peristaltic waves, and enhance the effect of the intrinsic neurones to cause increased motility, contraction of the rectum, and finally relaxation of the sphincters (Figure 1.6) (Smith, 2002).

It is beyond the scope of this thesis to discuss in detail the pharmacological properties of the mechanism of defecation, thus a basic overview will only be provided. Both the origin and the propagation of the propulsive waves, and in all probability the segmental contractions, are regulated via the intraluminal bowel wall plexus. Excitatory impulse is produced by the distension of the bowel wall by the stool bolus, after transversing the submucous plexus and being transmitted by the myenteric plexus. This further leads, to a cholinergic contraction proximal to the bolus and to a nonadrenergic, noncholinergic (NANC) relaxation that is mediated by nitric oxide (NO) containing inhibitory neurons, aboral to the bolus. Adrenalin modulates the acetylcholine release at cholinergic synapses. Nitric oxide has been recognised as a neurotransmitter that mediates relaxation of the smooth muscle of the gut including many other peptidergic peptides (VIP), substance P, neurokinin A and many others involved in the peristaltic reflex (Holschneider, 2006).

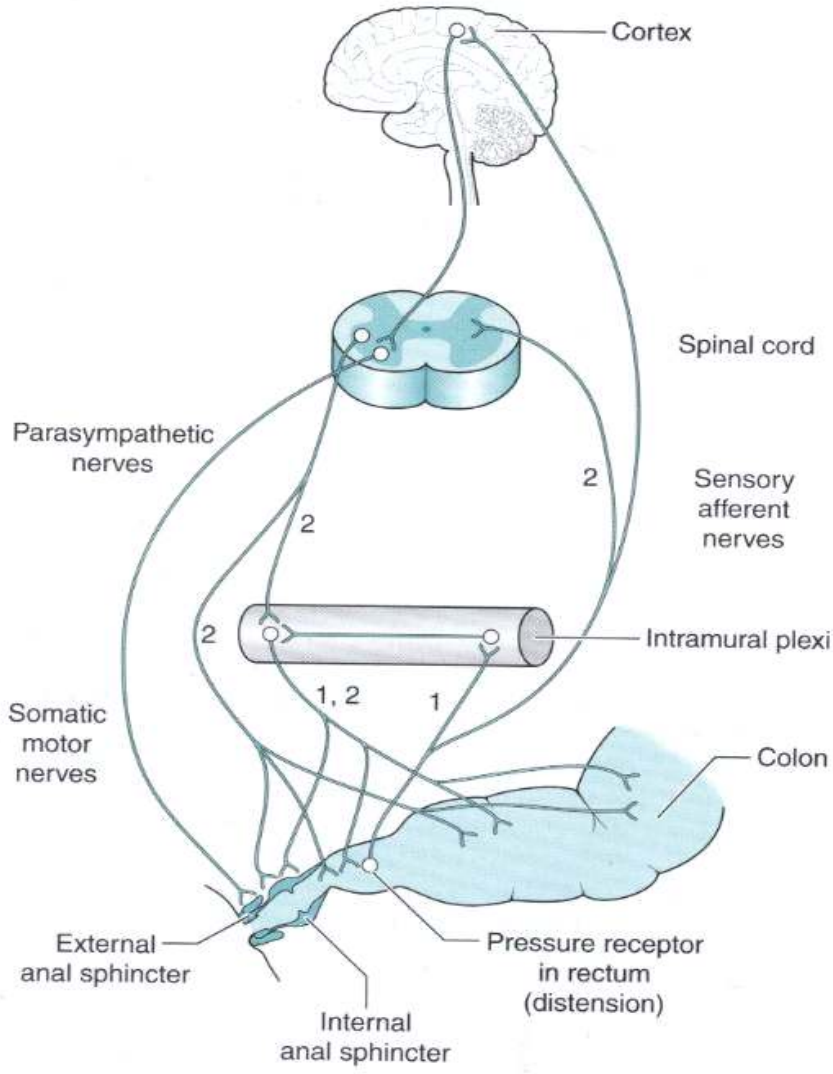


Figure 1.6: Neural control of the defaecation process. The basic reflex operates via the intramural plexi, and the spinal parasympathetic reflex reinforces the basic reflex. Control is also exerted by the conscious brain. Labels – 1 components of the basic reflex and 2 components of the spinal sympathetic reflex (Smith, 2002).

1.2 ANORECTAL ANOMALIES

1.2.1 Definitions

Anorectal anomalies (ARA) are a complex group of congenital anomalies resulting from abnormal development of the hindgut, allantois and sometimes the Mullerian duct, leading to incomplete or partial urorectal septal malformations (Davies et al., 2004, Rintala, 2005, Moore, 2006). Studying the morphology of ARA in human newborns, Bill and Johnson (Bill and Johnson, 1958) and later Gans and Friedman (Gans and Friedman, 1961) stated that in most forms of ARA the fistula may represent an ectopic anal opening. From these observations, they concluded that the rectum actually migrates during normal development, from a rather high position to the normal area of the anal opening. Thus, if this process of migration is stopped before the anus has reached its definitive position in the area of the perineum; an ectopic anal canal would result. Yet, embryological evidence wasn't used to support this theory. In 1986, van der Putte (van der Putte, 1986) modified the theory of a rectal or anal migration. This was done by studying normal and abnormal pig embryos, where it was proposed that a shift or rotation of the dorsal cloaca takes place. This shift should bring the dorsal cloaca down to the area of the tail groove, thus establishing there the future anal opening.

There are a number of existing classifications for ARA which are usually based on the level of bowel termination in relation to the perineum and descriptively on the site of the fistulous bowel outlet. In both sexes ARA can be divided into high, intermediate, and low anomalies as related to the level of the puborectalis portion of the levator ani muscle and whether there

is a fistula to the urinary tract in males or the vagina in females. In this thesis the Wingspread International Classification will be used (Table 1.1) which has been widely used in the literature, but it is important to keep in mind that categorising and describing such classifications can be difficult due to variations in the literature (Rintala, 2005) and our limited understanding of the embryology of ARA (Lambrecht and Lierse, 1987). There are few classifications in use in different centres throughout the world, making comparisons difficult. Furthermore, the number of variations seen in ARA makes the classification and operative treatment difficult. The key difference between the different types of ARA lies in the relationship of the terminal bowel to the pelvic floor muscles and of the levator ani muscle in particular.

Table 1.1: Wingspread International Classification

CLASSIFICATION	FEMALE	MALE
High	1. Anorectal agenesis A. Rectovaginal fistula B. Without fistula 2. Rectal atresia	1. Anorectal agenesis A. Rectovesical fistula B. Without fistula 2. Rectal atresia
Intermediate	1. Rectovaginal fistula 2. Rectovestibular fistula 3. Anal agenesis without fistula	1. Rectourethral fistula 2. Anal agenesis without fistula
Low	1. Anovestibular (perineal) fistula 2. Anocutaneous (perineal) fistula 3. Anal stenosis	1. Anocutaneous fistula 2. Anal stenosis
Rare	Persistent cloaca anomaly Rare malformations	Rare malformation

1.2.2 Classification and investigations in a newborn with an anorectal anomaly

The provisional diagnosis of an ARA and grading of its severity is usually straightforward in the newborn. In most patients, the type of anomaly can be determined by careful clinical examination and radiological investigation. The most important issue is to ascertain the level of the anomaly, because this determines the operative treatment in the neonatal period (Rintala, 2005). The importance of a complete medical history should not be neglected in order to focus on the examination of the perineum. A detailed evaluation and examination including family antenatal and birth history is necessary. Prenatal ultrasonography has a low sensitivity and specificity for the detection of ARA. A normal anus is visualised as a circular rim of hypoechogenicity in the perineum together with a central linear echogenic stripe. The absence of this circular rim is described as imperforate anus or anorectal malformation on the prenatal scan (Bekhit, 2006). Harris retrospectively viewed prenatal scans of children with ARA and demonstrated dilated colon on prenatal ultrasonograms (Harris et al., 1987). In this thesis, diagnosis will be discussed in relation to the classification of the anomaly for male and female below.

A low defect is classified when the developing bowel passes down through the pelvic floor musculature and anal sphincters (Hutson, 1999). The patient will have an ectopic anal opening in the perineum (Rintala, 2005). The most common type of low ARA found in males is called an anocutaneous fistula whereby the anus is covered by an excessive posterior fusion of the genital folds, with a fistula running forward subcutaneously to open along the midline of the perineum, scrotum or penis (Rintala, 2005, Cook, 1990). The anus is found somewhat displaced anteriorly, but the voluntary sphincter complex surrounds the main part of the anal canal. From the bowel termination, a narrow fistula runs anteriorly for

a variable distance within the median bar. This is diagnosed by distinctive appearance of perineum, fistula orifice visible or obscured by speck of meconium, fistulous track filled with meconium or probe is able to pass directly back along the fistula into anal canal (Murphy, 2006). A stenotic anus at the normal site may be due to partial covering by genital folds or to partial perforation of the anal membrane. A common term 'anal stenosis' is usually used to include both types, although most will be covered deformities. It is usually diagnosed by perineal appearance of hypertrophied folds (Murphy, 2006).

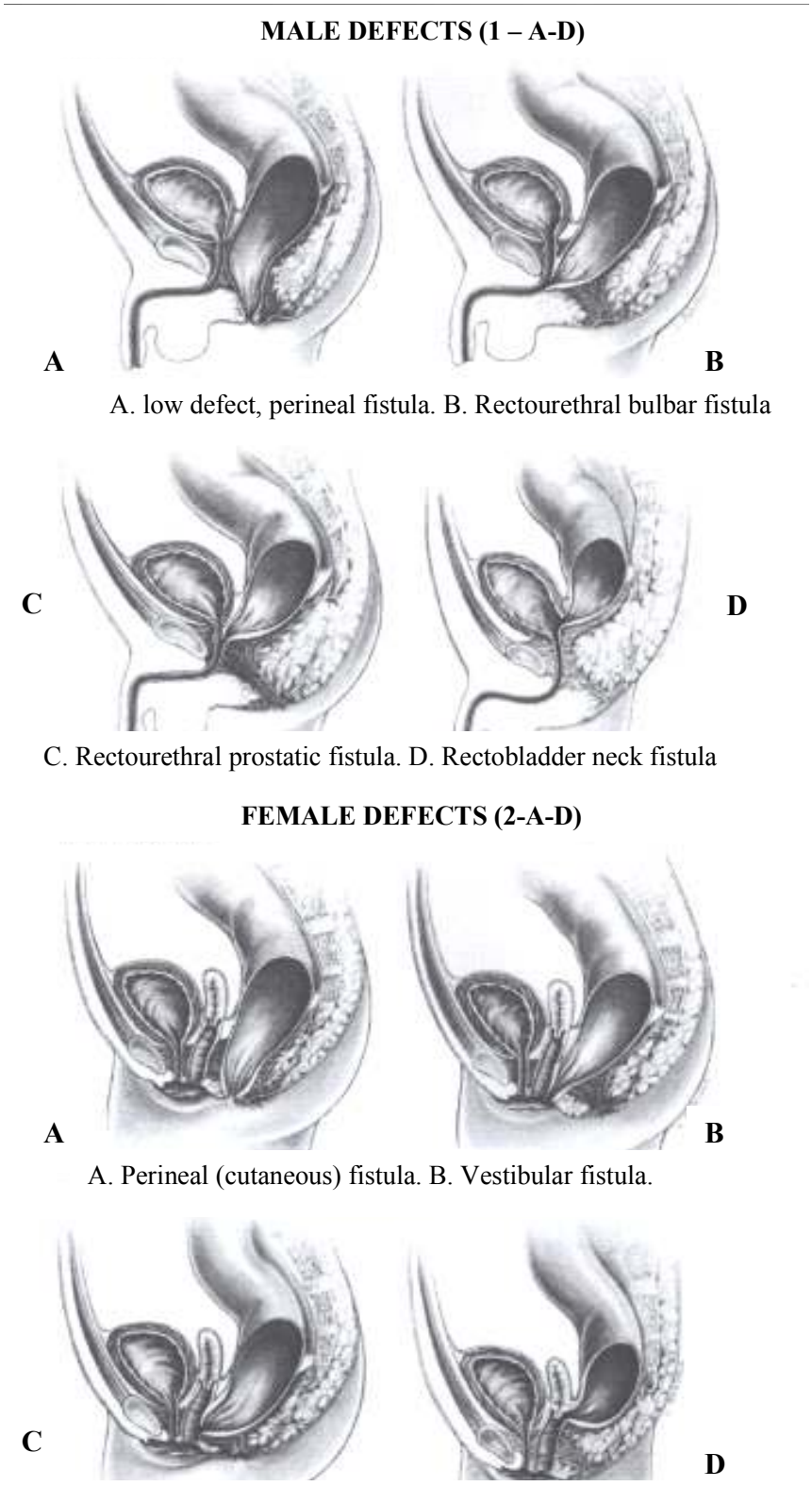
Low ARA are relatively found more frequently than high ones in females, with greater diversity in the fistulous opening than in the male. The anatomy, however, is similar in most respects to the equivalent lesion in the male. The anovestibular fistula lies close to the vaginal orifice and a probe passed into it will run subcutaneously in contrast to the direction of a rectovestibular fistula (Figure 1.7 2-B) (Cook, 1990). Also seen frequently in females is a perineal fistula (anterior perineal anus) (Figure 1.7 2-A) which is a normal looking anus found just behind the vestibule. In about half of the cases, the anterior anus is stenotic, and normal voluntary sphincters surround the posterior half of the anus but are very thin between the anal opening and the vestibular fourchette (Rintala, 2005). A 'covered' anal stenosis whereby the anal (fistula) opening is abnormally narrow (stenosed) is also common (Pena, 2000).

Anorectal anomalies are classified intermediate, when the bowel passes down into the levator ani muscle but does not reach the anal canal sphincters. In females, the most common defect is rectovestibular fistula (Figure 1.7 2-B), where the ectopic anus opens to the posterior vestibular fourchette, and the urethra and the vagina have normal appearances. In such cases, the opening can be difficult to see because of its small size and position under

the vestibular fourchette (Rintala, 2005). This is diagnosed by the appearance of three orifices in vestibule, urethra, vagina and a fine rectal fistula in fossa navicularis A rectovaginal fistula (with fistula) is when the fistula is found just above the hymen. The puborectalis muscle surrounds the caudal bowel, although the fistula may penetrate the sling anteriorly (Murphy, 2006). Anal agenesis (without fistula) is when the rectum terminates blindly at the upper border, with caudal end of blind gut near lower end of vagina. This is diagnosed with urethral and vaginal orifices with no distinguishing mark at the anal site. High anomalies in females include anorectal agenesis (without fistula), where the rectum ends blindly at any level in the pelvis above the levator, the blind strand if present, connects with vagina or perineum. Diagnosis is based on two perineal orifices (urethra and vagina) and no anus. Rectovesical fistula is when the rectum enters bladder between two separate vaginae which form a common cloaca at the bladder outlet, which is diagnosed by the appearance of a single cloacal orifice. Rectovaginal fistula is when the vagina is usually normal, rectal fistula opens in midline posteriorly, orifice largish (Figure 1.7 2–C). This is diagnosed by the appearance of normal two orifices in vestibule and evidence of meconium from the vagina. Rectal atresia is when the rectum terminates at any level, hence a short or long fibrous cord to the sacrum or to the distal bowel. On investigation, a normal anus is present but obstruction on digital examination (Murphy, 2006). A female patient who has only one external opening in the perineum has what is called a cloacal malformation – the rectum, vagina and urethra united to form a common recto-urogenital channel which opens at the perineum with a single opening. The opening may be found anywhere between the anal site and the base or tip of the clitoris. In most cases, the common channel opens between the normal vaginal site and the clitoris. The length of the common channel is variable; an anterior location of the external opening usually suggest a long common channel (Rintala, 2005).

Male patients, who have no detectable opening in the perineum, have a fistulous communication between the high-ending anorectum and the urethra. Usually, the urethral opening of the communication is found at or below the level of the prostate (Rintala, 2005). In high defects, bowel development is arrested superiorly to the pelvic floor muscles (Hutson, 1999). The most common high defect found in males is anorectal agenesis with a rectoprostatic urethral fistula (Figure 1.7 1-C). In rectoprostatic fistula, the rectal pouch lies above the level of the levator plate. On investigations, no anus or distinguishing diagnostic sign is evident and gas or meconium can be found in urine (Murphy, 2006). In rectobulbar fistula, the rectum terminates above the bulbocavernosus muscle by a wide fistula into the bulb (rectobulbar), or enters the urethra more distally as a fine fistula. The voluntary sphincter complex is always found to be hypoplastic, and the degree of hypoplasia has been shown to be associated to the severity of the sacral deformities, which are usual in these patients (Rintala, 2005). On diagnosis, there is often no distinguishing perineal sign, but there may be a thin perineum, hypospadias, or cleft scrotum and probe passes along urethra into rectum (Murphy, 2006). Rectal atresia in males, as in females is rare and is possibly acquired later in development than those deformities described as ageneses. In this case, the anus and anal canal are correctly sited and connected to the blind ending rectum by a cord of tissue which passes through the sphincter muscle complex (Cook, 1990). Anorectal agenesis, as in females, the rectum ends blindly at any level in the pelvis above the levator without a fibrous cord to the urethra or perineum.

Figure 1.7: Classification of anorectal anomalies. Reprinted with kind permission of Springer Science and Business Media (Pena, 1995)



A. low defect, perineal fistula. B. Rectourethral bulbar fistula

C. Rectourethral prostatic fistula. D. Rectobladder neck fistula

A. Perineal (cutaneous) fistula. B. Vestibular fistula.

C. Low rectovaginal fistula. D. High rectovaginal fistula

1.2.3 Epidemiology

Anorectal anomalies are a relatively uncommon congenital cause of intestinal obstruction in the newborn. The incidence of ARA has been reported as 1 out of every 3000-5000 births. A male predominance found in Western communities, with 55-70 percent of patients in larger series having been males (Pena, 2000, Rintala, 2005, Cuschieri, 2001). Anorectal anomalies may also be more frequent in developing countries (Moore, 2006). Evidence of both geographical and ethnic differences have been observed in ARA (Shija, 1986, Louw, 1959, Louw, 1965). It has been found that ARA form a significant clinical burden in Africa, where incidence has been found in 1:1,800 birth in Cape Town (Louw, 1965) and other parts of Africa such as Zimbabwe (Shija, 1986) and Nigeria (Adeyemo, 1997). Yet, despite these findings, there are others who have found no differences (Smith, 1988, Kiesewetter, 1964). There appears to be gender differences with respect to ARA. In general the male: female ratio associated with ARA is almost the same, with a 55:44 male: female ratio previously reported in large collective series (Endo et al., 1999, Smith, 1988). More severe malformations tend to be more common in male patients and tend to present with higher incidence of associated anomalies (Santulli, 1971, Ratan et al., 2004, Endo et al., 1999) In females with ARA, it is reported that the majority will have a defect of the low variety with a fistula to the perineum, fourchette or vestibule (Okada et al., 1992, Ratan et al., 2004, Endo et al., 1999). Cloaca anomalies are relatively rare, with an incidence of 1 in 50,000 births (Pena, 2000, Rintala, 2005). In both sexes, previous reports have shown the incidence of low ARA to be less than with high ARA (Javid et al., 1998).

1.2.4 Aetiology

The aetiology of ARA remains likely multifactorial (Falcone et al., 2007). Despite our lack of understanding of the normal development and pathologic variations found in ARA, the critical period of organogenesis is understood to be at or before the 6-7th week of gestation (Kluth D, 1995). Abnormal development would have to commence in early embryogenesis, possibly due to the limitations in the dorsal portion of the cloacal membrane resulting in persistent attachment of the hindgut to the urogenital sinus, resulting in the associated fistula (Kluth D, 1997). This may imply that the stimuli that induce abnormal development of the anorectum work throughout the developing foetus and may cause maldevelopment of several organ systems (Rintala, 2005). It is important to note that these anomalies not only lead to increased foetal mortality, but also result in significant morbidity (Ratan et al., 2004).

Despite the paucity of information on the genetic associations of ARA in humans and a fairly low familial incidence, the probability of a genetic association has increased due to the association with other chromosomal abnormalities and syndromes (Towne, 1972, Kaufman et al., 1974, Lowe et al., 1983)Approximately 36.4% are isolated lesions and 63.6% are associated with other anomalies (Cuschieri, 2001). Chromosomal defects are associated in 8% and a family history may be present (Cuschieri, 2001). In a large review of patients, 15% of cases had underlying chromosomal abnormalities, of which trisomies 21, 18 and 13 formed the largest group (Davies et al., 2004). Yet, ARA occur commonly in multi-anomaly sequences, such as the VACTERL (vertebral (e.g. hemisacrum), anorectal (e.g. malrotation, gastrointestinal duplication, duodenal obstructions, Hirschsprung's disease), cardiac (e.g. atrial/ventricular septal defects, tetralogy of Fallot, truncus arteriosis), tracheo-oesophageal, renal and limb (e.g. syndactyly, craniofacial anomalies) and CHARGE (colobomata, heart

disease, atresia choanae, retarded growth, genital anomalies (in males) and ear) associations (Davies et al., 2004, Moore, 2006). Czeizel et al (1985) suggested that babies with the VACTERL association were more likely to be male and of low foetal weight (Czeizel and Ludanyi, 1985). Levitt et al (1997) found that a tethered cord occurred in 24% patients, and this association was particularly noted amongst the patients with severe anorectal defects, sacral hypodevelopment, myelodysplasia, presacral mass', sacral hemivertebrae, or a single kidney (Levitt et al., 1997).

Genitourinary malformations form the main group of associated anomalies in ARA due to the closely associated embryology of the systems (Cook, 1990). Urinary tract abnormalities have been shown to occur in 20-54% of patients with ARA (Metts et al., 1997, McLorie et al., 1987, Belman, 1972, Hoekstra, 1983, Munn, 1983, Parrot, 1985). The most common upper tract anomaly has been found to be renal dysgenesis, which is seen in association with high ARA (Davies et al., 2004). Urological problems have also been found to be associated with a high incidence of fistulas encountered in ARA. Unlike in anorectal dysfunction, vesicoureteric dysfunction has the potential to cause permanent damage to other organs (Davies et al., 2004). Thus, due to the long term sequel of upper urinary tract damage, one of the main aspects of ARA treatment includes the preservation of renal function and the prevention of urinary tract infection. Those with a persistent cloacal anomaly, exhibit a relatively neuropathic dysfunction that is also commonly associated with spinal abnormalities, or iatrogenic injury to sacral nerves. In patients with high ARA, genital abnormalities are also frequently seen (Davies et al., 2004). Males have a higher incidence of genital anomalies occurring in low malformation and gastrointestinal anomalies (Ratan et al., 2004). Davies et al (2004) found that undescended testes and hypospadias were the most

frequent anomalies detected in males, with septate vagina most commonly seen in females (Davies et al., 2004).

It is uncommon to find genetically determined syndromes with ARA. There are however reasons to believe that there is a genetic component involved (Smith, 1988, Van Gelder, 1961). There is no real association between birth order, maternal age and relationship to parity has been established, although a slight preponderance among first-born infants has been suggested (Smith, 1988). As early as in the 1950s, it was acknowledged that the incidence of a malformation in a sibling, of a patient with ARA is increased and has been shown to be as much as 1 in 100, compared with an incidence of about 1 in 5000 in the general population (Falcone et al., 2007). Yet, it has also been suggested that heredity plays a minor role in ARA due to the low familial incidence (Murken, 1976). Since then, there have been several reports indicating families with 2 or more affected members and associations of ARA with multi-system syndromes. Particularly in patients having Townes-Brock's syndrome (Towne, 1972), Currarino's syndrome and Pallister-Hall syndrome (Falcone et al., 2007). Not only is there evidence of increased incidence of ARA in patients with trisomy 21, but that 95% of patients with trisomy 21 and ARA have imperforate anus without fistula, compared with 5% of all patients with ARA. Thus, it is likely that the mutation of a range of different genes can result in ARA, or that the aetiology of ARA is multigenic (Falcone et al., 2007).

Falcone at al (2007) (Falcone et al., 2007) showed in their large case series, an increased association of specific types of ARA, namely, perineal or vestibular fistulas, with affected family members. Based on their findings, parents of children with perineal or vestibular fistulas can now be told that there is a 3% chance of another family member being affected

(Falcone et al., 2007). Additionally, parents of boys born with a perineal fistula or girls born with a perineal/vestibular fistula can now be counselled that there is a 7% or 5% chance, respectively, of having a family member with a congenital ARA. There was also less family transmission among patients with either cloaca or prostate fistulas.

There is also a considerable body of evidence from animal experiments to substantiate the genetic associations. There have been animal studies in lines of mice (Kluth et al., 1991), pigs (Vianna and Tobias, 2005) and even in some breeds of dogs (Van der Putte and Neeteson, 1984) with inherited ARA which point to genetic causes of ARA. Gene targeting in mice has also demonstrated the importance of a number of genes, acting in isolation or in combination, for normal hindgut development. Thus, it is very likely that ARA is similar to the prototypical congenital anomaly of the digestive system, Hirschsprung's disease, which also affects about 1 in 5,000 live births (Bates, 2002, Kapur, 1999, Tam and Garcia-Barcelo, 2004)

1.2.5 Surgical Management in ARA

1.2.5.1 Historical reference to anorectal anomalies and surgery

It is beyond the scope of this thesis to go into detail about the historical journey of ARA, however, it is interesting to note that this condition was recognised in animals since the time of Aristotle in the third century BC (Grosfeld, 2006). Soranus was the first paediatrician (from Rome), who changed the attitude in the second century AD by not allowing neonates with ARA to die and who described dividing a thin anal membrane and dilating the opening (Scharli, 1978). It is important to note that ARA was a source of concern from earlier times,

yet no record has been found of surgical intervention until the seventh century Byzantine physician Paul of Aegina (625–690 AD) - author of the Epitome of Medicine, which was first printed in Greek by the Aldine Press in Venice in 1528 (Gurunluoglu and Gurunluoglu, 2003). He opened the bowel by piercing the anal membrane and used a wedge-shaped tent dilator in the seventh century (Matas, 1897). Galen in 1576 described the anal sphincters, levator muscles and coccyx (Grosfeld, 2006). There some records regarding ARA until 1676, when Cooke treated a child by making a small incision over a blind anal membrane and dilated the aperture with elder pith. He emphasised the importance of the sphincteric mechanism to other medical professionals who aimed to duplicate his success (Cooke, 1685, Cule, 1965). In 1693, Saviard was the first to attempt treatment of high bowel termination by plunging a trocar through the perineum (Grosfeld, 2006). This was followed by Benjamin Bell in 1787 who underwent a dissection in two newborns via the perineum to locate the rectal ampulla (Cook, 1990). Prolonged 'bouginage' was required to preserve the open passage using a sponge tent, gentian root, or other substances that swell with moisture (deVries, 1984). Bell also managed to describe instances of rectovaginal and bladder fistulas.

The colostomy became well recognised in the eighteenth century in France. Littre (1710) performed a autopsy in an infant with rectal atresia and proposed that the bowel be brought to the surface of the abdomen to function as an anus (Grosfeld, 2006). Durret in 1793 performed the first successful sigmoid colostomy (termed an 'inguinal colostomy or procedure of Littre). Roux (1834) identified the significance of keeping the perineal dissection strictly in the midline and preservation of the EAS (Grosfeld, 2006, Matas, 1897). Amusat was the first individual who sutured the rectal wall to the skin edges in 1853, which has been considered the first actual anoplasty. This was the landmark procedure at the time

and gained wide acceptance, and was used frequently for the rest of the nineteenth century. Several techniques were further used from splitting, dislocating or excising the coccyx in order to gain better exposure, and some surgeons even opened the pelvic peritoneum to obtain greater length of bowel. The first indication of a combined abdominal and perineal exploration was by Neil McLoed in 1880. In 1886, McCormac was one of the few to suggest a two-stage procedure preliminary colostomy and subsequent anoplasty (McCormac, 1886). In 1887, Matas combined a sacral approach to rectal atresia with sacrotomy to aid exposure in instances of high-lying anomalies and predicted that this would be the route of choice of these procedures in the future (Matas, 1897). During the pre 1900 era, appreciation of the pelvic and perineal anatomy was influenced by the observation of Vesalius (1543), Galen (1576) and Santorini (1724) who described the anal sphincters, the levators, and the coccyx (Grosfeld, 2006). Textbooks of Surgery in 1908 recommended colostomy as a life-saving measure only, otherwise the perineal approach was employed for all other cases (Keen, 1908).

Debate about surgical management continued over the centuries from a number of surgeons (Grosfeld, 2006). Following World War II, things began to change with introduction of antibiotics and improvements in anaesthesia had a positive influence on reducing the septic complications associated with bowel surgery. The abdominoperineal approach initially explored by McLoed, was well accepted eventually and further modified by Norris in 1943 (Norris et al., 1949) and Rhoads in 1944, whereby successfully tried one-stage abdominoperineal procedures in several neonates (Rhoads et al., 1948). Rhoades, Piper and Randall in 1948, published the first description of the above operation (Rhoads et al., 1948).

There are several operative techniques that took into consideration the importance in understanding the anatomical basis of continence. This was firstly appreciated by Stephens' sacroperineal (or sacro-abdominoperineal) approach, first described in 1953, which will be discussed in detail later, with emphasis on the role of the levator ani muscle and lack of significance of the EAS and IAS (Stephens, 1953, Grosfeld, 2006). Others included Rehbein and Kiesewetter who both advocated submucosal resection to avoid damaging pararectal nerves and muscles (Kiesewetter and Chang, 1977, Kiesewetter et al., 1976). Because of the high incidence of faecal incontinence (FI) in the abdominoperineal approach, in 1963 Kiesewetter and Pittsburgh modified Stephens' operation by performing the abdominosacroperineal procedure (Kiesewetter and Turner, 1963). This procedure involved using the abdominal approach isolating the fistula and the sacral route to enter the supralevator space by splitting the pubococcygeus and iliococcygeus in the midline. Unlike Stephens, Kiesewetter believed the EAS was present and worth saving. Two years earlier (1961), Smith had identified the normal sized EAS in 15 out of 16 autopsied cases of imperforate anus (Smith, 1961). Kiesewetter and Nixon found the EAS muscle present in all nine cases studied at autopsy, but found a gap between the sphincter and the puborectalis muscle (Sukarochana and Kiesewetter, 1968). Another significant moment in the reconstruction of the anorectum is Mollard's anterior dissection to define the puborectalis muscle which was considered a key role in continence. This was first reported in 1975 using an anterior perineal approach for high ARA (Laberge et al., 1983, Mollard et al., 1978). Finally, the posterior sagittal approach first described by deVries and Pena which became well accepted due to the wide exposure it gave by dividing the entire pelvic floor (Pena and Devries, 1982). In the 1970s and early 1980's comparing results among authors became difficult due to the different subjective criteria for grading and definitions used to assess function of ARA – this still in the case today (Grosfeld, 2006).

1.2.5.2 The anatomy debate in anorectal anomalies

Stephens (1986) has laid maximum stress on the puborectalis sling being the principle muscle responsible for maintaining continence (deVries and Cox, 1985, N'Guessan and Stephens, 1986). Despite this, De Vries and Pena (1982) avoid reference to a specific sling: *'too much emphasis has been placed on the value of the puborectalis for continence'* and they prefer to accept the concept of a *muscle complex* which includes the fusion of levator and EAS muscles (Pena and Devries, 1982, deVries and Pena, 1982). This paradigm is in direct conflict to studies which clearly demonstrate the anatomical and physiological function of these muscles. In practice clinically if the puborectalis is damaged, and the EAS left intact, the patient is left faecally incontinent. Conversely, if the EAS is divided too extensively (e.g. during fistula-in-ano surgery) whilst the puborectalis is left undamaged, the patient may leak mucus but is not necessarily incontinent (Holschneider et al., 2001).

As anatomists have noted for centuries and Smith (Smith, 1987, Holschneider et al., 2001) summarises: 1) the lowest and most medial fibres of the levator do not have this so called 'sling' like structure from the pubis anteriorly, back to and behind the rectum, and forward again to the pubis; 2) behind the bowel the rest of the levator acts on the floor of the pelvis; 3) the EAS is a intricate structure from skin up to levator divided into strata, some of which are circular, with some fibres orientated anteroposteriorly, attached at the perineal body, and posteriorly to the skin or coccyx; 4) it is difficult to distinguish between the lowest levator fibres and the deep part of the EAS; 5) the EAS is further divided by cephalic to caudal bands derived from the pubococcygeal part of the levator and the longitudinal muscle coat of the rectum (smooth muscle); and 6) the IAS is the expanded end of the circular smooth muscle of the rectum (Smith, 1987). Reflecting on the current knowledge of anatomy which

has been known for centuries, the whole muscle complex is not merely a striated muscle complex; in fact it has been suggested that it be called a *'sphincteric muscle complex'* instead. This would allow it to include all its elements (Smith, 1987). Pena and De Vries (Pena and Devries, 1982), do show appreciation that there is a muscle complex, but derive their observations purely on operative material and unfortunately counter-intuitively during their operative technique, the full extent of the puborectalis is divided before actual recognition of the muscle.

Poor functional outcomes may result from anal sphincteric dysfunction (N'Guessan and Stephens, 1986, deVries and Pena, 1982) either as a result of organ dysgenesis or from iatrogenic damage during surgery, yet the EAS is always represented in ARA (Pena and Devries, 1982, deVries and Pena, 1982). Embryological and histological studies have shown that the IAS is also present in ARA (Holschneider et al., 2001, Lambrecht and Lierse, 1987), and that the integrity of the IAS is important for a good functional result following repair of ARA (Rintala and Lindahl, 1995, Fukata et al., 1997). These findings have led to surgical techniques that try to preserve as much of the distal bowel as possible. Defects of the EAS typically result in urge incontinence whilst IAS pathology usually results in passive leakage (Gladman, 2005). However, the anal sphincter is only one contributor to the normal continence mechanism with 'suprasphincteric' contributions from the rectum and colon considered increasingly important (Siproudhis et al., 2005, Bharucha et al., 2005, Chan et al., 2005a). In particular, reduced or increased sensation and compliance can compromise continence. Our preliminary data on the pathophysiology of incontinence in a series of patients with repaired ARA confirm these finding and will be later discussed in detail (Athanasakos et al., 2008).

1.2.5.3 Operation rational based on the anatomy in ARA

Despite modern developments, modern surgical techniques are unable to offer normal anorectal function in many children who are born with ARA (discussed in detail later). A significant number of these children suffer from FI or severe constipation. Some have urinary incontinence and others have poor sexual function as adults. Given the known importance of sphincter preservation during surgery, there remains controversy as to the exact surgical techniques used to perform anorectal reconstruction. Some procedures lead to division of the sphincter complex (deVries and Cox, 1985, N'Guessan and Stephens, 1986) as opposed to pull through techniques with efforts to conserve particularly the IAS (Smith, 1987). The consequences of scarring on function can result in a relatively narrow and incompliant sphincter after preservation. This can lead to a particularly unfavourable clinical pattern of obstructed defecation, overflow and megarectum, which is commonly encountered in those with poor functional outcome.

1.2.5.3.1 Surgery for low ARA

Generally low ARA are repaired in the neonatal period with relatively simple perineal procedures that do not require a proximal colostomy (Nivatvongs Santhat, 1997). As mentioned previously, males who have a *perineal (cutaneous) fistula* can be treated during the neonatal period, since the anal canal is at least partly within the voluntary EAS complex, thus the operation can be limited to a simple opening of a passageway for the bowel contents (Rintala, 2005). The *anocutaneous fistula*, can be treated by a classic 'cutback' procedure, which involves a haemostat placed in the anus and the tissue is cut back with cautery precisely in the midline to the posterior border of the EAS (Fonkalsrud Eric W, 2004). Another approach is the 'V-Y anoplasty' of the fistula, where the anterior fistula or anal

orifice is opened posteriorly, simply dividing the perineum to the EAS, which is identified by muscle stimulation (Rintala, 2005, Fonkalsrud Eric W, 2004, Nivatvongs Santhat, 1997). The skin is incised in a Y fasion and the sphincter muscles are retracted posteriorly. A long posterior midline incision is then performed in the rectal pouch to convert the Y incision to a V, widening the opening extensively. The mucosal edges of the bowel termination are then sutured to the perineal skin (Nivatvongs Santhat, 1997). In many females and sometimes in males the anterior margin of the anus is found to lie too far anteriorly to use the Y-V anoplasty technique (Nivatvongs Santhat, 1997). Under these circumstances to use the 'anal transposition' is more appropriate, creating an anterior perineal skin bridge and a satisfactory perineal body in the processes. One way of doing this is known as the 'tennis racket' incision (i.e. around the fistula extending back in the midline to the posterior extent of the EAS). This is followed by complete dissection of the fistula from the vagina in the female and transposition of the rectum to a position within the EAS; resulting in the formation of a neoanus. The perineal body is then reconstructed (Nivatvongs Santhat, 1997). Some surgeons use anal transposition by limited 'posterior sagittal anorectoplasty' (PSARP) for anocutenous fistulae which will be discussed later. There is evidence to suggest that this procedure is more extensive and more prone to operative complications than the cutback. However, there is no evidence that PSARP would give better outcomes than a simple cutback in low anomalies. In fact, it can be argued that restoration of normal anorectal anatomy is of great concern for both the cutback and PSARP procedures due to the division of the sphincteric mechanism (Pakarinen et al., 2006, Rintala, 2005).

Females with *perineal (cutaneous) fistula* usually require more extensive surgery, as the anal canal is less contained within the sphincter complex than in males. Today the most

commonly used approach for female perineal fistula is the 'limited PSARP'. The timing of the operation is critical; it is safer to proceed with surgery during the first two or three days of life, because meconium is then less likely to be colonised by pathogenic bacteria.

1.2.5.3.2 Surgery for intermediate and high ARA

It has been suggested, all ARA in males without an anal opening in the perineal region need an initial colostomy to relieve the obstruction. However, some surgeons prefer to use the one stage reconstruction during the neonatal period without a protective colostomy for high anomalies (Rintala, 2005). One of the main concerns related to a neonatal single-stage repair without a colostomy is that it involves more or less blind dissection of the rectal termination and recto-urinary fistula in a meconium-stained field, without precise information of the exact anatomy of the defect (e.g. radiological, endosonography) (Rintala, 2005). Generally, the pull through procedure is performed between 9 and 18 months of age. There is no doubt, that several approaches have been suggested yet no single approach has superior results, and all have drawbacks. However, all the procedures share four objectives: 1) to place the rectal pouch on the perineum, 2) to eliminate rectal obstruction, 3) to position the pull through rectum as normally as possible within the striated complex muscle and 4) to close the rectourinary fistula (Rintala, 2005).

Today, the 'abdominoperineal' exploration is credited to Rhoads (Cook, 1990). Although this method enables the surgeon to free the blind-ending rectum very close to the rectal wall, it may lead to nerve injury in the true pelvis and damage the blood supply to neighbouring organs. This is of particular concern, if as in most cases, the lowest part of the rectal pouch descends distally to the fistula (Rehbein, 1959, Cook, 1990), is distended as in newborns, is

filled with meconium or has a thin wall (Cook, 1990, Browne, 1951). Swenson and Donnellan adopted a similar approach to Rhoads, in which there was no sacral exposure (Swenson and Donnellan, 1967). Yet, they took into consideration Stephen's concept, to define the correct plane through the puborectalis sling from the abdominal route, and feeding the neorectum through this sling to the perineum (Smith, 1987, Swenson and Donnellan, 1967). The main drawback with this technique is defining the puborectalis from the abdominal route (where it is hidden behind the bladder and pelvic fascia), thus interfering with pelvic parasympathetics outside the rectum, and the EAS is not well defined.

Other repairs with similar appreciation of defining the puborectalis include the Stephens and Smith's 'sacroperinal approach' (Pena, 1995, Ong and Beasley, 1991). Stephens (Stephens, 1953), was the first to recognise the essential prerequisite for continence; that is the placement of the neorectum through the levator complex, especially its puborectalis position. Simplistically, through a relatively short sacrococcygeal incision, the plane of the puborectalis is firstly made by right-angled forceps pressing against a metal sound in urethra or vagina; the fistula is ligated from within the rectum and the rectum mobilised either through the sacral or abdominal incisions, and threaded down through the sling, where it is anastomosed to skin flaps (Stephens, 1953, Smith, 1987). It is important to note that in this procedure the puborectalis is defined and interference with the bladder nerve supply is limited; the anus is skin-lined for sensation; and the procedure may be completed by the sacral route alone (for intermediate anomalies) or the abdominal route (if further bowel mobilisation is required in high anomalies) (Stephens, 1953, Smith, 1987). However, some surgeons have found that the puborectalis sling itself is not visualised in this procedure, especially by a surgeon inexperienced, where the forceps may diverge from the midline either missing the puborectalis entirely or penetrating it eccentrically. Access to the fistula

and urethra is to some degree limited with a potential chance of damaging the latter, and there is lack of recognition given to the EAS, which is penetrated blindly (Stephens, 1953, Smith, 1987). Despite this, Stephens procedure revolutionised the treatment of anorectal anomalies, particularly at the time when it was introduced, and most importantly formed the basis of every advance since then.

Modifications of the 'anterior perineal approach' described originally by Mollard are still used by some surgeons today (Smith, 1987). Mollard accessed the sphincter complex by a curved transverse perineal incision anterior to the new anus. A plane to the fistula and to the puborectalis is thus opened up directly behind the urethra (or vagina) with positive detection of both fistula and levator being visualised (Smith, 1987). The benefit of this procedure is the clear recognition of puborectalis, yet once again limited detection of the EAS.

Throughout the 19th and early 20th centuries, perineal exposure of the anorectal region was the standard approach (Smith, 1987). De Vries and Pena (N'Guessan and Stephens, 1986, Smith, 1987), reintroduced the perineal approach to the rectum despite the fact that this procedure fell into disrepute as it lacked the respect of the sphincteric musculature which often resulted in very poor results (Smith, 1987). However, today the most well accepted and used operation for repairing high and intermediate ARA is Pena's PSARP (Pena and Devries, 1982, Rintala, 2005). Basically, the dissection is aided by electrostimulation of all muscle fibres, starting with precise definition of the maximum confluence of EAS components at the proposed anal site (Rintala, 2005, N'Guessan and Stephens, 1986). Each muscle is divided in the sagittal plane, this includes going through the external-puborectalis complex, allowing a wide access to divide a fistula under vision, mobilise and taper the terminal rectum, and then reconstitute all muscle elements accurately around the neorectum

in precisely the correct anatomical position (Rintala, 2005, N'Guessan and Stephens, 1986, deVries and Pena, 1982, Smith, 1987). This procedure is unique from other procedures discussed above, in that the fistula can be directly visualised and therefore, damage to the urethra is minimised by the wide exposure of the fistula (Rintala, 2005, N'Guessan and Stephens, 1986, deVries and Pena, 1982, Smith, 1987). Despite these advantages, the concept of intentionally dividing surgically the entire muscular complex on which the continence mechanism depends on, especially the deep portion (EAS, puborectalis), is of great concern.

The 'Durham Smith' or 'perineal rectoplasty' procedure is used in patients with an intermediate or high ARA (such as rectoprostatic urethra fistula/high rectovaginal fistula) (Smith, 1987). This procedure is similar to Pena and De Vries in that an incision from the sacrum to the proposed anal site is made, using electrostimulation to define all muscles. The subcutaneous and superficial components of the EAS are divided sagittally, as are the levator portions (iliococygeus and ischiococcygeus muscles) but not the combined puborectalis, pubococcygeus, and deep portion of the EAS. These essential muscles are kept intact with total preservation of the essential musculature for continence (Smith, 1987).

In some high anomalies, there is insufficient mobilisation of the rectum and this has been corrected using a perineal route: the 'perineal abdominoperineal rectoplasty' (Smith, 1987). It is initiated in the perineum, with preservation of the deep sling of the muscle complex, which is defined by a Penrose drain. This is followed by placing the patient in the lithotomy position (the patient lies on their back with the hips and knees flexed and the thighs apart). This is followed by opening the abdomen and mobilising the bowel; the rectal pouch is preserved and by submucosal sleeve dissection (Romualdi, 1960), the fistula is divided from

within; the neorectum, tapered if necessary, is brought down within the rectal sleeve to the base of the pouch through which a hole is made to identify the Penrose drain, preserving any circular muscles of the rectal pouch (Smith, 1987). From the perineum the tapered bowel is then pulled down through the undamaged sling, and the anoplasty completed by the Nixon technique (Smith, 1987).

Lately, some surgeons have chosen to repair high ARA using the laparoscopic approach. This involves 'laparoscopic' mobilisation of the rectal termination and fistula closure and subsequent pull-through of the fistula to the anal site through the sphincter funnel, which is identified by muscle stimulation (Rintala, 2005). This procedure still remains in its infancy and there is a lack of follow up results at present. This approach generally involves less manipulation of the voluntary sphincteric complex than the PSARP procedure mentioned above (Rintala, 2005).

As mentioned previously, the most common ARA in females is the vestibular fistula. The treatment still remains controversial, yet most surgeons prefer to do a colostomy to begin with in order to minimise the risk of potentially deleterious complications (Rintala, 2005). It has been well accepted for vestibular fistula to do a simple neonatal 'cutback' procedure in order to make the anal opening wide enough for passage of stool (Rintala, 2005). A traditional alternative to a cutback has been 'anal transposition' to the normal anal site. This operation which is of medium complexity has been suggested as it produces excellent cosmetic results and a normally situated anal opening (Demirbilek and Atayurt, 1999). Today the preferred method for repairing a rectovestibular fistula is limited PSARP (Rintala, 2005, Demirbilek and Atayurt, 1999).

One of the most challenging groups among female patients with anorectal anomalies are those with persistent cloaca (Rintala, 2005, Demirbilek and Atayurt, 1999). Unusual arrangements of the urogenital and rectal anatomy exists, thus there is no particular standard operation for a cloaca. Therefore, there is no doubt that a neonate with a cloacal anomaly requires close attention in comparison to other types of ARA. Reconstructive surgery for a cloacal anomaly requires precise and detailed description about the anatomical defect present. The significant anatomical issue is the length of the common channel, since this dictates the type of procedure that is necessary for full reconstruction (Rintala, 2005, Demirbilek and Atayurt, 1999).

In conclusion, there still remains no ideal operative procedure for patients with ARA. It needs to be stressed that surgeons today, need to pursue physiological means of investigations postoperatively (e.g. anorectal manometry, endosonography, barostatis measures) in order to move forward in this challenging area. But before one begins to suggest new surgical interventions, the surgeon must first appreciate the anatomical and physiological significance of preserving structures important to the continence mechanism to achieve any improvement in their patients.

1.2.6 Outcomes for patients with ARA

The treatment of ARA either by perineal, sacral, abdominal, or combined approach is technically demanding and requires strict adherence to the finer anatomical and physiological details to achieve good results. Despite surgical advances mentioned in the previous section, voluntary bowel control is frequently poor following surgical care for ARA (Heikenen et al., 1999) with high rates of faecal incontinence (FI), and also constipation after

all grades of reconstructive surgery (Rintala and Lindahl, 1995, Ong and Beasley, 1991, Rintala et al., 1993b). With regard to continence, poor functional outcome may be due to anal sphincteric dysfunction either as a result of organ dysgenesis or from iatrogenic injury. The integrity of both the IAS and the EAS are important for a good functional result following repair of ARA (Rintala and Lindahl, 1995, Ong and Beasley, 1991, Rintala et al., 1993b). Traditionally, sphincteric dysfunction was considered as the sole contributory factor to FI. However, patients without a history of ARA and with an anatomically intact and normal functioning sphincter complex can also experience episodes of FI, indicating that there must be other pathophysiological mechanisms contributing to their symptoms (Williams et al., 2001, Lunniss, 2007). It is now clearly recognised that disturbances of 'extra-sphincteric' sensorimotor function are also crucial to the development of symptoms of FI (Bharucha, 2004, Bharucha et al., 2005, Chan et al., 2005a, Salvioli et al., 2001, Williams et al., 2001, Lunniss, 2007). Further discussion is necessary to understand the symptoms of FI and constipation in the context of ARA and furthermore, to comprehend the pathophysiological mechanisms involved in these symptoms.

1.2.6.1 Faecal incontinence

1.2.6.1.1 Definition

Even though the task of defining faecal incontinence (FI) is difficult, as it varies amongst the literature a great deal. For this thesis, FI may be defined as the *'involuntary loss of stool or soiling at a socially inappropriate time or place'* (Lamah and Kumar, 1999), or *'the involuntary loss of flatus, liquid or stool that is a social or hygiene problem'* (Chatoor et al., 2007). Clinically, FI has been classified into three specific types: 1) urge incontinence

which is the unwanted loss of stool despite active attempts to inhibit defecation; 2) passive incontinence which is unwanted loss of stool without patient awareness or 3) a combination of urge and passive incontinence (Deutekom et al., 2007).

1.2.6.1.2 Epidemiology

It is important to appreciate that FI affects all ages and both sexes and is estimated to affect approximately 2% to 7% of the adult population (in the US and Europe) with an equal prevalence in males and females (Perry et al., 2002, Deutekom et al., 2007, Kalantar et al., 2002, Walter et al., 2002, Whitehead et al., 1999)increasing to up to 15% in the elderly (Roberts et al., 1999). Additionally, 63% of affected elderly patients are women (Perry et al., 2002). This finding relates to the commonest aetiologies, in particular obstetric perineal trauma, which remains one of the most common aetiological factors in young women (Chatoor et al., 2007). However, reports of the prevalence and incidence of FI in the community show significant variation. This can be due to many factors such as sampling, non-response and self selection. Enck et al (1991) has shown that 5% of patients with FI had incontinence symptoms noted in the medical charts, data from which therefore highlights bias that systematically underestimates the real prevalence of FI (Enck et al., 1991). Functional FI which is defined as recurrent uncontrolled passage of faecal material in a person, who has no underlying neuropathic or structural aetiologies, occurs in about 1.4% of children aged seven years (Whitehead et al., 1999).

There is a relationship with FI and social and psychological disability. One of the reasons for this is that FI is such a distressing and embarrassing symptom and has a major impact on quality of life (Chatoor et al., 2007). A patient suffering from FI, is not suffering from a

purely physical, but also psychological disability that comes with it, leading to social isolation and loss of independence (Chatoor et al., 2007). Faecal incontinence also constitutes a substantial economic burden to individual patients and health care resources (Chatoor et al., 2007, Malouf et al., 2001). Most importantly, the social embarrassment experienced by sufferers means they are often unwilling to admit to symptoms, and doctors are reluctant to embarrass patients by asking about it (Malouf et al., 2001, Bharucha, 2003). Therefore, we are likely to grossly underestimate the true prevalence of this disabling condition.

1.2.6.1.3 Diagnosis

A clear diagnosis of FI starts with a detailed history of the patient's complaint, which requires a good rapport between patient and clinician (Tuteja and Rao, 2004). The type of incontinence may imply the cause of the symptom; e.g. passive soiling of stool suggests an IAS or sensory problem, urge incontinence suggests EAS or luminal disease (Chatoor et al., 2007). Questions need to be directed to the volume of stool lost, the frequency of episodes of incontinence, how long they can defer defaecation for (if needed) and the social implications it has on them, in order to have an insight into the type and severity of FI and its severity. A history of obstetric or symptoms of other pelvic floor problems (urinary incontinence, pelvic floor prolapsed) should also be elicited (Table 1.2).

Once a detail history has been accomplished, clinical examination should begin by checking for perianal excoriation and dermatitis from prolonged exposure to faeces, and for damaged sphincters (Chatoor et al., 2007). Physical examination should be performed without prior enema or laxative use. In patients with FI related to constipation, a large mass of stool in the

rectum on digital examination and/or in the colon on abdominal palpitation is usually found (Whitehead et al., 1999). If the patient is able to contract the EAS, efferent denervation is unlikely. Rectal prolapse can be evaluated by asking the patient to strain as if defecating while seated on a commode chair. On observation, perineal scarring, small perinal body size and a wide genital hiatus implies obstetric trauma. The digital examination should assess for pelvic floor dyssynergia (decreased anal canal pressures reliably exclude the diagnosis of pelvic floor dyssynergia, but abnormal findings require confirmation) (Whitehead et al., 1999). However, if the history and physical examination do not support a clear diagnosis of function FI, further tests are required such as physiological investigations (e.g. endosonography), which will be discussed later in this thesis.

1.2.6.1.4 Pathophysiology

The mechanism of normal continence relies on, amongst other factors, a complex physiological communication between motor and sensory components of the anorectum (Rao, 2004a, Rao, 2006, Cheetham et al., 2001, Chan et al., 2005c). Thus abnormalities of one or more of these mechanisms, that maintain continence may results in FI. It is valuable in clinical practice to classify incontinence according to underlying pathophysiology, as this will hopefully dictate appropriate and better management for the patient. Anal sphincter disruption or weakness (i.e. due to obstetric or congenital) (Table 1.2), pudendal neuropathy, impaired rectal accommodation, or incomplete evacuation may all contribute to the pathogenesis of FI. These changes may be a consequence of local, anatomical or systemic disorders. Thus it is important to keep in mind throughout this thesis that the origin of FI is multifactorial (Table 1.2).

As mentioned in our understanding of the normal anatomy of the anorectum, the anal sphincter consists of two muscular components: the IAS and EAS. The IAS contributes about 85% of the total pressure of the anal canal at rest (Cooper and Rose, 2000). The EAS is recruited to increase anal canal pressure, especially when continence is challenged (e.g. raised intra-rectal or intra-abdominal pressure) (Chatoor et al., 2007, Cheetham et al., 2001). Impairment of the IAS can result in decreased resting pressures, leading abnormalities such as passive FI. Dysfunction of the EAS leading to decreased squeeze pressures has been linked to urge FI (Deutekom et al., 2007, Engel et al., 1995, Gee and Durdey, 1995). In our practice, sphincter dysfunction accounts for the majority of cases of FI (GI Physiology Unit, Royal London Hospital). As in other tertiary referral centres, trauma to the anal sphincter during childbirth, followed by iatrogenic injury after anal surgery are the two most common identifiable causes of sphincter injury (Table 1.2) (Kamm, 1998, Lunniss et al., 2004). Dysfunction of the IAS can arise due to many factors including structure damage, usually during childbirth or anal surgery or in the absence of structural damage either due to primary idiopathic degeneration or secondary to tissue disorders such as scleroderma (Kamm, 1998). As stressed throughout this thesis, there are contributions of other pelvic floor muscles responsible for the mechanism of continence which can easily be under-appreciated. Fernandz-Fraga et al (2002) demonstrated that levator ani weakness is strongly associated with severity of FI (Fernandez-Fraga et al., 2002).

Nevertheless, patients with an anatomically intact and normal functioning EAS also experience episodes of urge FI, indicating that other pathophysiological mechanisms may contribute to symptoms. It is known that alterations in suprasphincteric mechanisms influence continence but their precise role in urge FI remains undetermined (Rao, 2004a, Rao, 2006, Rao, 2004b). The reservoir function of the colorectum may be compromised, for

example, by disturbance of sensorimotor function. As visceral sensory and motor mechanisms of the anorectum and colon are themselves inextricably linked, alterations in the motor component may effect change in sensory function, and vice versa. Faecal incontinence is influenced by higher cortical centres and spinal reflexes, stool consistency, rectal compliance and capacity and, anal sphincter function (Hill et al., 2002).

Anatomically, the rectum and anal canal lie adjacent to one another; yet they are innervated by different sensory pathways. In the rectum, sensory information comes via the parasympathetic pathways to reach the dorsal horn of the spinal cord, whereas the sensory pathway from the anal canal is via the pudendal nerves (somatic). But there may be a degree overlap evident in the transition zone. These pathways originate from the sacral plexus (S2, S3 and S4) and are closely related anatomically at this level. The branches of the pudendal nerve, providing efferent and afferent pathways to the EAS and perineum, are susceptible to stretch injury, which may result in muscle weakness and FI. Examples of such injuries may occur during childbirth (Snooks and Swash, 1984, Sultan et al., 1994, Tetzschner et al., 1997, Rieger and Wattchow, 1999), with chronic straining of stool or secondary to rectal prolapse (Snooks and Swash, 1984, Kiff et al., 1984, Engel and Kamm, 1994). It is now known that structural damage to the anal sphincteric mechanism is the underlying cause in most patients (Kamm, 1998, Burnett et al., 1991, Law et al., 1991, Deen et al., 1993, Nielsen et al., 1993) rather than pudendal neuropathy, and true isolated neuropathy may be rare (Vaizey et al., 1998). Having said this, there is a strong relationship between pudendal neuropathy and EAS weakness in patients with FI, which suggests that pathological process affecting pudendal nerve conduction impairs anal sphincter function (Hill et al., 2002).

The rectum has both viscous and elastic properties which allows it to maintain low intraluminal pressure, even if the volume is large (Arhan, 1976). Thus, the rectum has the

ability to adapt to an imposed stretch enabling rectal contents to be accommodated and defaecation to be delayed, known as rectal compliance. However, if this mechanism is altered, decreased rectal capacity and heightened sensory perception (known as 'hypocompliance' i.e. a stiffer rectal wall) or increased rectal capacity and blunted sensory perception ('hypercompliance' i.e. more elastic rectal wall) will result. In cases where a patient is suffering from FI, the rectum is often poorly compliant (Salvioli et al., 2001, Rasmussen et al., 1990), resulting in reduced reservoir function/capacity and symptoms of urgency/frequency of defecation (Rasmussen et al., 1990). This is due to the functional reduction in rectal volume.

Rectal sensory function is regularly quantified by recording the threshold volumes required to elicit a range of rectal sensations (first sensation, urge sensation, and maximal tolerance volume) (Farthing and Lennard-jones, 1978). In the rectal wall, mechanoreceptors are present, however, the rectum itself is not needed for certain sensations, as patients with a coloanal anastomoses or ileal pouch are able to feel the desire to defecate (Gladman et al., 2006). Thus, it is possible that such stretch receptors located in the puborectalis, levator ani and sphincteric musculature contribute to sensory discrimination (Rasmussen, 1994). Injury to the afferent nerve pathways will therefore disturb sensory perception which may be associated with FI, as intact sensory function is an integral part of the continence mechanism (Vasudevan et al., 2007, Gladman, 2005). If the afferent pathway is altered, hyposensitivity (elevated sensory threshold), can result, which has been associated with patients with idiopathic FI (Gladman et al., 2003) (Hancke and Schurholz, 1987). Decreased sensory thresholds of the rectum (hypersensitivity) maybe responsible for the heightened perception of rectal filling and act as an independent trigger of FI (Chan et al., 2005c). Our knowledge on rectal sensation in the context of patients with ARA remains limited, however, it is

expected that the rectum will be affected by sacral neurodysgenesis and by the nature of the reconstructive surgery (Smith, 1987, Emblem et al., 1997, Emblem et al., 2007).

Table 1.2: Aetiology of Faecal Incontinence (FI)

Aetiology	Examples
Anal sphincter weakness	Traumatic: obstetric, iatrogenic related to surgical procedures: haemorrhoidectomy, sphincterotomy, fistulotomy, anorectal infection, colectomy, pouch procedures. Non-traumatic: scleroderma, IAS thinning of unknown aetiology.
Puborectalis muscle	Ageing, excessive perineal descent, trauma.
Neuropathy	Stretch injury, obstetric trauma, diabetes mellitus, cauda equina syndrome.
Urogynaecological	Pelvic organ prolapse Associated with urinary incontinence
Anatomic disturbance of the pelvic floor	Fistula, rectal prolapse, descending perineum syndrome
Congenital	Anorectal malformation Anal agenesis
Inflammatory conditions	Crohn's disease, ulcerative colitis, radiation proctitis.
Central nervous system disease	Dementia, stroke, brain tumours, spinal cord lesions, multiple system atrophy (Shy-Drager syndrome), multiple sclerosis.
Diarrhoea	Irritable bowel syndrome, postcholecystectomy diarrhoea. Inflammatory bowel disease Infectious diarrhoea Laxative abuse Malabsorption Drugs (any that cause diarrhoea) Foods (caffeine, alcohol, aspartamine)
Sexual	Anal intercourse (non-consensual more than consensual)
Psychiatric illness	Behavioural

This table is an integration of several resources (Rao, 2004b) (Chatoor et al., 2007) (Andrews and Bharucha, 2005) (Cooper and Rose, 2000)

1.2.6.2 Constipation

1.2.6.2.1 Definition

As with FI, defining constipation is difficult due to the variation and subjectivity found amongst the literature. It is important to remember when discussing constipation, that it is not a disease, but a symptom. Constipation is a symptom reported by patients who believe that there is a disturbance of the events that they perceive to comprise normal defaecation. Patients use a variety of symptoms with the term constipation, including those apparently directly related to defaecation e.g. infrequency of bowel action, loss of urge to defecate, straining, incomplete, painful or unsuccessful evacuation, or more diverse symptoms such as abdominal pain, bloating or nausea. It is beyond the scope of this thesis, to discuss constipation in great depth. Clayden and Agnarsson (1991) defined constipation as (Clayden, 1991);

> *". . . the difficulty or delay in the passage of stools (not a description of the hardness of the stool, although this is often but not always associated)* (Clayden & Agnarsson, 1991 p. 1).

The evaluation of the degree of severity (i.e. mild, moderate, and severe) is highly subjective, limiting comparisons between various reports. This thesis has adopted Clayden's definition with the following modifications. Constipation is defined as one or more of the following:

i) Difficulty or delay in the passage of stools

ii) Difficulty in passing stools because they are hard or small

iii) Pain when passing stools

'Acquired constipation' which is not due to an aganglionic segment of the colon, rectum or anal canal often commences in childhood. The principle symptom is one of soiling due to

overflow incontinence around a solid faecal bolus (Silverberg, 1984). Many of these children have behavioural problems and complex social background. 'Idiopathic constipation' is a diagnosis which is made by exclusion of all other causes of altered bowel habits. Typically the colon is of normal length and diameter on barium enema and of normal appearance on colonoscopy, although there may be areas of melanosis coli (Holdstock et al., 1970). A subgroup of patients with functional constipation has persistent dilation of the rectum and/or colon, termed idiopathic megarectum (Gladman et al., 2007, Holdstock et al., 1970). This means a large capacity rectum as a result of underlying nerve supply abnormalities or muscle dysfunction, which remains large after disimpaction of the rectum (van der Plas et al., 2000).

1.2.6.2.2 Epidemiology

Constipation is the second most commonly self-reported gastrointestinal symptom, affecting between 2-34% of (Clayden and Keshtgar, 2003) populations studied (Drossman et al., 1982, Sonnenberg and Koch, 1989, Camilleri et al., 1994). As found in FI, the lack of consistency in the description of constipation may be responsible for such vast discrepancies in estimation of prevalence and epidemiological factors associated with constipation.

Constipation is also a common problem in children, accounting for about 3% of consultations in an average paediatric practice and as much as 25% in a paediatric gastroenterology clinic (Taitz et al., 1986, Loening-Baucke, 1993, de Lorijn et al., 2004). Only those children unsuccessfully treated by their general practitioners are referred, and this percentage highlights the severity and longevity of childhood constipation and soiling.

Constipation, with, or without soiling occurs often in children, and is one of the ten most common problems seen by general paediatricians (Clayden and Keshtgar, 2003, Cladyen, 2005, Mason et al., 2004). No specific organic cause can be found in approximately 90% of the children (Hinton and Lennard-Jones, 1968, Hinton et al., 1969). The diagnosis is mainly based on clinical history and physical examination. Patients and/or their parents refer to the number of stools per week, to stool volume, to difficulty in defecation, and/or to sensation of abdominal fullness (Clayden and Keshtgar, 2003, Cladyen, 2005).

1.2.6.2.3 Diagnosis

Most clinicians can make a decision based on history and physical examination regarding investigations for constipation which may include blood tests for electrolyte imbalances, thyroid function, calcium metabolism, rectal biopsy, radiological studies, anorectal manometry (Halverson and Orkin, 1998, Clayden and Keshtgar, 2003). A plain abdominal radiograph is frequently used to confirm the presence of retained stool or enlargement of the colon or rectum (Barr et al., 1979, Rockney et al., 1995, Keshtgar et al., 2004a). Anatomic studies such as colonoscopy or barium enema may reveal pathology of the patient's symptoms (Halverson and Orkin, 1998). Rectal biopsy is a gold standard for diagnosis of Hirschsprung's disease where there is a lack of ganglion cells in submucosa on haematoxylin and eosin staining and presence of hypertrophic nerve fibres in lamina propria or acetylcholinesterase staining.

In patients with constipation, the term megarectum is often used indiscriminately. For some it means a large rectal mass on rectal examination, while for others it means a wide rectum

on an abdominal x ray, the presence of impaired rectal sensation, or the finding of large maximal rectal volumes on anorectal manometry (van der Plas et al., 2000, Clayden, 1992, Schnaufer et al., 1970, Leon et al., 1987, Meunier et al., 1984, Verduron et al., 1988). Dilation of the rectum may be evident on a plain radiograph of the abdomen, although diagnosis on this basis is somewhat subjective because no specific criteria exist. Therefore, the diagnosis is usually made when the rectal diameter at the pelvic brim is greater than 6.5cm on a lateral radiograph obtained during double contrast barium enema (Preston and Lennard-Jones, 1985). A simple radiopaque marker study with plain abdominal films taken three to five days later is adequate for detecting transit abnormalities (Gladman, 2005, Hinton et al., 1969). Studies have found an important delay in the rectosigmoid colon in patients with constipation (van der Plas et al., 2000, Benninga et al., 1995).

1.2.6.2.4 Pathophysiology

The pathophysiology of chronic idiopathic constipation is not fully understood and it is beyond the scope of this thesis to go into great detail. The most widely accepted hypothesis found in paediatrics, is that fear of defecation and voluntary retention of stools lead to the formation of a functional megarectum with loss of rectal sensitivity and of the normal need to defecate, causing overflow incontinence and non-voluntary expulsion of faeces, or encopresis (Loening-Baucke, 1984b). Most studies in small children have investigated various anorectal functional parameters because the distal bowel is more accessible to study by methods such as manometry (Arhan et al., 1972, Loening-Baucke and Younoszai, 1982, Loening-Baucke, 1984b, Loening-Baucke, 1984a, Keren et al., 1988, Meunier et al., 1984, Loening-Baucke and Cruikshank, 1986).

It is important to keep in mind when taking a history of the patient, to exclude common disorders causing constipation including endocrine and metabolic diseases such as diabetes mellitus or hypothyroidism; neurological diseases such as spinal cord injury or multiple sclerosis, rectoanal problems such as anal strictures or proctitis, iatrogenic conditions such as constipation due to drug, previous surgeries or dietary factors such as a low residue diet.

Chronic idiopathic constipation may be due to a disorder in the mechanism of defecation, sometimes known as outlet obstruction or anismus (Watier et al., 1983, Duthie and Bartolo, 1992). These patients have difficulty in rectal evacuation due to a failure of the puborectalis muscle and external sphincter to relax during attempted defecation, or due to a hypertonic IAS. Alternatively, constipation may be due to colonic inertia or a failure of the bowel to propel its contents in an orderly prograde manner. This disorder of colonic motility may be confined to a segment of the colon or the rectum or to the whole of the large bowel (Arhan et al., 1981, Poisson and Devroede, 1983, Metcalf et al., 1987). Colonic inertia is usually identified by the delay in the excretion or passage of radio-opaque markers, isotopic scans or a failure of the colon to respond to a stimulant (Hinton et al., 1969, Touchais et al., 1988, Krevsky et al., 1986, Preston and Lennard-Jones, 1986, Roe et al., 1986, Shouler and Keighley, 1986, Bassotti et al., 1988, Varma and Smith, 1988).

Those with significant loss of the ability to sense distension may have passive (overflow) incontinence. The symptoms related to faecal impaction are a decreased defecation frequency, passing massive stools, abdominal pain, abdominal distension, and overflow incontinence (Clayden, 1992, Meunier et al., 1984, Stabile et al., 1992, Callaghan and Nixon, 1964, Preston and Lennard-Jones, 1985). Studies in children with constipation have shown relations between night time soiling and paediatric slow transit constipation and

between faecal overflow incontinence and the presence of rectal faecal impaction (Benninga et al., 1996). Karlbom et al (2004) found constipation with symptoms of infrequency defecation to be associated with impaired rectal sensitivity (Karlbom et al., 2004). Patients with infrequent defecation have shown increased rectal compliance which could be due to either lower muscular tone in the rectal wall or to altered viscoelastic properties of the rectal wall. Engel and Kamm (Engel and Kamm, 1994) previously reported that straining has acute, as well as chronic effects on pudendal nerve function. Stretch, neural ischemia and venous stasis are possible effects of straining. This is a mechanism for development of sensitivity impairment in patients with outlet obstruction. Hosie and Spitz (1997) demonstrated an association with a thickened IAS and children (5 months and 13 years) with idiopathic constipation using endosonography (Hosie and Spitz, 1997). Children who had constipation displayed significant thickening of the IAS independent of of the length of the history, however no difference in the morphology of the EAS between the control and constipation group. Keshtgar et al (2004) also demonstrated thickening of the IAS in patients with constipation (144 patients) which significantly correlated with duration and severity of symptoms, size of megarectum, and amplitude of rectal contraction. It was suggested that the pathogenesis was secondary to the continuous presence of faeces in the rectum, resulting in chronic abnormal stimulus to the IAS, which leads to hypertrophic changes in the rectum wall and IAS (Keshtgar et al., 2004b).

1.2.6.2.5 Is the age of the child a useful guide to the main cause of constipation?

One of the main focuses of this thesis is idiopathic constipation in children above 11 years of age. It is beneficial to take into consideration the age and developmental stage of the child when it comes to the diagnosis and practical management of patients with IC (Table 1.3).

Firstly, symptoms of constipation occurring in the newborn should raise the suspicious of an obstructed large bowel by a short aganglionic segment in Hirschsprung's disease or ARA with anal stenosis (Clayden and Keshtgar, 2003, Cladyen, 2005). This is essential especially if the newborn presented with other structural problems such as VACTERL related anomalies. In infancy (beyond 4 weeks of age) toddlers and preschool age, it could be due fluid/feed intake or if early constipation (e.g. due to prematurity or gastro-oesophageal reflux disease) has gone unreported and the family have been using regular anal treatments or procedures (suppositories, enemas, or digital evacuation). In severe cases of feeding problems and constipation, especially in association with gastro-oesophageal reflux and poor thriving, rare gut motility problems such as intestinal pseudo-obstruction should be considered (Table 1.3) (Schuffler et al., 1978, Krishnamurthy et al., 1993).

Withholding is a common behavioural factor of constipation in young children which can be due to psychological stressors (Mason et al., 2004, de Lorijn et al., 2004) or fear of using the toilet or potty (Clayden, 2004, Cladyen, 2005) or episodes of painful defaecation, often due to constipation. Repeatedly withholding involves ignoring the urge to defecate, and eventually the stool retained in the rectum becomes impacted leading to constipation (Rogers, 2003, Clayden and Keshtgar, 2003). Clayden & Keshtgar (2003) presented a case study of a 2 year old boy to illustrate this point:

"The boy has been noticed to have episodes of straining, as if to defecate, throughout the day and he eventually screams as he passes a large hard stool often streaked with fresh blood. Over the past two weeks, the intervals between the stools have extended to four days. He tends to hide behind the furniture during these episodes of straining and resists contact with his parents even though he appears afraid. He has no problems with defecation either as a newborn or as an infant, but since age 1 year had occasional dry stools described as 'rabbit droppings' by his mother. This has been

explained a result of his high cows's milk intake and poor eating. He has a family history of a similar but milder problem occurring in his older sister at the same age. . ." (Clayden and Keshtgar, 2003)

Clayden et al (2003) suggested that this boy may have a familial predisposition to delayed defecation by having a unusually larger rectal capacity than the norm (Clayden and Keshtgar, 2003). This behaviour allows the boy to accumulate stool instead of passing it as his rectal contractions, provoke the rectoanal inhibitory reflex which leads to more prolonging (Clayden and Keshtgar, 2003, Callaghan and Nixon, 1964). He has learned to perceive this sensation as the precursor to anal pain and thus strains to withhold the stool by contracting his EAS and associated pelvic floor muscles by a change of posture (extended legs, arched back – known as the 'banana posture'). Hiding behind the furniture allows the boy not to become distracting during the withholding period, as he knows what it is like to allow the stool to descend. Repeated treatment failures have a psychosocial impact on the child and family (Clayden, 1991) and psychosocial problems may lead to non-compliancy with treatment regimes whether it is medication, toileting regimes, diet or behaviour modification, which then maintains the constipation (Clayden, 1991).

School age children who have constipation become more of an issue of struggle with the resulting overflow FI (Clayden and Keshtgar, 2003, Cladyen, 2005). It has been often found, that the childs' constipation has gone unnoticed for many months or years where the continuous loose stool in the underclothing has been accepted as laziness, immaturity or attention seeking. Childhood constipation is often compounded by FI that becomes the dominant complaint as peer and social pressures increase with age (Clayden and Keshtgar, 2003). Most childhood constipation clinics report a 2-3 to 1, male to female ratio whereas with adults there is a marked female predominance. It has been suggested that constipation

in children is mostly caused by the conscious or unconscious postponement of defecation (withholding behaviour) due to learned behaviour and pain with evacuation of a large faecal bolus (de Lorijn et al., 2004) or problems with faecal retention in the megarectum with overflow FI or it is the early onset of more adult type pancolonic slow transit constipation (Clayden and Keshtgar, 2003).

In older children and teenagers with persistence of the megarectum and FI, there is a tendency for increasing denial and dissociation that infuriates their parents and teachers, limits the effectiveness of psychological input and sabotages any physical treatments (Clayden and Keshtgar, 2003, Cladyen, 2005, Ludman and Spitz, 1996). This leads to poor compliance of medication, disregarding routine use of the lavatory, and ignoring FI when it occurs.

There is continuous debate over the association between constipation and psychosocial problems, and whether constipation causes psychosocial problems or vice versa (Benninga et al., 2004). Benninga et al (2004) mentions some of the terms use to describe this: *"psychogenic constipation and some consider that unexplained encopresis is triggered by unconscious anger" (Benninga et al., 2004).* Studies have found that psychosocial and behavioural problems are the main cause of chronic idiopathic constipation (Coughlin, 2003, Southwell et al., 2005). Coughlin (2003) says *"psychosocial and behavioural factors are often the source of constipation in children"* (p297), but does not acknowledge the role that psychosocial and behavioural problems can have in maintaining constipation (Coughlin, 2003). Some studies have found the importance of behavioural disturbances or personality disorders, suggesting that constipation and encopresis require psychiatric treatment (Gabel et al., 1986, Friman et al., 1988).

Table 1.3: Inter-related physical and psychological factors in childhood constipation

Borrowed from (Clayden and Keshtgar, 2003)

Early physical factors	**Early behavioural factors**
Familial high capacity stools High milk, low fibre intake Hard non-malleable stools Anal fissure Perianal group A streptococcal infection Cow's milk allergy/eosinophilic proctitis Medication – for example, diuretics, analgesia. Rare: Hirschsprung's disease, anal stenosis, hypocalcaemia, hypothyroidism, celiac disease.	Poor or faddy eating Fear of pain related withholding of faeces Avoidance of defecation Too early or coercive pot training Pot/lavatory refusal Parental anxiety, tension, and anger Fear of medication (particularly by anal route)
Later physical	**Later behavioural**
Hypertrophied rectum (megarectum) Residual stool (faecaloma/faecalith) Episodic rectoanal inhibition and overflow faecal soiling. Poor rectal sensation Less common: child abuse (anal sexual abuse), celiac disease, cerebral palsy, lead poisoning.	Embarrassment/shame related to soiling Parental blame/anger related to soiling and lavatory refusal Teasing and bullying related to incontinence Dissociation and denial Medicine and lavatory routines refusal Decreased mobility/activity.

1.2.7 Management of symptoms of faecal incontinence and constipation

A brief account will be discussed about some of the current treatment modalities for constipation and FI in childhood. But before we embark on the cocktail of laxatives given to children with FI and constipation or discuss the advanced treatment modalities up for suggestion, we need appreciate the need to firstly educate our audience, the child and family involved. There is no point in offering solutions, without the patients and carers involved, understanding the purpose and physiological mechanism involved in dealing with these symptoms on a day to day basis. Thus, education about basic physiological mechanisms involved in continence, at an early stage should be introduced. They need to be aware, that the rectum regularly contracts when impacted and so any soft or loose stool in the vicinity of the IAS will leak out, especially as the persistently full rectum produces very little sensation during its contractions. As the leaking stool is of the same temperature as the skin, it is not surprising that the child is unaware of this type of FI (Cladyen, 2005, Clayden and Keshtgar, 2003). Then there is the balance between effective emptying of the rectum and the ability to reach the lavatory in time is particularly difficult if the child needs high dosage laxatives to avoid faecal impaction. The amount and timing of the dose along with a good fluid intake will hopefully encourage a stool to be passed at a regular time of the day.

1.2.7.1 Medication

The goal of treatment for patients of any age suffering with FI and/or constipation is to restore continence and to improve the quality of life. Pharmacological therapies involve using a variety of drugs (Table 1.4), each with a different mechanism of action to improve FI

and constipation. All laxatives act in the lumen of the colon. Some form a greater bulk (bran, carboxymethyl-cellulose, ispaghulla, sterculia) (Table 1.4). Others soften the stool (Arachis oil, liquid paraffin, docusate sodium or calcium salt, given as an enema) which facilitates the expulsion of the bolus (Table 1.4) (Briejer et al., 1999). Other laxatives are able to stimulate the mucosa and induce secretion and mass movements. These include i) antranoids such as senna, aloe and dantron; ii) polyphenol derivatives such as Phenolphthalein, Bisacodyl, Sodium Picosulphage and; iii) miscellaneous compounds such as Castor oil, Glycerol and Docusate Sodium or Calcium salt (Table 1.4) (Briejer et al., 1999). Osmotic laxatives (Movicol, Mannitol, Sorbitol, Lactitol, Lactulose, Magnesium salts, Phosphates, Sodium citrate) (Table 1.4) aim to increase the fluid content of the stool and facilitate expulsion of the bolus by lubricating and softening it (Briejer et al., 1999).

Clayden & Keshtgar (2003) have suggested that the first stage for a child with a hard stool extending to the umbilicus on abdominal palpation is to soften it. Examples of softeners include Lactulose, Sodium Docusate and Polyethylene Glycol (Macrogol) (Table 1.4) (Clayden and Keshtgar, 2003). There is no doubt, that the evacuation phase is one of the most challenging areas for the clinician and the patient. The risk of using forceful but effective physical means to clear the stool must be balanced against the stress caused to the anxious child as this may intensify the psychological factors that operate in the persisting problem (Clayden and Keshtgar, 2003). This can be achieved with multi-disciplinary support from the clinician, surgeon, specialist stoma nurses, parents and most of all, the child. If the mass is not evacuated spontaneously, then a high dose of stimulant laxative such as Senna ('sennakot'), Bisacodyl or Sodium Picosulphate may successful clear the retained stool (Table 1.4). However, this risks increasing FI, provoking abdominal pain to such a degree that it undermines the child and family's confidence in the medication that will be so

essential in the maintenance phase (Clayden and Keshtgar, 2003). Suppositories and enemas are effective but disliked to the point of phobia in some children (e.g. Glycerol rectal suppositories). Other medications can include Polyethylene glycol (Klean-Prep, Golytely or Movicol) (Table 1.4). If the child has had to undergo any of the evacuation methods, there is a degree of motivation from child and family to avoid that being needed again. They are likely to start to take regular stimulant laxatives regularly if they have had the rationale for the treatment explained carefully. Once the pattern of defecation has been established, parents are tempted to reduce the medication to see if it is still necessary. Unfortunately, this is likely to provoke a relapse that might even require a repeat of the rigours of the evacuation phase (Clayden and Keshtgar, 2003) (Table 1.4).

But what happens if the patient is not responding to treatment? Firstly, we need to address the issue of compliance of the medication and whether it is being taken regularly or properly. Sometimes it is the intensity of the child's behavioural response to the defecation problems that blocks the effectiveness of the medication regimen. Rewards for overcoming the fear of pots/lavatories in the form of star charts are surprisingly effective especially if the design of the star or token is changed with time and parents encouraged using their creativity in designing the chart (Clayden & Keshtgar). Dealing with the denial and dissociation problem of the older child is more likely to need expert psychological input (Clayden and Keshtgar, 2003, Ludman and Spitz, 1996).

Table 1.4: Medication for symptoms of faecal incontinence (FI) and constipation

Borrowed from: (Clayden and Keshtgar, 2003)

Medication	Advantage	Disadvantage
Lactulose	Increase colonic water and gut flora, acceptable to most children	Appears to lose effectiveness over time, increases 'wetness' of soiling.
Docusate	Emulsifying effect on hard faeces	Increases 'wetness' of soiling, taste often disliked by children.
Liquid paraffin/mineral oil	Increases lubrication of hard stools	Disliked by most children, increases soiling penetration into clothing, theoretical lung aspiration risk.
Methylcellulose Senna	Provides fibre and bulk Provides rectal filling and contraction after a time delay that helps school age children plan their day	Only the tablet form is currently licensed. Provokes abdominal pain and increases soiling if used when large retain stool is in rectum.
Sodium picosulphate	Provokes rectal filling and contraction after shorter time delay than senna	May be difficult to find the ideal time in day for use in school age children
Polyethylene glycol/macrogol (Kleanprep/Movicol)	Flushes unabsorbable water into colon without having to resort to enemas.	High volumes needed to clear large stools may be difficult to drink and require hospital admission for nasogastric tube.
Enema/suppository	Direct immediate action on the loaded rectum.	Provokes fear/humiliation in children and young people unless able to administer it themselves.

1.2.7.2 Advanced treatments when medication fails

When the child has undergone rigorous measures of medication or compliance has become an issue for the patient, other treatment modalities need to be seeked. In children anal dilation or IAS partial myectomy under anaesthetic have been done for constipation because of the perception that there is a degree of hypertrophy and increased activity of the IAS as part of the pathophysiology of the idiopathic megarectum. It is believed that these procedures reduce the anal sphincter tone and allow pain-free defecation. In a double blind randomized controlled trial of sixty children who underwent anal dilation versus no dilation for treatment of chronic idiopathic constipation, no significance was found in outcome with regards to improvement in symptom severity score between these two groups at 3 and 12 months follow up (Keshtgar et al., 2005). Sphincterotomy and sphincter myectomy involves division or excision of upper half of IAS, respectively. The purpose of these procedures is to treat idiopathic constipation in children caused by IAS achalasia in Hirschsprung's disease (Clayden and Lawson, 1976, Loening-Baucke, 1984a). Improvements have been shown in symptoms using these techniques which were attributed to shortening and widening of the functional anal canal after anal stretch and myectomy which allows the faecal bolus to reach the sensory sampling area and be expelled easily. However, one should note the detrimental effects of any procedure that weakens the sphincters may not become apparently for many years.

Newer treatment is botulinum toxin injections in the treatment of chronic idiopathic constipation without risking permanent damage and weakness of anal sphincter (Keshtgar et al., 2007b). Botulinum toxin inhibits the local release of acetylcholine from presynaptic cholinergic nerves (Simpson, 1981) which would cause loss of junctional acetylcholine

receptors and result in loss of excitatory sympathetic input to the IAS tone. Jones et al (Jones et al., 2004) has suggested that the major effect of botulinum toxin on the IAS is through blockade of sympathetic stimulation, which is caused by a reduction in the release of noradrenalin neurotransmitters at the neuromuscular junction. The effect of botulinum toxin in reducing contractions of striated and smooth muscle fibre is focal, transient and reversible without having a systemic effect. Such injections have been used in children for the treatment of constipation after a pull-through operation for Hirschsprung's disease (Langer and Birnbaum, 1997) and in adults for the treatment of anal fissures (Brisinda et al., 1999). Basically, the rationale is that during the period of maximum activity of the toxin in reducing the sphincter pressure, ordinary laxatives and lavatory routines allow the rectum to begin to shrink. By the time the toxin has worn off, the frequency and the completeness of defecation will have improved due to; the partial resolution of the megarectum, as well as the boost to confidence that is produced by symptom improvement. Thus, botulinum toxin achieves the same effect as myectomy, of the IAS done chemically, by reducing the resting sphincter pressure for a short period. Physiological results have indicated that botulinum toxin is equally effective and perhaps less invasive than myectomy of the IAS, yet results only lasts short term (Keshtgar et al., 2007b). Anal plugs have been designed to temporarily occlude the anal canal. It has been shown that these plugs can be useful in patients with impaired anal canal sensation, those with neurological disease and those who are institutionalised or immobilised (Mortensen and Humphreys, 1991).

A surgical treatment offered to children suffering from chronic constipation and FI is the antegrade continence enema (ACE), also known as the Malone antegrade continence enema. The ACE stoma was first used in the 1990s for children with faecal soiling due to neuropathic (neurological) disorders such as Spina Bifida (Yerkes et al., 2003) and is now

also used to treat chronic constipation and FI. The ACE is a catheterisable stoma usually made using the appendix, which allows access to the colon via the abdomen. It is seen as a more pleasant alternative to rectal washouts because it allows easier administration of enemas to promote complete colonic emptying (Malone, 2004). The empty rectum prevents soiling, whilst regular colonic emptying prevents constipation. The ACE stoma has been shown to benefit patients with neuropathic rectum or where there residual sphincter zone is extremely narrow or weak after repair of ARA (Keshtgar et al., 2004b). The procedure is well tolerated and effective in achieving more regular and predictable stools with reduced episodes of incontinence. However, one needs to keep in mind that the ACE stoma is unlikely to be successful unless the psychological factors or fear or dissociation are addressed but the quality of life of the child who is enema dependent is likely improved if spared the apparently endless repetition of the 'per anal' treatments they dread. There has been mixed perceptions about the success of the ACE. Studies have found that the ACE stoma is an effective treatment for constipation and soiling (Yerkes et al., 2003, Searles et al., 2000, Herndon et al., 2004, Hutson et al., 2001, Clayden, 2004). Other studies have not rated the ACE as highly (Rubin and Dale, 2006) due to the instances of repeated treatment failures and they identify that complication are common (stomal stenosis and pain with the enemas) (Dey et al., 2003). The literature also highlights that the ACE is believed to be less successful in the treatment of children younger than five years of age, and those with chronic idiopathic constipation because of increased non-compliancy (Ekmark and Adams, 2000, Dey et al., 2003, Herndon et al., 2004, King et al., 2005). However, studies (King et al., 2005) (Yerkes et al., 2003, Ekmark and Adams, 2000) have found that the ACE stoma significantly improves the quality of life of children with chronic idiopathic constipation.

Biofeedback therapy is based on the principle of operant conditioning which has been shown to improve bowel function and FI (Engel et al., 1974, Rao, 1998). Tuteja & Rao (2004) illustrate the main purpose of this therapy is to: improve the strength of the anal sphincter muscles improve the coordination between the abdominal, gluteal and anal sphincter muscles during voluntary squeeze and following rectal perception and enhance the anorectal sensory perception. After biofeedback therapy, symptomatic improvement has been reported in 70 to 80% of patients with either incontinence or obstructive defecation (Rao, 1998, Norton et al., 2006, Norton et al., 2003, Lunniss, 2007). Yet, evidence is contracdictory as to which patients are most likely to benefit from a biofeedback programme, and there are no clear predictors of success or failure (Whitehead et al., 2001, Norton et al., 2006).

The above is achieved by using a rectal balloon (anal manometry) device, patients are taught to contract the EAS when they perceive balloon distension. The perception of balloon distension can be reinforced by using visual tracings (or in some cases verbal or auditory) of balloon volume and anal pressure, and the procedure is repeated with progressively smaller balloon volumes. Some studies have shown improvement after a year of therapy, yet ongoing controlled studies are needed (Tuteja and Rao, 2004).

A surgical technique that involves the continuous electrical stimulation of the gracilis muscle, which is surgically transposed around the anal canal, is called ‘graciloplasty’ (Rotholtz and Wexner, 2001, Wexner et al., 2002, Williams et al., 2001). Electrical stimulation facilitates anal tone by converting type II (fast-twitch, fatigue-prone) to type 1 (slow-twitch, fatigue resistant) muscle fibres. After having the surgery, studies have found a reduction in the frequency of incontinent episodes in some but not all of their patients

(Wexner et al., 2002, Chapman et al., 2002). A review showed this technique to be associated with 2% mortality and a significant risk of re-operation (Chapman et al., 2002).

Sacral nerve stimulation was first reported for use in patients with urinary difficulties (urinary incontinence) in the 1960s (Habib, 1967). Sacral nerve stimulation (for neuromodulation) is a relatively new technique for treating FI and is used in patients with an intact or repaired sphincter complex (Matzel et al., 1995). It is a less invasive technique and its main advantage is that a temporary procedure can be carried out prior to the final operation to make a reliable estimate of its outcome. The procedure involves placing a percutaneous electrode in a sacral foramen (usually S3) and if a two week test period is successful a permanent pulse generator can be implanted. Recent studies suggest that notable improvement can be achieved with little impact (Matzel et al., 1995, Jarrett et al., 2004, Malouf et al., 2000). Vaizey et al (1999) investigated the efficacy and possible mode of action of short term stimulation of sacral nerves in patients with FI and a structurally intact EAS (Vaizey et al., 1999b). It was found that sacral nerve stimulation does decrease episodes of FI. The actual mechanism as to why this procedure only seems to work in some patients remains unknown. Although, it has been implied that the effect may be mediate via facilitation of striated sphincter muscle function and via neuromodulation of sacral reflexes which regulate rectal sensitivity, contractility and anal motility (Vaizey et al., 1999b). It has also shown changes in sacral nerve reflexes and rectal sensitivity (Vaizey et al., 1999b, Rosen et al., 2001, Malouf et al., 2000). It has also been suggested that sacral nerve stimulation might modulate higher cortical function through alterations in corticoanal exitability (Turnbull et al., 1999) The cortical part of the human anal spincter and pelvic floor can be mapped non-invasively to the motor cortex in healthy subjects, and after stimulation of the the pudendal nerve or lumbosacral roots can produce shorterm increases in

corticoanal excitability (Turnbull et al., 1999). Thus, there is indication that nerve stimulation can modulate motor cortical centres relecvant to anal function, and that this might be important in altering continence behaviour. The cost of this treatment is of great concern because the total cost of the equipment for both temporary and permanent sacral nerve stimulation is approximately £7000 (Kenefick and Christiansen, 2004).

Others measures include excision of the megarectum, when all other treatments have failed and there is clear evidence of the extreme capacity of the rectum (Cheu and Grosfeld, 1992, Lee et al., 2002, Keshtgar et al., 2007a). As a last resort, colorectal resections have been used in the most extreme cases, where patients have failed to respond to care provided my multidisciplinary teams. The technique involves resection of the lower sigmoid colon, which is often almost normal in calibre, to the lower third of the rectum below the peritoneal reflection, without tapering of this part of the rectum. The sigmoid colon is spatulated to match the calibre of the rectal ampulla (Williams et al., 2000). Results have illustrated that resections rarely show a complete and immediate cure in the context of idiopathic constipation (Keshtgar et al., 2004a). Keshtgar et al (2007) investigated 62 children born with ARA, 16 of who had resection of their megarectum. In this study about a half (n = 7) became continent (Keshtgar et al., 2007a).

1.3 PHYSIOLOGICAL ASSESSMENT

Physiological assessment will be briefly discussed in this section with greater detail in Chapter 2.

A detailed interview in collaboration with the patients' clinical history and physical examination is the first step in diagnosing a patients' bowel problem. Yet, to gain a thorough comprehension of the patients' symptoms, physiological assessment is needed for the aetiology of the incontinence or constipation to be deduced, coexisting pathology to be excluded and a decision regarding choice of suitable, rather than empirical therapy to be made on individual basis. For this thesis, we will discuss briefly some of the physiological tests usually undertaken as a form of assessment for FI and constipation. These tests should provide characterization of the sensory and motor disorders responsible for presenting symptoms, and thus promote evidence based guidance of management strategy.

1.3.1 Anorectal manometry

Anorectal physiological investigations play an essential role in the assessment of patients with FI and/or constipation, because they provide an objective measurement of motor and sensory function. Furthermore, it provides measurement of pressures in the anal canal, to evaluate the muscular contraction and relaxation of the sphincters (Azpiroz et al., 2002, Rao and Patel, 1997). It is a widely used and well established tool to specifically assess for:
functional deficits in anal sphincter tone the presence or absence of rectoanal reflexes normal or abnormal rectal sensory function and compliance

The major draw back when using this tool is that lack of uniformity regarding equipment and technique among different institutions. Lack of standardised method makes it difficult to compare between research centres; therefore, each individual institution is encouraged to develop its own control values or, if using normative data from the literature, adopt similar methodology (Gladman, 2005). The main purpose for using this tool is to identify the

functional anal canal length and to record the maximum resting anal canal pressure and voluntary anal squeeze increment. A station pull through (Gladman, 2005) continuous pull through or stationary technique is usually employed.

The IAS contributes approximately 85% of the total pressure in the anal canal and is chiefly responsible for anal continence at rest (Fernandez-Fraga et al., 2002). In patients with FI, the functional anal canal length has been found shorter compared to normal control subjects (Gladman, 2005). Several studies have shown that symptoms of passive FI (unwanted loss of stool without patient awareness) are related to low resting anal tone due to impairment of the IAS (Salvioli et al., 2001) (Read et al., 1984) (Gladman, 2005) (Engel et al., 1995, Vaizey et al., 1997). This is usually due to IAS rupture (e.g. obstetric trauma, iatrogenic injury), but also may be secondary to smooth muscle degeneration. Urge FI (unwanted loss of stool despite active attempts to inhibit defecation) has been related to EAS dysfunction (Chan et al., 2005a). Symptoms of urge or 'stress' FI often correlate with low anal squeeze pressures along with reduced squeeze duration. Although low or poorly sustained voluntary anal squeeze pressures implies EAS weakness, standard manometry alone cannot differentiate between compromised muscle integrity or impaired innervation, or both, as a cause of that weakness. Anal squeeze pressures has been demonstrated to be relatively sensitive and specific for discrimination of patients with FI; nevertheless, the correlation between anal canal pressures and incontinence is not perfect, given the range of normal values and the contribution of various other factors that are crucial to anorectal continence. Resting and squeeze pressures may be normal in idiopathic constipated patients but a few have increased resting internal sphincter activity (Kamm, 1987). Heikenen et al (1999) found in ARA, low anal resting and squeeze pressure were associated with FI (Heikenen et al., 1999).

Relaxation of the cauda anus in response to rectal distension called the 'rectoanal inhibitory reflex' (RAIR) is believed to play an important role in the continence mechanism. The normal RAIR has been found to be most likely mediated by both the sacral cord and myenteric neurones (Kaur et al., 2002). This reflex can be elicited by simply inflating a rectal bag or balloon; the anal response can be measured using a manometric probe (Azpiroz et al., 2002). Abnormal RAIR in response to rectal distension has been described in the literature in patients with FI (Sangwan et al., 1996, Sangwan et al., 1995, Zbar et al., 1998, Sun et al., 1990). It has been found that in FI, there is a greater relaxation of the IAS in response to rectal distension (Kaur et al., 2002) (Farouk and Bartolo, 1993, Duthie and Bartolo, 1992). Presence of a normal RAIR in which distension of a rectal balloon causes relaxation of IAS excludes Hirschsprungs' disease (Keshtgar et al., 2004b). In patients with idiopathic constipation, RAIR has shown to be preserved (Poisson and Devroede, 1983, Bartolo et al., 1988). The clinical significance of the IAS has been brought to our attention with the advent of sphincter saving surgery and has lead to a renewed interest in the RAIR and its role in continence (Smith, 1987). Studies have shown that greater IAS relaxation in patients with FI occurs in response to rectal distension at each volume when compared with both healthy controls and constipated patients (Kaur et al., 2002, Farouk and Bartolo, 1993). The excitatory component of the RAIR is caused by the brief contraction of the EAS which maintains the anorectal pressure gradient. It has been shown that parametric assessment of the RAIR may correlate with FI where a more rapid recovery of the inhibitory wave occurs in patients with demonstrable EAS atrophy (Kaur et al., 2002, Zbar et al., 1998). This suggests that IAS plays a significant role, especially in patients in whom the EAS function is impaired.

1.3.1.1 Rectal sensation

Intact anorectal sensation is fundamental to normal defaecation and continence. In clinical practice, rectal sensation is most easily assessed by simply volumetric distension using intrarectal balloon (Bharucha, 2006) and anal sensation is measured by recording thresholds to electrical stimulation (Roe et al., 1986).

Rectal sensory function is most normally quantified using simple latex balloon distension (Bharucha, 2006, Chan et al., 2005a, Chan et al., 2005b). It is an important factor in the defaecatory stimulus, because distension has been implied to initiate rectal wall contractions, creating the desire to defecate (Denny-Brown and Robertson, 2004, Duthie and Gairns, 1960, White et al., 1940). The technique involves using inflation, which include i) ramp (continual) or ii) intermittent which can be either phasic (volumes injected and then withdrawn) or stepwise (volumes are maintained between inflations) in nature. Thresholds for first sensation, desire to defecate and maximum toleration as volunteered by the patient, are recorded. Alterations of afferent pathways can result in elevated thresholds, 'hyposensitivity' (Gladman et al., 2005) which has been seen in patients with idiopathic FI (Gladman et al., 2003, Hancke and Schurholz, 1987). Decreased sensory thresholds, 'hypersensitivity' may be responsible for the heightened perception of rectal filling and act as an independent trigger of FI (Gladman, 2005). When faecal contents reach the rectum, resulting in the desire to defecate, a mainly voluntary increase in EAS activity will result in delay of defaecation. But, when patients are unable to generate adequate maximal squeeze pressures, this will inevitable lead to incontinence, i.e. urge FI (Engel et al., 1995, Chan et al., 2005c). Those with rectal hypersensitivity typically complain of urgency/urge incontinence and increased frequency of defecation. Association between higher thresholds

for rectal sensory perception has been shown with autonomic neuropathy, congenital neurogenic anorectal malformation (spina bifida, Hirschsprungs' disease, myelomeningocele) and functional and somatic alterations of the rectal reservoir, such as megarectum and descending perineum syndrome (Hancke and Schurholz, 1987). Both abnormalities have been reported in some patients with FI (Tuteja and Rao, 2004, Lubowski and Nicholls, 1988, Gladman et al., 2003, Vasudevan et al., 2007, Rogers et al., 1988). Rectal sensation is known to be impaired in patients with a megarectum (Gladman et al., 2003) and constipation (Vasudevan et al., 2007); it is also abnormal in children with idiopathic constipation (van der Plas et al., 2000).

1.3.1.2 Rectal Compliance

The rectum has elastic properties that allow it to maintain low intraluminal pressure, even if the volume is large (Arhan, 1976). Compliance is the pressure/volume relationship during rectal distension. This can be measured by injecting air into the intrarectal bag and measuring the pressure or using a barostat that distends the rectum to given pressure levels and determines the volume at each distending step (Azpiroz and Malagelada, 1987, Whitehead and Delvaux, 1997, Gladman et al., 2005, Bharucha, 2006). Intra-balloon (intrarectal) pressure and the balloon volume must be monitored simultaneously; compliance is calculated as change in volume divided by change in pressure ($\Delta V/\Delta P$) over that part of the pressure-volume curve between first sensation and maximum toleration. Changes in compliance can affect continence. If compliance is decreased, smaller volumes of stool can cause increased pressure and impair rectal storage function (Cooper and Rose, 2000). In a

proportion of patients with FI, the rectum has been shown to be poorly compliant (i.e. the rectal wall is 'stiffer', primarily related to urgency (Gladman, 2005). Studies have shown in constipated patients to have increased rectal volumes at constant defecation urge and maximum tolerable volume (Gladman et al., 2005, Gosselink et al., 2001). When increased volume tolerance and compliance are found in a patient with FI, an underlying constipation contributing to the incontinence should be suspected (Rasmussen et al., 1990).

1.3.2 Endoanal Ultrasonography

The imaging modalities currently used to examine the anal sphincter complex and levator ani muscle are endoanal ultrasonography (EUS) and endoanal magnetic resonance (EMR) (Fukata et al., 1997, Nievelstein et al., 2002, Nielsen et al., 1993, Hussain et al., 1995, deSouza et al., 1997, Keshtgar et al., 2004b, Keshtgar et al., 2008). EUS is for the evaluation of sphincter integrity and now provides the cornerstone for clinical investigation of patients with FI (Emblem et al., 2007, Keshtgar et al., 2008). It has also been suggested that endosonography is a validated technique that can be applied with confidence to children with repaired ARA (Keshtgar et al., 2007a).

Given the predominately cylindrical nature of the anal structures, imaging is best suited to a 360 degree axial view obtained at right angles to the lumen, and this is achieved using a 10-megahertz (MHz) transducer attached to a mechanically rotating endoprobe. Although operator-dependent, sensitivity and specificity approach 100% for the identification of anatomical defects if carried out by an experienced research doctor. Structural damage to either the IAS or EAS can be identified clearly, as well as degenerative changes in the smooth muscle.

In incontinent patients, EUS has revealed that obstetric trauma followed by anal surgery, are the major risk factors. Of those physiological and imaging techniques available for the evaluation of patients with FI (Tankova et al., 2001) and patients with ARA (Jones et al., 2003, Athanasakos et al., 2008, Fukata et al., 1997, Emblem et al., 2007, Emblem et al., 1997) ultrasound is the test most likely to influence a change in management. Keshtgar et al (2004) investigated children with chronic idiopathic constipation using endosonography and found that the thickness of IAS correlated with duration and severity of symptoms, size of megarectum, amplitude of rectal and IAS activity and age of children (Keshtgar et al., 2004b). Based on ultrasonographic findings (in conjunction with other test results), rational treatment can be planned, including the selection of patients who may benefit from surgery.

A sphincter defect may be diagnosed on the basis of discontinuity, thinning and/or scarring of the sphincters, and/or asymmetry of the anal canal (Sudol-Szopinska and Jakubowski, 2002). The 3D modification of 2D endosonography offers a longitudinal perspective and has improved the appreciation of spatial relations in the anal canal (Gold et al., 1999) extending the utility of 2D endosonography. The interpretation is less operator dependent, and the data are able to be stored for review. Several studies have now examined the application of 3D endosonography in healthy volunteers (Knowles et al., 2008) and in the assessment of patients with FI (West et al., 2004, Gold et al., 1999).

1.3.3 Electrophysiology

The pudendal nerve supplies sensory fibres to the anoderm of the distal anal canal and motor fibres to the EAS, and arises from the sacral roots S2, S3 and S4. It has been shown

previously that in healthy volunteers, anal sensory function, but not distal rectal sensitivity, could be blunted by distal pudendal nerve blockade, supportive of separate distinct afferent innervation (Vasudevan et al., 2007) (Chan et al., 2005b). The pudendal nerve terminal motor latency (PNTML) is a measurement of the conduction time from stimulation of the pudendal nerve at the level of the ischial spine to the evoked EAS contraction. This is achieved using a disposable glove-mounted stimulating and recording electrode (St Mark's pudendal electrode) connected to a suitable recorder. Prolonged latencies are suggestive of pudendal neuropathy and have been demonstrated in incontinent patients who have suffered obstetric trauma, have excessive perineal descent or a recognised neurological disorder (Hill et al., 2002) (Gooneratne et al., 2007). Although, 'grouped' data show that incontinent patients with bilaterally prolonged PNTMLs have reduced anal squeeze pressures compared to controls, thus supporting the concept that neuropathic process impairs EAS function, the sensitivity and specificity of this test is poor; many patients with delayed latencies have squeeze pressure within the normal range and vice versa (Gooneratne et al., 2007, Hill et al., 2002). This lack of agreement is likely to be due to methodological limitations:

- PNTMLs increase with age, independent of continuous status
- The PNTML reflects the function of the fastest conducting motor fibres, and thus normal latencies may be recorded in a damaged as long as some fast-conducting fibres remain
- The test is operator-dependent and may be technically difficult to perform in some patients.

Thus, recording of PNTML may contribute little to the management of individual patients with FI and its routine use should now be questioned. It has been found that unilateral pudendal neuropathy is a common abnormality in individuals with FI and has been significantly associated with both attenuated resting pressure and squeeze increments (Gooneratne et al., 2007). Yet, unilateral prolongation of PNTMLs is probably without clinical significance.

1.3.4 Evacuation Proctography

Evacuation proctography (defecography) is a radiographic test (contrast material is placed into the rectum), whereby anorectal anatomy and pelvic floor motion are recorded on video and the subject is asked to rest, squeeze, cough or expel the contrast (Gladman, 2005, Andrews and Bharucha, 2005) It is during these manoeuvres, that the anorectal angle and the position of the anorectal junction are shown. Such observation allows the identification of excessive perineal descent, internal rectal intussusceptions, rectocoele, sigmoidcoles, or enteroceles (Andrews & Bharucha). Passive (overflow) incontinence or post-defecation leakage may occur secondary to disorders of rectal evacuation (Gladman, 2005, Ferrante et al., 1991).

1.3.5 Transit Studies

Methods used to measure gut transit may be classified as radiological, calorimetric, particulate, chemical, and isotopic (Hinton et al., 1969). The first description of methodology, employing radiopaque polythene cylindrical pellets, was that of Hinton *et al.* (Hinton et al., 1969) who measured the disappearance of 20 such markers from the gut and

their appearance in the stool by serial radiographs. They were able to establish that this marker was not absorbed, and was completely recoverable in the stool. Normal ranges for both men and women have subsequently been determined, with abnormal transit defined as retention of more than 20% of markers on a single plain radiograph at 5 days (Bassotti et al., 1988)

In patients in whom 'constipation' and incontinence coexist, transit studies provide objective confirmation of subjective complaints of infrequent defecation. Assessment of total and segmental colonic transit time using radio-opaque markers is a non-invasive method which provides information about colorectal motor function (Arhan et al., 1981, Chaussade et al., 1989, Metcalf et al., 1987). Furthermore, this technique has been used to localise a delayed transit in the colon and to evaluate the response to treatment (Benninga et al., 1996, Chaussade et al., 1989, Papadopoulou et al., 1994). It has been widely used in children with chronic constipation (Benninga et al., 1996, de Lorijn et al., 2004, van der Plas et al., 2000, Gutierrez et al., 2002). Some investigators have shown a good relation between symptoms of constipation and colonic transit time in adults (Glia et al., 1999, Verduron et al., 1988). However, for accurate assessment of segmental colonic transit, radionuclide scintigraphy is required.

1.4 PSYCHOLOGY AND CHRONIC CONDITIONS

1.4.1 Definition of Chronic Conditions

Generally, definitions of chronicity vary because they are derived from different conditions, severities, causalities, treatment settings and psychosocial backgrounds. Thus, definitions of chronic conditions should remain flexible yet comprehensive to cater for a variety of conditions. However common factors may pertain across different conditions; the most obvious being that the condition does not remit. A universal definition will not necessarily cater to all conditions. With this in mind, it is vital to specify definitions used by medical professionals and/or institutions and justify their use in particular situation. This will minimize confusion and complexity when discussing and comparing between different chronic conditions. The National Health Interview Survey conducted in Britain defined that chronic conditions included all problems lasting longer than three months (Pless, 2008). Although a complete or almost complete cure is now available for many children with ARA some children have to learn to adjust with some degree of ongoing illness. Thus, this definition seems reasonable and useful when later discussing the long-term outcomes for children with ARA in this thesis.

Conceptualisation of chronic illness has been generally based on categorical, non-categorical models and a mixture of the two. The 'categorical' model concentrates on the adaptations for the child/parent/family with one specific chronic condition and its association with specific social or emotional functioning (World Health Organisation, 1982). This approach characteristically groups chronic conditions in terms of specific conditions, such as asthma

or haemophilia and/or body system impairment (such as metabolic, hearing, cardiac defects). Pless and Perrin (1985) (Pless, 1985) and Davis (1993) (Davis, 1993) have each discussed the failure of categorical diagnostic approaches to consistently predict psychological outcomes in children with chronic conditions and their families. The non-categorical approach (Pless, 1975, Stein and Jessop, 1982) proposes that there are commonalities between different chronic conditions. Furthermore, it recognizes that it is the natural history of the condition and its severity, and not its specific characteristics that is significant in the risk of psychological maladjustment. This approach emphasizes:

> *". . . that children face common life experiences and problems based on generic dimensions of their conditions rather than on idiosyncratic characteristics of any specific disease entity"* (Stein and Jessop, 1982 p. 354) (Stein and Jessop, 1982).

Yet, rather than accepting an either or approach to defining a chronic condition a 'mixed' or 'partial' or 'modified' categorical approach has been suggested (Pless, 1985) (Perrin et al., 1993) (Thompson, 1996). This mixed approach involves a combination of the categorical and non-categorical models:

> *". . . there are likely to be both illness-specific and generic approaches of importance to adaptation of children and families to chronic illness and that it is premature for the field to adopt solely a categorical or non categorical approach"* (Thompson & Gustafson p. 5 (Thompson, 1996).

This thesis has adopted this frame of thinking when talking about a chronic condition because it recognizes variations between diagnostic categories yet continues to appreciate the commonalities across multiple conditions.

1.4.2 Perspective of the chronic condition in paediatrics

Chronic illness poses considerable stress for children and adolescents. Epidemiologic surveys show that children and adolescents with chronic disease are at a significantly greater risk than their healthy peers of developing major psychosocial problems (Cappelli et al., 1989).

One of the main areas this thesis will focus on will be the psychosocial functioning of the adolescent and adult living with ARA. This involves accepting the physician/s, parent/s and/or childs' perception on the impact of the condition. Analysis and comparisons between research studies becomes difficult when assessing psychosocial adjustment in children with chronic conditions. This is because levels of adjustment vary depending on the informant. Research studies centred on parental responses generally reveal more maladjustment than those based on teacher or physician reports, or those indicated by objective measures (Kashani et al., 1988). Generally, it is easy for adults to make assumptions what a child is thinking because they have passed the period of childhood. Yet, this frame of thinking may lead adults to impose an adult view of the world instead of a childs' (Waksler, 1986).

Children's' views on illness are neglected or their perception of illness is understood within the context of stage developmental theories (Bibace and Walsh, 1980). Piaget's (1929) general theory of cognitive development proposes a child's developmental understanding of their body and illness as being within a systematic and predictable order of stages. Concepts of illness are derived from a childs' acquisition of informal reasoning (Burbach and Peterson, 1986). Thus, the majority of children of a particular age will have grasped a level of understanding of illness. Piagets' stages propose that the young child (4 to 11years) is

able to make sense of the world with limited knowledge acquired through direct experience and with concrete basis. At this stage, children lack the ability to generalize to related experiences and to understand the variations that can exist in one situation. Yet, with increasing age thinking becomes more mature and logical (i.e. with reason about real objects or events). As children reach adulthood they are able to rationalize, think in abstract terms and explore problems systematically.

The child may not hold specific knowledge about their condition; however they are often aware of their condition and make their own sense of it. The staged development paradigm is useful for making sense of a childs' growing awareness and understanding of their body and illness. However, it is not a substitute for listening to a childs; own view and feelings about their experience with the condition. It is therefore important to explore each childs' unique understanding. For example, children who have experienced a significant illness in their life either establish less, equally, or more advanced illness concepts compared with children who have none/little experience of illness (Burbach and Peterson, 1986).

This thesis will be focusing a great deal on adolescents with a chronic illness. In the care of adolescent patients, all aspects of clinical medicine are played out against a background of rapid physical, psychological and social developmental changes. For chronically ill adolescents, the development problems normally associated with adolescence are no doubt magnified (Boice, 1998). An overarching concern relates to social acceptance. An issue for all adolescents, this becomes more serious for those with chronic illnesses, who may spend a great amount of time isolated from other teenagers or in the company of adults.

1.4.3 Anorectal anomalies and psychosocial functioning

"For a child, if you are labelled 'difficult', without those around having the knowledge as to why you are being 'difficult', it creates severe social problems for you. You may have been considered 'difficult' before you developed the soiling problem, be that as it may be, but once you have a soiling problem, you are likely to be a whole lot more 'difficult'. Being 'difficult' implies that it is somehow your fault" (Buchanan, 1992).

The above quote, addresses the problems involved when dealing with such a taboo subject as ARA and the ongoing symptoms experienced. As one would expect, when surgical treatment is carried out on the paediatric patient, attention is focused on the immediate outcome. More often than not the immediate outcome for ARA is satisfactory, with improvement of the symptoms, treatment of the anatomical defect, a quick return to a normal pattern of life and little, if any doubt concerning the ultimate prognosis. Adolescents and adults with ARA who continue to have problems are particularly difficult group to treat. They have undergone years of disruption to schooling and normal social interactions, as well as medical and surgical interventions which have failed them. They may understandably be unwilling to undergo further invasive evaluation and be sceptical about the efficacy of alternative or newer treatments. Additionally, a patient with ARA there are no obvious disfiguring or physical signs (e.g. as you would with someone who has Down's syndrome) to know they are ill. Although a discreditable condition allows an individual to appear to be without illness, it becomes necessary to decide how much to reveal to strangers or new acquaintances, which causes anxiety, especially when it comes to talking about issues such as FI and constipation. In patients with ARA, often not much thought is given to the

possibility that problems may develop in the long-term, and that consideration should be given to the question: 'What happens to a paediatric surgical patient when adulthood is reached?'

Several studies have found more psychosocial problems among children and adolescents with a chronic condition in comparison to children without a chronic condition (Eiser, 1990, Gortmaker, 1990, Lavigne, 1992, Varni et al., 1992, Wolman et al., 1994). Other studies have found no difference (Orr et al., 1984, Kellerman et al., 1980, Cappelli et al., 1989, Logan et al., 1990). Possible reasons for such psychosocial problems include physical limitations associated with the condition, severity of the condition, difficulties adhering to long-term medical treatments, high rates of school absence, limited opportunities for socialisation, feelings of helplessness, depression and increased dependency, and self-consciousness (Bennett, 1994).

Schlenk et al (Schlenk et al., 1998) found that patients with incontinence, chronic obstructive pulmonary diseases, acquired immunodeficiency syndrome and fibromyalgia have substantially lower quality of life. Faecal incontinence has had the greatest impact on the overall psychosocial functioning of children with ARA. This is because soiling is embarrassing and is considered shameful and socially unacceptable. An accurate measure of continence is often difficult to obtain due to definitional variation and failure to make a clear distinction between occasional soiling and significant soiling. Faecal incontinence, however defined has been found to be associated with poorer psychosocial functioning and parental criticism (Catto-Smith et al., 1995, Damon et al., 2004, Diseth, 1995). This relationship between psychosocial function and severity of physical impairment is consistent with other

studies of congenital malformations (Heller et al., 1985, Diseth, 1995, Spurkland et al., 1993).

Varying degrees of constipation and FI in patients with ARA have profound effects on quality of life as illustrated in our literature summary (Table 1.5) (Ditesheim and Templeton, 1987, Ludman et al., 1994, Rintala et al., 1992, Diseth et al., 1998a, Diseth et al., 1998b). ARA has shown to have an impact on the patients' day to day activities from school/work, family, participation in sport, 'sleepovers' and social life (Hassink et al., 1994, Hamid et al., 2007, Poley et al., 2004). Hamid et al (Hamid et al., 2007) found issues such as, loss of body image, teasing from peers, offensive odour and pre-occupation with toileting some factors which affect patients with ARA. On the contrary, others have found that children with ARA have significantly worse bowel function than their peers, depending on the type of lesion, yet, despite this, their quality of life is not significantly impaired (Ludman and Spitz, 1996, Ludman et al., 1994, Goyal et al., 2006, Iwai et al., 2007, Bai et al., 2000). Ludman and Spitz (1996) (Ludman and Spitz, 1996) found that the psychological problems, though high, were not related to the level of FI and that young incontinent girls tended to have statistically significant psychological maladjustment. Sexual issues also may produce anxiety, yet often ignored or denied when during a clinical consultation. It has been revealed that sexual problems such as erectile dysfunction and ejaculatory incompetence are common in male patients with high and intermediate type, ARA with sacral anomalies (Iwai et al., 2007, Konuma et al., 2006, Hamid et al., 2007).

It may be expected that the more severe the condition is, the greater the probability of psychosocial difficulties. Surprisingly no relationship between severity and problems with psychosocial adjustment has been found (MacLean et al., 1992) (McAnarney et al., 1974)

(Perrin et al., 1989). In fact more emphasis is placed on the presence of the condition rather than its level of severity. However, it has been found in adolescence with ARA that had psychological morbidity tended to be more severe as the degree of FI worsened (Funakosi et al., 2005, Diseth et al., 1998b). While others found no association with severity of the condition or symptom to psychological functioning (Ludman and Spitz, 1996)

Morbidity has been found to coexist in patients with ARA even after surgical repair, resulting in significant emotional and social difficulty for both the patients and their families (Table 1.5) (Ludman and Spitz, 1996, Hamid et al., 2007, Ditesheim and Templeton, 1987, Diseth and Emblem, 1996, Hassink et al., 1994, Ginn-Pease et al., 1991, Ludman and Spitz, 1995) Children with chronic conditions or disabilities have psychosocial maladjustment, behavioural problems and more difficulties in everyday functioning than healthy children (Athanasakos et al., 2006). Hamid et al (Hamid et al., 2007) found 80% of their patients with ARA to have one or more forms of psychological morbidity, including feedings of extreme anxiety and embarrassment, depression and low self esteem. It has been suggested that bowel dysfunction is one of the most important factors that influences the level of depression of children with ARA (Table 1.5) (Amae et al., 2008, Hamid et al., 2007). Funakosi et al (Funakosi et al., 2005) found that in children with ARA, depression tended to be more severe as the degree of FI worsened as the child reaches adolescence, yet the association failed to reached statistical significance. Clayden (Clayden, 1992) has suggested that a childs' physical development may be disturbed by disordered bowel function and that faecal soiling has a critical effect on psychosocial factors such as self-esteem and confidence (Clayden, 1992). This is to our own data contrast (Athanasakos et al., 2006) that children and young adults with Hirschsprung's disease have minimal psychiatric morbidity, but experience condition-specific psychosocial problems (despite significant impairment of FI).

Hope has been defined as an expectation of positive events (Nunn, 1996b). Nunn (Nunn, 1996b) suggested that differences might exist between individuals in the need for perceived control in order to feel positively about the future. Children at any age may have difficulties in perceiving their future. This can have specific implications for children with a chronic condition when trying to cope with the condition and/or encourage adherence to treatment regimens. From an adolescents' outlook, there may be a greater comprehension of the long-term of their condition – specifically the realisation that they will have if for the rest of their lives. Existing limitations become more obvious and may place greater emphasis on future choices (such as career) and ambitions, such as living independently or having a family. Thinking about what one 'can do' and 'can not do' in the future, may cause the child to fear, resent or become perplexed about their purpose in life. More so, adolescents will become aware of the sole responsibility for their condition as they reach adulthood (rather than parents or doctors) which could produce a deep sadness and despair, a sense of mourning for the loss of the perfect 'picture' or future. Cappelli et al. (Cappelli et al., 1989) suggested that adolescents with chronic illness (such as diabetes) are in fact not at greater risk of developing psychopathology, yet becoming more concerned about their health and future. There is currently limited literature investigating personal hopefulness in children with ARA to date. Despite the reported high level of psychosocial morbidity found in patients with ARA, Hamid et al (Hamid et al., 2007) found their level of hopefulness of the future to be positive (Table 1.5). Similar findings have been found in patients with Hirschsprung's Disease (Athanasakos et al., 2006).

Coping consists of both emotional and cognitive features (Holden, 1995). Discovering what children with chronic conditions find troublesome and recognising the strategies and support

networks they use to cope with these stressors are vital for future clinical intervention. Studies have indicated that both environmental and biological factors facilitate effective coping (Compas and Boyer, 2001, Sinnema, 1991, Sharrer and Ryan-Wenger, 1995, Tyc et al., 1995) Factors which determine the way a child copes with a chronic condition includes their conceptualisation of the condition, characteristics of the condition (such as life threatening, ongoing treatments) and adjustment of others in their environment (i.e. parents, relatives, peers, medical professionals). Ludman and Spitz (Ludman and Spitz, 1996) found that children with ARA will be able to adapt themselves to society. However, other results indicate that intrinsic depression became more severe in adolescence and suggested that some patients may not be able to integrate themselves into society (Funakosi et al., 2005). Boekaerts and Roder (Boekaerts and Roder, 1999) found children with chronic conditions use coping strategies in relation to common stressors that appeared to be similar to those of healthy children. Boyd and Hunsberger (Boyd and Hunsberger, 1998) proposed that chronically ill children who were frequently hospitalised became adept at recognising and implementing a repertoire of coping strategies. Specifically, using family and friends as supportive resources and/or gaining knowledge of their condition from supportive health care professionals.

Adolescents experience numerous changes; coping with a chronic condition adds yet another dimension to their lives. Adolescents with ARA have often adopted coping strategies to manage their chronic disability, which has nevertheless interrupted their social, emotional, physical and academic growth and development (Ludman and Spitz, 1996). Ludman and Spitz found that children aged 8 to 11 years with FI used denial as a coping strategy to handle difficult situations

Table 1.5: Summary of the literature found in patients with anorectal anomalies investigating psychosocial and quality of life measures

Author	Year	N	Age range (years)	Psychosocial Measures	Who filled out questionnaire?	Comparison groups
Amae et al	2008	66	0-16	• Kovacs Children Depression Inventory – CDI: 6-16 years. • Symptom scores Assessed mothers of patients: • Spielberger's' State-Trait Anxiety Index - STAI • Zung's self-rating depression scale (SDS)	Parent and child filled out questionnaire together	None
Iwai et al	2007	29	20-40	• Bowel function assessed by Japanese Study Group for ARA • Interview about social and sexual function	Patient with ARA – questionnaire posted	None
Hamid et al	2007	84	3-27	• Athanasakos et al: The Hirschsprung's Disease Family Impact Questionnaire modified for ARA included: questions on continence, quality of life and level of hopefulness (Athanasakos et al., 2006)	Parent and child filled out questionnaire together – questionnaires posted	None
Goyal et al	2006	80	4-18	• Pediatric Quality of Life Inventory (PedsQL 4) • Functional outcome questionnaire - non standardised for assessment of continence.	Child filled out questionnaire during outpatient visit with parent or posted.	20 healthy controls (4.5-14.8 years).
Poley et al	2005	286	1-51 (ARA) 1-42 (CDH)	• Health related quality of life (HRQol/TAIQOL) for children 1-4 years of age including symptom and quality of life subscales. • SF-36 (> 16 years)	Parent and child filled out questionnaire together where questionnaire was posted.	Congenital diaphragmatic hernia (CDH)
Funakosi et al	2005	50	0-16	• 7-16 years Children's Depression Inventory (CDI) Assessed mothers of patients: • Zung's self-rating depression scale (SDS) • Mothers had the Spielberger's State Trait Anxiety Index (STAI)	Parent and child filled out questionnaire together with a child psychiatrist.	None
Bai et al	2000	71	8-16	• Self-structured disease impact questionnaire • Child Behavior Check List (CBCL).	Not known	None

Author	Year	N	Age range (years)	Psychosocial Measures	Who filled out questionnaire?	Comparison groups
Hassink et al	1998	109	1-18	• Nijmegen Questionnaire on Chidering Situations (NQCS) • Child Behaviour Checklist (CBCL). • Teachers Report Form (TRF)	Parents were interviewed about day to day life with their child and questionnaires sent home.	None
Ludman et al (Same sample of patients were used for both papers).	1996 2000	160	6-17	Semi-structured interviews carried out by clinical psychologist including : • Child Assessment Schedule (CAS) • DSM-III-R • Depression self-rating scale (DSRS) • Chid Behaviour Checklist (CBCL) • 30 item General Health Questionnaire • Kelly score (faecal continence) • Teachers Report Form (TRF)	Child was separately interviewed (semi-structured) from parents. Parents were also interviewed (semi-structured).	None
Diseth et al	1998	17	12-20	Child interviewed (semi-structured) separate from parents: • Wingspread classification for continence scoring • Flatus continence assessed using analogue scale • Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) • Youth Self-Report (YSR) • Children's Global Assessment Scale (CGAS) Parents interviewed (semi-structured) separate from child: • Child Behavior Checklist (CBCL) • Parental Account of Children's Symptoms (PACS) • Chronic Family Difficulties (CFD)	Child was separately interviewed (semi-structured) from parents. Parents were also interviewed (semi-structured).	Hirschsprung's Disease (n=19; 10-20 years)

Author	Year	N	Age range (years)	Psychosocial Measures	Who filled out questionnaire?	Comparison groups
Diseth et al	1996	33	12-20	• Clinical and anorectal manometry • Wingspread classification for continence • Flatus continence assessed using analogue scale • Child Assessment Schedule (CAS) • Child Behavior Checklist (CBCL) • Youth Self-Report (YSR) • Children's Global Assessment Scale (CGAS) • DSM-III-R	Adolescent assessed on their own in a semi-structured interview	None
Rintala et al	1992	83	Mean age 35 years (range not mentioned)	• Fecal incontinence – Holschneider Score • Interviewed patients about overall well being including social problems and difficulties in sexual life.	Patient with ARA Healthy volunteer	78 healthy controls (Mean age 33.4 years) without history of anorectal surgery

1.5 KNOWLEDGE GAPS

1.5.1 Summary and current limitations

As discussed in great detail in this chapter, there is extensive literature on the bowel difficulties that patients with ARA experience (Zia-ul-Miraj and Brereton, 1997, Hettiarachchi et al., 2002, Rintala et al., 1992). We know that despite surgical advances and advanced treatment modalities, voluntary bowel control is frequently poor following surgical care with high rates of FI, and also constipation after all grades of reconstructive surgery (Ong and Beasley, 1991, Rintala et al., 1993b, Rintala and Lindahl, 1995). Furthermore, there remains conflicting views as to whether symptoms of constipation and FI in patients with ARA have profound effects on quality of life. Yet, despite various perspectives in the literature, morbidity has been found to coexist in patients with ARA even after surgical repair, resulting in significant emotional and social difficulty for both the patients and their families.

Currently, there are obvious limitations in the literature when it comes to discussing about quality of life and psychological morbidity in patients with ARA. Firstly, the majority of questionnaires administered to access bowel and psychosocial functioning, included parental/familial influences. Such influences will have an impact on how the child or adolescent views their condition and may alter their true perspective of their experience. The child or adolescent involved is the one who is living with it and is of a different age and developmental stage in comparison to their parents. Thus, questionnaires need to be administered in a way that encourages the child or adolescent to answer the questions in relation to their condition from their

experience and make them feel comfortable that no one will judge their answers. Thus posting questionnaires or asking patients to fill out questionnaires with others will encourage input from others and possibly alter their answers. Secondly, in order to comprehend how poor patients with ARA are doing in terms of continence and psychosocial functioning, we need to use control groups to draw comparisons which few authors have done so far (Table 1.5).

Lastly, our knowledge about the pathophysiological mechanisms involved in patients with ARA remains limited. Traditionally, sphincter dysfunction was considered as the sole contributory factor to FI. However, patients without a history of ARA and with an anatomically intact and normal functioning sphincter complex can also experience episodes of FI, indicating that there are other pathophysiological mechanisms contributing to their symptoms (Lunniss, 2007, Williams et al., 2001). It is now clearly recognised that disturbances of 'extra-sphincteric' sensorimotor function are also crucial to the development of symptoms of FI (Bharucha et al., 2005, Williams et al., 2001, Lunniss, 2007, Salvioli et al., 2001) Yet, currently, our knowledge of the pathophysiology of FI relates almost exclusively to information gained in adults with acquired symptoms (i.e. usually post-obstetric or following anal surgery). Thus, the pathophysiology of FI in congenital ARA, however, remains unclear and our understanding rudimentary. Notably, the importance of extra-sphincteric mechanisms has not been adequately addressed and is a current limitation.

1.5.2 Aims and hypothesis

The two main aims of this study were to determine the;

- impact that FI and constipation has on psychosocial functioning in the context of ARA and
- pathophysiological mechanisms that might contribute to poor bowel function in patients with ARA.

Furthermore, two control groups were introduced to our study. These included:

Group 1 (Positive disease controls): Idiopathic constipation (IC) refers to an incapacity to regularly pass stool, where the cause remains unknown. It is one of the most common bowel movement disorders among children and adolescents. This group shares similar symptoms of constipation and FI to our ARA group but are a functional disorder with no anatomical defect as in ARA.

Group 2 (Negative disease controls): Patients who have been diagnosed with appendicitis and have had surgery (appendectomy). They have been treated for a condition entirely separate from the area that our patients ARA and IC individuals share in common.

We hypothesized the following:

- There would be a positive relationship with type of ARA (high, intermediate, low) with symptom scores (i.e. FI, constipation)

- Symptom scores assessing constipation and FI would be major determinants for poor psychosocial functioning.
- Patients with ARA would have poorer symptom and quality of life scores, mental state and coping strategies in comparison to the control groups which have normal anatomical anorectum with intact sphincters and associated structures.
- Patients with ARA would represent higher levels of neuroticism and introversion in comparison to the control groups.
- There would be a relationship between symptom scores and the structural/function integrity of the anal sphincter and supra-sphincteric anatomy.
- The pathophysiology in ARA would involve extra-sphincteric mechanisms.

CHAPTER 2

MATERIALS &

METHODS

2.0 MATERIALS AND METHODS

2.1 INTRODUCTION

This chapter provides a detailed description of the methodologies undertaken to measure the impact of FI and constipation have on psychosocial functioning in the context of ARA and the pathophysiological mechanisms that might contribute to poor bowel function in patients with ARA. General methodology relating to the preparation of the thesis and recruitment and selection of patients for participation in this study will be included. Control and comparison subjects are described. The methodology of gastrointestinal physiological investigations is discussed in detail. Standardised psychiatric measures have been reviewed in this chapter in relation to its theoretical background, development and use in other research samples. Each instrument used has been discussed in relation to its purpose, validity, reliability and why it was chosen for this research project.

2.2 ETHICS APPROVAL

Ethics relates to a set of rules or strict criteria as to whether or not the research study conforms to existing guidelines set out by government bodies, professional associations or local committees (Jackson, 2000). The research protocol was firstly peer reviewed prior (Appendix - A) to ethical approval (Appendix – B). The use of patients and healthy volunteers was approved by the East London and the City Health

Authority (ELCHA) Research Ethics Committee. The following ethics committee references cover the body of work contained within this thesis. ELCHA no: 07/Q0605/2 (Appendix – B).

2.3 ARA PATIENTS

2.3.1 Recruitment

Patients for study were recruited by written invitation from the author, or directly approached in person at times of clinical presentation to the Royal London Hospital (Barts & The London NHS Trust) and St Thomas' Hospital (Guys, St Thomas' and King's NHS Trust). All clinicians in care of patients with ARA, were informed about our research project and criteria, and were asked to inform the author when a patient presented to the hospital. In order to gain a representative of the ARA population as a whole, a request was made to medical records to both hospitals, to code for any patients who have been diagnosed with 'anorectal malformation/anomalies', 'imperforate anus' and 'ectopic anus'. This allowed 'all comers' to become involved in our research project rather than selecting patients with poor bowel function.

Since ARA is a rather rare congenital condition, we were unaware of how many possible patients could be recruited. Thus, an estimate number was calculated based on information provided from surgical colleagues, and from lists of patients used in previous research audit studies of this condition. Altogether, a number of 80 patients were found between the two institutions. We consulted a statistician (Fiona Warburton) from Research and Development from Queen Mary University of

London, who performed a power calculation in order to see how many patients were required for recruitment (was concluded to be 50 patients), which was based on the psychiatric tools we would be analysing and the availability of patients that could be attained.

2.3.2 Selection

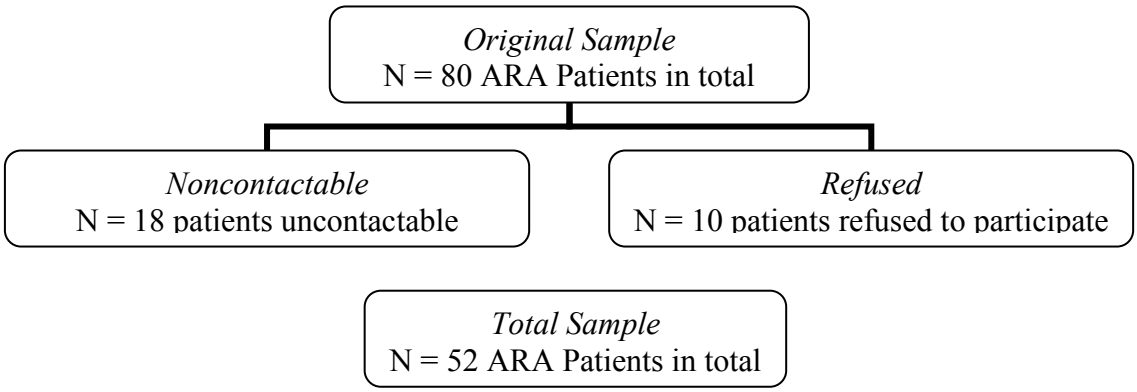
Patients with ARA were initially contacted by a letter inviting the patient (Appendix – C) to our study which was either posted or given in person (i.e. during their clinic visit) along with a Patient Information Sheet (Appendix – D). The letters included the purpose of the study, important aspects of their involvement and requesting their participation followed. Patients and parents/carers (especially if the patient was under the age of 16 years) were able to call the medical researcher in charge to answer any enquires they had. They were assured anonymity at all times and were under no circumstances pressured to be part of the study. Every effort was made to ensure the smooth and consecutive recruitment of eligible subjects which was succeeded with good rapport and patience.

Written consent (Appendix – E) was received from patients. Ten patients did not wish to participate in this research due to emotional burden, time constraints (due to work or school or travel commitments) or language barrier (however, interpreters were provided if needed.

2.3.2.1 Inclusion criteria

Patients who have been diagnosed and/or surgically treated for ARA between 1963 - 1996 were included. Patients will be divided into groups based on clinical (using symptomatic scores), physiological and psychosocial outcomes. The original ARA sample (Figure 2.1) comprised 80 patients aged between eleven and forty-five years at the time of our research follow-up and resided in United Kingdom. Eligibility criteria excluded patents with limited medical history, no contact details and who had died. Out of 80 patients with ARA, 18 (23%) patients could not be located, one who was deceased and died due to Hirschsprung's disease and associated cardiac defect (Figure 2.1).

Figure 2.1: Selection of total population sample in anorectal anomalies



Patients who have been diagnosed and/or surgically treated for ARA between 1963 - 1996 were included in this study. Patients were included on the basis of:

i) ARA is defined as a range of congenital conditions ranging from a slight malposition of the anus to complex anomalies of the hindgut and urogenital organ reconstructed anorectal anomaly.

ii) Patients were classified according to the Wingspread international classification (as mentioned in Chapter 1).

iii) Patients who underwent reconstructive surgery for ARA.

iv) Both symptomatic and asymptomatic patients were included in order to gain a representative population sample.

v) Age range was between 11-45 years of age. This age group will allow us to investigate a widespread of patients from all ages and thus gain a preview of how these patients cope after surgery in terms of their bowel function and everyday life.

2.3.2.2 Exclusion criteria

Patients were specifically excluded for the following:

i. Downs/Autism or developmental delay: the main reason for this exclusion was due to the several questionnaires that need to be filled out by the patient themselves without parental/carer input. It was important to obtain patient's perspective entirely.

ii. Pregnancy: some physiological tests involved exposure to x-rays.

iii. Patients who have had their rectum excised prior to participating in physiological investigations which needed the rectum to be intact.

2.4 DATA COLLECTION

2.4.1 Methods of collection

Clinical information was obtained by interview and review of records (patient hospital notes and computerised records using a number of software packages (patient administration system [PAS] or Electronic Patient Record [EPR]). Data were collected retrospectively. This assured consistency and accuracy in patient medical history. When there was still missing information after viewing the patient's record and on interview, the author consulted their clinician or simply entered 'missing' in the research database.

2.4.2 Data storage

All data, regardless of method of acquisition, were stored on a dedicated, password protected database, which was established at the start of the study, and modified subsequently as required. Data were stored on Microsoft ® Excel 97 for Windows (Microsoft Corporation, Santa Rosa, CA, USA) and statistical package SPSS Version 16.0 for Windows (Coakes, Steed and Ong, 1999 John Wiley & Sons Australia) and hard copies (if required) in a secure locked cabinet.

2.4.3 Clinical data

Medical history reviewed included general medical background of the patient with ARA from time of birth to present date of this research study. A detailed patient history included gestation period (32-37 weeks), family medical history, other associated conditions, the nature of the patients presenting symptoms, mode of onset, personal past medical, treatment history, family history, and systematic enquiry was obtained, and included the variables listed in Table 2.1.

2.4.4 Operative technique

As discussed in Chapter 1, several operative techniques exist for the reconstruction of patients with ARA. As part of the learning process and appreciation in understanding the techniques, the author attended several operations during the research period in order to gain an insight of the techniques and for descriptive purpose for this thesis.

Table 2.1: Clinical data collected for patients with anorectal anomalies

Basic details	Date of birth
	Sex
	Gestation period
	Ethnicity
	Contact details and next of kin if patient < 16 years old
	Associated medical conditions (VACTREL) and other conditions
Family history	History of anorectal disorders in the family and other associated conditions
History of ARA	Obstetric history
	Age of diagnosis
	Type of anorectal anomaly
	Type of reconstructive operation
Investigations	Physical examination
	Physiological assessment (if any)
	Psychological reports (if any)
History of symptoms	Type and onset of symptoms: constipation, faecal incontinence, abdominal pain.
Treatment (excluding original reconstructive operation)	*Medication (such as laxatives):*
	Type of medication
	Duration of medication
	Did the medication work?
	Other treatments
	Botulinum toxin
	Sacral nerve stimulation
	Antegrade continence enema or other stomas
	Anal dilatation
	Myectomy
	Graciloplasty
	Other
Psychosocial History	Psychosocial difficulties

2.5 CONTROL GROUPS

As discussed in Chapter 1, the current literature lacks a control groups when discussing bowel and psychosocial function in patients with ARA. The two control groups included in this research study are discussed below.

2.5.1 Positive disease control group

Idiopathic constipation (IC) refers to an incapacity to regularly pass stool, where the cause remains unknown. It is one of the most common bowel movement disorders among children and adolescents. This group shares similar symptoms of constipation and FI to our ARA group but are a functional disorder with no anatomical defect as in ARA. Medical history reviewed included general medical background of the patient with ARA from time of birth to present date of this research study. A detailed patient history included gestation period, family medical history, other associated conditions, the nature of the patients presenting symptoms, mode of onset, personal past medical, treatment history, family history, and systematic enquiry was obtained, and included the variables listed in Table 2.2

2.5.2 Negative disease control group

In this thesis, the negative disease control group included patients who have been diagnosed with appendicitis and have had surgery (appendectomy). They have been treated for a condition entirely separate from the area that our patients ARA and IC individuals share in common. Medical history included those listed in Table 2.3.

Table 2.2: Clinical data collected for patients with idiopathic constipation

Basic details	Date of birth
	Sex
	Gestation period
	Ethnicity
	Contact details and next of kin if patient < 16 years old
	Associated medical conditions (VACTREL)
	Other medical conditions
Family history	History of constipation or other gastrointestinal disorders
History of IC	Age of diagnosis
	Duration of constipation
Investigations	Physical examination
	Physiological assessment (if any)
	Psychological reports (if any)
History of symptoms	Onset of symptoms
	Duration of symptoms
Treatment (excluding original reconstructive operation)	*Medication (such as laxatives):*
	Type of medication
	Duration of medication
	Did the medication work?
	Other treatments
	botulinum toxin
	sacral nerve stimulation
	Antegrade continence enema
	Stomas
	Anal dilatation
	Myectomy
	Other
Psychosocial History	Psychosocial difficulties

Table 2.3: Clinical data collected for healthy controls

Basic details	Date of birth
	Sex
	Gestation period
	Ethnicity
	Contact details and next of kin if patient < 16 years old
	Other medical conditions
History of gastrointestinal symptoms	Examples include: constipation, faecal incontinence, piles etc.
Appendicitis	Age of onset and operation
Psychosocial History	Psychosocial difficulties

2.6 SYMPTOM ASSESSMENT

Symptom assessment was obtained in a short interview with the author, when the patient came to fill out other required questionnaires in a private room

2.6.1 Constipation

As mentioned in Chapter 1, constipation is a poorly defined clinical symptom, not a definitive diagnosis. Previous studies have investigated the symptoms associated with constipation, and scoring systems have been used in its diagnosis (Agachan et al., 1996).

The Knowles-Eccersley-Scott-Symptom (KESS) questionnaire (Appendix – F) is a modified version of that used in the Cleveland Clinic Score (Agachan et al., 1996). Changes in questions were based on clinical impression of those symptoms most likely to be discriminatory. Knowles et al (Knowles et al., 2000) questionnaire design involved a structured interviewer-led questionnaire consisting of eleven questions which was devised by incorporating internationally agreed-upon criteria (Whitehead, 1991). This questionnaire was designed to be simple enough to be completed in less than five minutes. Each question had four or five possible linear integer scale to produce a range of between 0 and 3 or 0 to 4 points. Lower scores represented symptom free sates and higher scores, increased symptom severity. The total KESS score was the sum of all scores gained on individual questions with a maximum possible of 39 points. The answers to each question were worded such that any patient who fitted agreed criteria (Whitehead, 1991) for constipation would be likely to score at least one point per question. KESS score for constipation: includes items such as duration of constipation, laxative use, frequency of bowel movement, unsuccessful evacuatory attempts, feeling of incomplete evacuation, abdominal pain, bloating, enemas/digitations, difficulty in evacuating, time taken and stool consistency and use of laxatives and effectiveness.

This structured symptom scoring questionnaire was completed by 71 chronically constipated patients and 20 asymptomatic controls. The symptom score correlated with a previously validated constipation score (Cleveland Clinic Score) ($r = 0.90$). Discriminant analysis using cross validation estimated that pathophysiology could be predicted correctly for 55% (95% confidence interval = 43-67%) of patients using just give symptoms (Knowles et al., 2000). This scoring system is a valid technique to

assist in the diagnosis of constipation and is the first study using appropriate statistically methodology to demonstrate a discriminatory ability of multiple symptoms in constipation. Further, validation of the classification performance of this method of symptom analysis in a prospective cohort of patients was undertaken (105 patients referred to their institution for specialist investigation of intractable constipation) (Knowles et al., 2002).

2.6.2 Faecal Incontinence

A scoring system for the assessment of severity of faecal incontinence (FI) is required to gain an objective comparison of outcomes of both conservative and surgical treatments. A number of scales have been published (Browning and Parks, 1983, Millar, 1988, Pescatori et al., 1992, Jorge and Wexner, 1993). The Wexner Continence Grading Scale has become a widely used for the assessment of severity of FI. Vaizey et al (Vaizey et al., 1999a) felt that there were three areas in which this scale could be improved. Firstly, the scale does not take account of faecal urgency, which can be present without overt FI. Secondly, the need to wear a pad is given equal weighting to the occurrence of incontinence. However the use of a pad may not be fastidiousness. The use of a pad also often relates to the presence of coexistent urinary leakage. Finally, in the comparison of degree of incontinence preoperatively and postoperatively, the introduction of antidiarrhoeal drugs should be taken into account. These are often given as a part of the treatment package and a failure to recognise this could give a false impression of the surgical success rate. In developing a new scale, Vaizey (Vaizey et al., 1999a) felt that the Wexner scale formed an excellent basis, but with these modifications mentioned above. The new scale or

called the ‘Vaizey Incontinence Questionnaire’ or ‘St Mark’s incontinence score’ (Appendix – G) has introduced an assessment of the ability to defer defecation and an additional score for the use of antidiarrhoeal, and reduced the emphasis on the need to wear a pad. Vaizey et al (Vaizey et al., 1999a) found the ‘Vaizey Incontinence Questionnaire’ to correlate closely with a detailed clinical assessment by two independent observers, and has demonstrated the highest test-retest reliability, reproducibility and sensitivity to change produced by definitive treatment than Pescatori, Wexner and American Medical Systems. Many studies have assessed FI along with physiological measurements using the new scale (Maeda et al., 2008, Terra et al., 2006b, Beddy et al., 2004, Kushwaha et al., 2003, Badvie and Andreyev, 2005, Olopade et al., 2005, Deutekom et al., 2005, Terra et al., 2006a, Dobben et al., 2007).

The ‘Vaizey Incontinence Questionnaire’ consists of seven questions (Appendix – G). A score of 0 suggests no problems with bowel continence (complete continence), and a score of 24 suggests very severe problems with incontinence (complete incontinence). The scale consists of three items about the type (gas, liquid, solid) and frequency of incontinence (all scored from 0 to 4) and four additional items addressing social invalidation (0 to 4), the need to wear a pad or plug (0 to 2), the use of constipating medication (0 to 2) and the presence of urge incontinence (0 to 4). A Vaizey Incontinence score of at least 12 is considered poor (Felt-Bersma et al., 2007, Terra et al., 2006a, Terra et al., 2008, Terra et al., 2006b, Dobben et al., 2007, Deutekom et al., 2007, Deutekom et al., 2005). The Vaizey Incontinence score has gained wide acceptance and has found to correlate well with patients’ subjective perception ($r = 0.55$; $P<0.001$) and is reliable regardless of type of incontinence, patient’s age, or gender (Maeda et al., 2008). It is also suitable for the severity

assessment of FI and the evaluation of a treatment outcome (Maeda et al., 2008). For patients who are suffering from FI on a daily or regular basis, further questions were asked using the diary card (Appendix – G).

2.7 GASTROINTESTINAL PHYSIOLOGICAL TESTS

A number of tests have been developed, principally in the last 30 years, to examine the physiological function of the colon and anorectum. Comprehensive clinical evaluation of the patient, along with clinical history, physical examination and investigations, allows the aetiology of their symptoms (such as FI) to be deduced, coexisting pathology to be excluded and the best suitable treatment to be offered. An introduction to some of these physiological investigations in Chapter 1, have been discussed. This section specifically describes the tests used routinely to assess patients presenting with symptoms of constipation and FI to the Gastrointestinal Physiology Unit (GIPU) and which have been used in assessing the pathophysiology of FI and constipation in patients with ARA. The study population includes 32 consecutive patients comprised 15 females and 17 males. Age range of the population sample included ranages bewteen 11-42 years of age and mean of 24 (+/- 9). All patients included those who have underwent surgery for ARA as infants and were referred for investigation of their symptoms of faecal incontinence (FI) between 1998-2006. The cohort of subjects who will undergo physiological testing are not all drawn from the ARA group for this part of the study. Only 14/32 patients were from the original ARA population group. The data from the following tests are included in this thesis:

1. Transit studies	Radio-opaque marker and / or radioisotope
2. Anal manometry	Anal sphincter resting and squeeze pressures
	Rectoanal inhibitory reflex testing
3. Rectal sensory testing	First constant sensation

	Defaecatory desire volume
	Maximum tolerated volume
4. Evacuation proctography	Mechanical and functional outlet obstruction
5. Pudendal Latency Test	Conduction time of pudendal nerve
6. Endosonography	Integrity of anal sphincters

The study population comprised of a small group of consecutive patients, who have undergone surgery for ARA as infants and were referred for investigation of their symptoms of FI between 1998-2006 to our GIPU.

2.7.1 Transit Studies

As discussed in Chapter 1, idiopathic constipation could be due to colonic motility disorder that is associated with a reduction in the rate of progress of colonic intraluminal contents (MacDonald et al., 1993). Colonic transit studies allow patients' subjective complaints to be objectively confirmed, and further allow the investigator to distinguish between those patients with a slow and normal colonic transit time. This is achieved by a simple radio-opaque marker study which detects transit abnormalities in everyday clinical practice, involving the ingestion of non-absorbable cylindrical pellets that are of similar density to food residue, and that have no effect on gut activity (Hinton et al., 1969) followed by a plain abdominal radiograph taken 3 to 5 days later (Arhan et al., 1981, Hinton et al., 1969, Roberts et al., 1993, Metcalf et al., 1987).

For this thesis, patients presenting with infrequency of defaecation were assessed predominately by colonic transit studies, using radio-opaque marker studies (Figure 2.2). For this thesis, laxative medication and opiate analgesics were stopped 24 h prior to the start of the study and avoided until its completion. Patients remained on their normal diet during the study period. Studies were carried out as previously described (Roberts et al., 1993), with a single plain abdominal radiograph performed at 100 h after administration of a gelatin capsule (broken down rapidly in the stomach) containing 50 radio-opaque markers, cut from a length of 2.5 mm (external diameter) diameter radio-opaque vinyl tubing (SIMS Portex Ltd., Hythe, UK). Delayed transit was defined as >20% of 50 administered markers remaining at 100h (Roberts et al., 1993, Hinton et al., 1969).

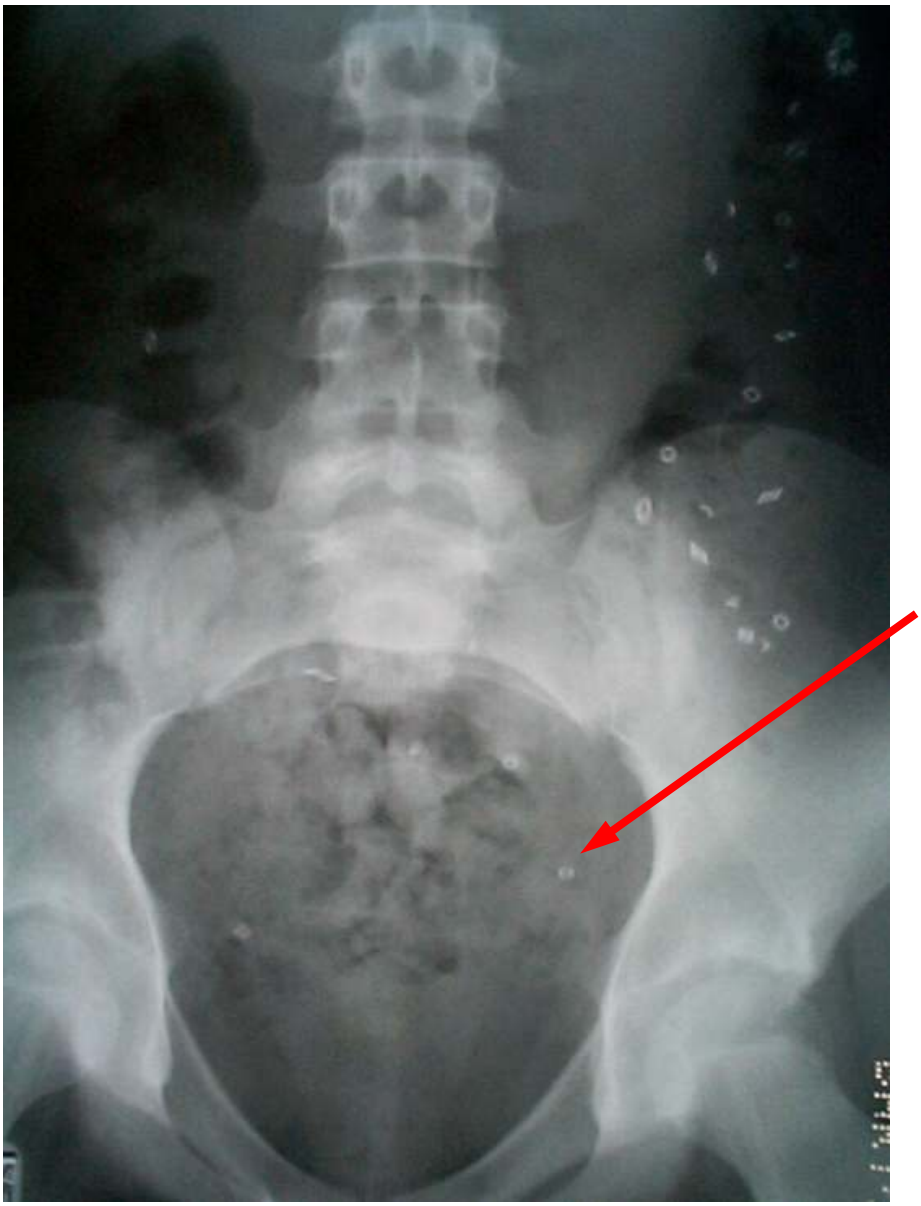
2.7.2 Anal manometry

Measurements were undertaken of functional anal canal length, maximum resting and voluntary anal squeeze pressures using standard methodology (station pull-through manometry). These measurements are performed with open-tipped or side-opening water perfused catheters, direct online solid-state transducers, or air-or water filled balloons of various sizes and configurations. Normal anal pressures vary according to sex, age and technique used (Diamant et al., 1999). It is found, that pressures are higher in men and younger people (Jameson et al., 1994).

In this thesis, manometry was performed using a single channel side hole catheter linked to an Arndorfer-type pneumohydraulic water perfusion system: a pull back technique allowed assessment of functional anal canal length, maximum resting tone,

and maximum voluntary squeeze pressures (Figure 2.3) (Read et al., 1984, Chan et al., 2005c). Anal resting tone and squeeze pressures were considered abnormal if they were below 50 cm H20, which are the lower limits of the normal for our unit.

Figure 2.2: Colonic transit studies, using radio-opaque markers. This can be seen in the x-ray below with remaining markers in a patient (see arrow).



Presence or absence of the recto-anal inhibitory reflex (RAIR) was also confirmed by positioning the manometry catheter in the high-pressure zone of the anal canal and distending the rectum with an air-filled balloon tied to a Foley-catheter (Farthing and Lennard-jones, 1978). Such values are comparable to those obtained from the literature for this technique (Read et al., 1979).

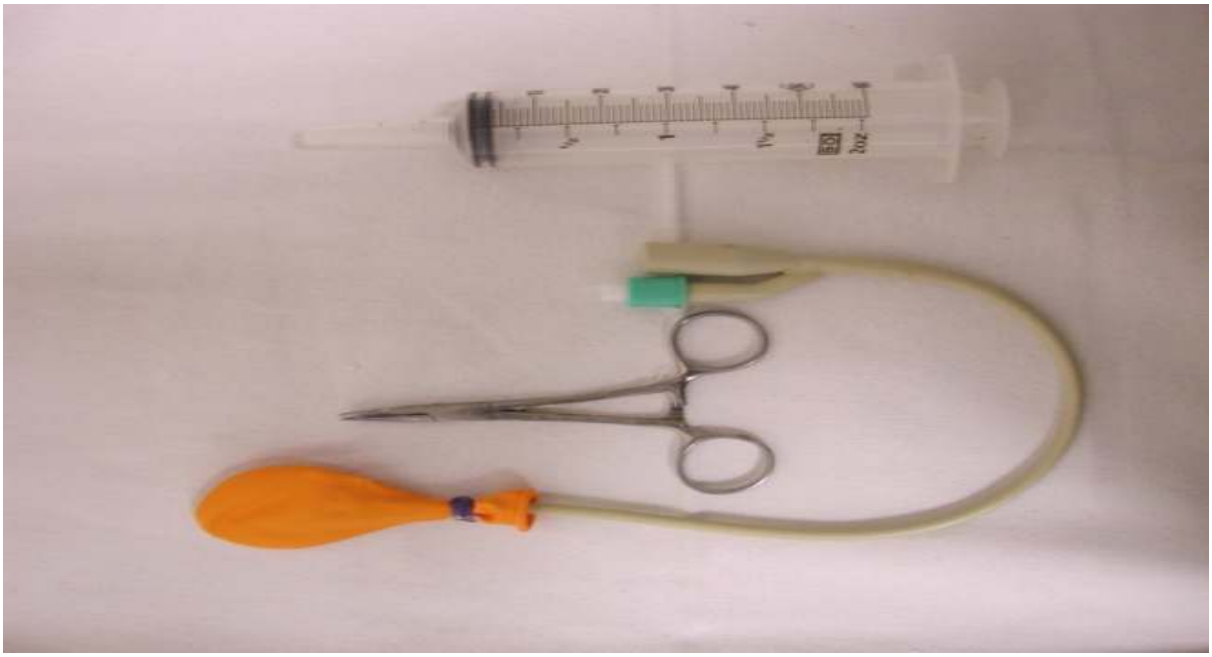
Figure 2.3: The apparatus required to perform anal manometry. This is done at our GI Physiology Unit, Royal London Hospital (UK). An intraluminal pressure- sensing water perfused catheter is connected to pressure transducers, and the analogue signals are amplified and digitalised by an interface converter and transmitted to a personal computer for display.

2.7.3 Rectal sensory testing

Rectal sensation was assessed by inflating a simple latex balloon (same rubber party balloon used before) with air at 1 ml/sec (Figure 2.4), positioned 10 cm from the anal verge and determining the threshold volumes for first constant sensation (FCS), defaecatory desire volume (DDV) and maximum tolerable volume (MTV) (Farthing

and Lennard-jones, 1978). Values obtained for each sensory threshold were compared with normal ranges matched for age and sex (Jameson et al., 1994). Patients were considered to have rectal hyposensitivity if MTV was < 100 ml in females or < 80 mls in males (Chan et al., 2005a).

Figure 2.4: Apparatus used to assess rectal sensory function during anorectal physiological investigation.



2.7.4 Evacuation Proctography

Additionally to colonic dysmotility, constipation could be due to secondary outlet obstruction (Martelli et al., 1978). Evacuation proctography (Figure 2.5.a) is a technique which involves imaging the rectum with instilled contrast material, which allows the observation of the process, rate and completeness of rectal evacuation using fluoroscopic techniques (Diamant et al., 1999). The image (Figure 2.5.b) will

also provide information about the anatomy of the rectum including any anatomical abnormalities (e.g. rectocoele, rectal prolapse/intussusception and others).

Firstly, the semisolid contrast medium was prepared by mixing barium sulphate and scotch porridge oats at body temperature to make a thick paste. The test involved instilling barium paste (artificial stool) into the rectum to the previously determined maximum tolerable volume and allowing the patient to evacuate under fluoroscopy (Mahieu et al., 1984) (Womack et al., 1985). The contrast was injected into the rectum using a wide tipped syringe via a proctoscope. With the patient seated on a radiolucent commode (Figure 2.5.a), lateral fluoroscopy was performed using an image intensifier (Siemens Plc., Bracknell, UK). The amount of contrast voided, and the time taken to void were recorded. Any radiological abnormalities in the rectum were identified.

In this thesis, normal evacuation proctography was classified when the patient had no difficulty expelling rectal contents (which included radiological abnormalities of the rectum that did not constitute a 'physical obstruction' to defaecation), and abnormal (outlet obstruction) when there was a clear difficulty expelling rectal contents.
Patients with an abnormal proctogram were further subdivided into:

i) 'mechanical' outlet obstruction – presence of anatomical abnormalities (e.g. rectocoele, rectal intussusception etc) that is due to a physical barrier to defaecation or
ii) 'functional' outlet obstruction (Wald, 2001) – difficulty expelling rectal contents in the absence of radiological abnormalities (e.g.

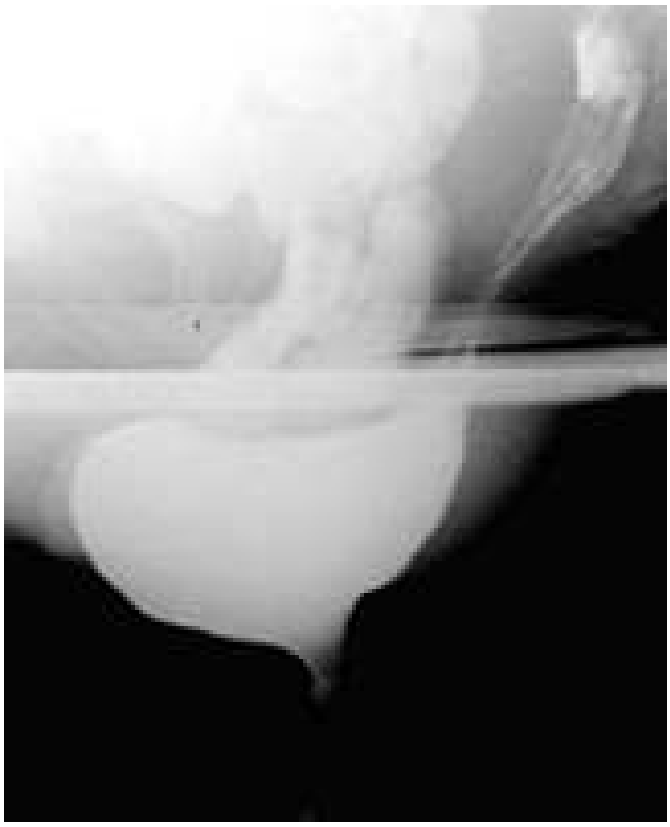
failure of pelvic floor muscle relaxation when the anorectal angle or anal canal remains closed despite adequate expulsive effort or slow prolonged evacuation – 180 seconds or early termination of evacuation despite normal opening of the anorectal angle and relaxation of the anal canal, with most of the neostool retained (>25%) and those with exaggerated rectal adaptation and loss of the sensation of rectal fullness (Chan et al., 2001).

2.7.5 Pudendal Latency Test

As mentioned in Chapter 1, branches of the pudendal nerve provide both efferent and afferent pathways to the pelvic floor, EAS and perineum. Thus, pathological processes affecting pudendal nerve conduction could impair the functioning of the anal sphincter and pelvic floor, and such neuropathy may be important in the aetiology of idiopathic or 'neurogenic' FI and other functional anorectal disorders (Hill et al., 2002). The pudendal nerve motor latency test (PNTML) is a measurement of the conduction time from stimulation of the pudendal nerve at the level of the ischial spines, to the evoked EAS contraction. Prolonged latencies are suggestive of pudendal neuropathy, and have been demonstrated in patients with idiopathic incontinence (Kiff et al., 1984), yet, with the advent of endosonography, many patients previously thought to have 'idiopathic' incontinence are now recognised as having identifiable muscle damage or degeneration (Vaizey et al., 1997, Kamm, 1998).

Figure 2.5: Evacuation proctography. This involves imaging the rectum with instilled contrast material radiolucent commode (a) as seen below at our GI (b) Physiology Unit (Royal London Hospital, UK)

(a)



(b)

For this thesis, PNTMLs were determined using a disposable glove-mounted stimulating and recording electrode (Figure 2.6) (St Mark's pudendal stimulating electrode: Dantec Electronics Ltd, Bristol UK) (Kiff et al., 1984) connected to a recorder (Kiff et al., 1984). The index finger bearing the electrode array was inserted into the rectum, and the ischial spine sought. Square wave stimuli of 01 ms duration and 50 V were applied at 1 s interval. PNTML are known to increase with age (Laurberg and Swash, 1989), patients were considered to have a pudendal neuropathy (either unilateral or bilateral) if PNTMLs exceed 2.3 ms in those <40 years or age, and exceeded 2.5 ms in those ≥ 40 years of age. These values represent the upper limit of normal for our unit (Chan et al., 2005a).

2.7.6 Endosonography

Endosonography or endoanal ultrasound is a technique used to accurately image the sphincter muscles. This has revolutionised our understanding of the pathogenesis of FI as mentioned above, showing that structural damage rather than pudendal nerve damage is the underlying cause in most patients (Nielsen et al., 1993, Burnett et al., 1991, Law et al., 1991). It now forms the cornerstone for the evaluation of sphincter integrity.

In this thesis, we know that the cylindrical nature of the anal structures, imaging is best suited to a 360^0 axial view obtained at right angles to the lumen. This achieved using 10MHz transducer attached to a mechanically rotating endoprobe (transrectal probe type 1850 and ultrasound machine, model 1846 and; B-K Medical Berkshire, UK) (Figure 2.7.a). A hard plastic cone surrounding the transducer is filled with

distilled water and protected with a condom, covering liberally inside and out with ultrasound gel to ensure good acoustic contact. During the evaluation, the probe was inserted into the rectum and slowly withdrawn through the anal canal with images Figure 2.7.b) being recorded from the upper, mid and lower levels. Although operator dependent, sensitivity and specificity approach 100% for the identification of anatomical defects if carried out by an experienced practitioner (Sultan et al., 1994). Structural damage to either the internal or external anal sphincter was clearly identified, as well as degenerative changes in the smooth muscle (Vaizey et al., 1997).

Figure 2.6: The St Mark's pudendal nerve electrode. This consists of a pair of stimulating electrodes mounted on a fixed array together with the recording electrode.

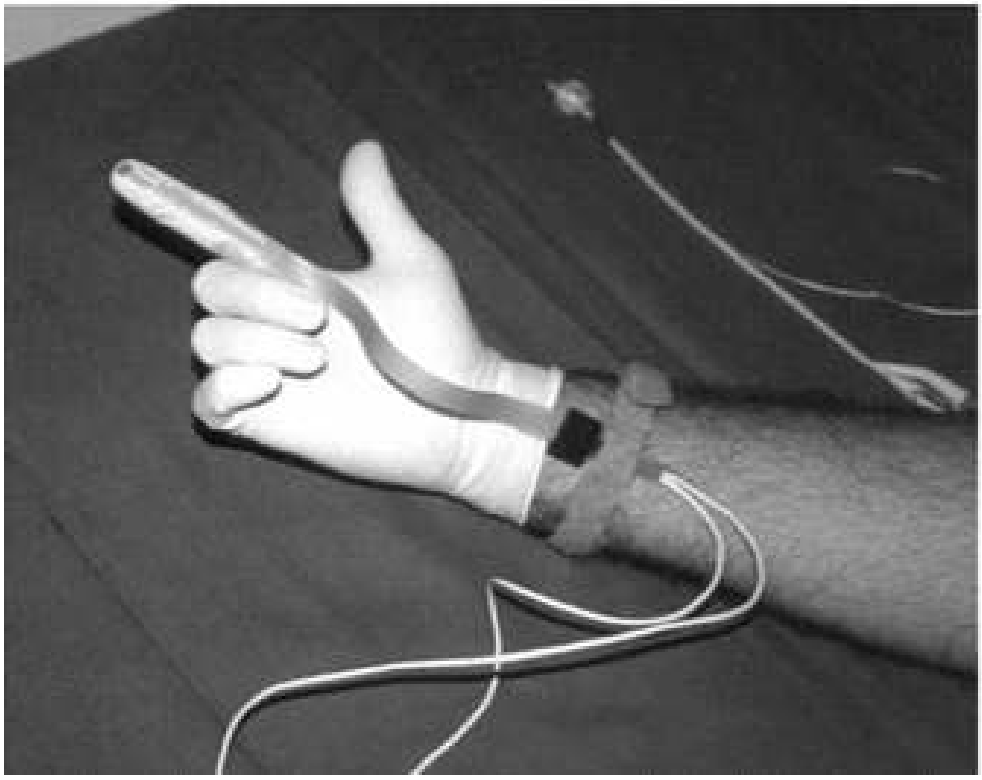
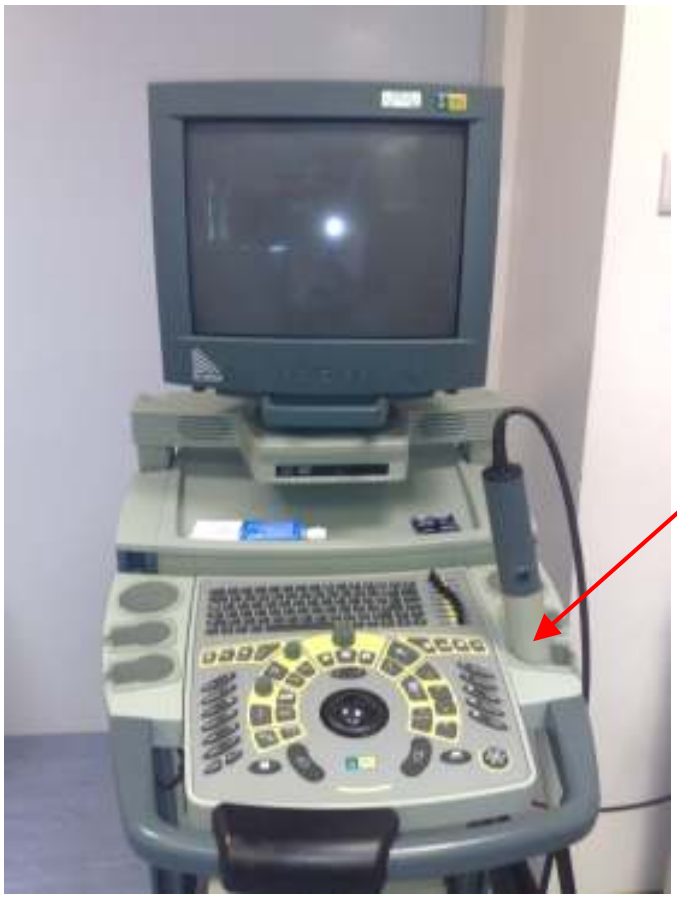


Figure 2.7: a) Endosonography machine. Probe (see arrow) (a) and b) image produced showing sphincteric muscles and puborectalis.



2.8 PSYCHIATRIC AND QUALITY OF LIFE INVESTIGATIONS

Psychiatric tests included specific measures of depression, anxiety, personality, general health, gastrointestinal quality of life and level of hopefulness (Table 2.4). These questionnaires were done in a private room where the subject was entirely on their own with an identification number, in order to encourage anonymity and confidentiality. As seen in Chapter 1 literature review table, most studies investigating quality of life and psychiatric measures in patients with ARA, the questionnaires were posted to the subject's home address or done in clinic (i.e. in an interview format or with parent). The presence of other parties (e.g. parent/s, other family, researchers, and clinicians) could influence the subject's answers to the questions and thus not encourage an honest answer. All subjects were given an envelope (with an ID number) which was provided at the beginning of the visit. This allowed the subject to put all questionnaires in the envelope once completed, sealing it and avoiding the author in charge to become bias when analysing the results. If the subject was unable to attend the research unit or hospital, visits were made to the subject's home/work place from the author, where the questionnaires were filled again in a private room. One subject was in prison during the time of the research study, and since they fitted the inclusion criteria, they too were included in this research following the same format as above.

2.8.1 Gastrointestinal Quality of Life

Quality of life measurements have become increasingly important in surgical research

and are nowadays often one of the endpoints of clinical trials, besides the more established outcome measures such as morbidity, mortality and survival rates (Okike et al., 1979, Andreollo and Earlam, 1987, Vantrappen and Hellemans, 1980). Measurement of quality of life in patients with various medical conditions is used to evaluate the nature and extent of functional and psychosocial impairment. Furthermore, it allows the monitoring of quality of care and comparison of different therapeutic approaches. Measuring quality of life necessitates use of instruments that are consistent, reproducible, sensitive and applicable. To date the gastrointestinal quality of life index (GIQLI) (Appendix - H) first published in the German version in 1993, developed by Eypasch and colleagues to measure health related quality of life (HRQOL) in multiple chronic gastrointestinal disorders (Eypasch et al., 1995). The

Table 2.4: Psychiatric instruments for all subject groups

Variables	Ages Administered	Instrument
Quality of life	≥ 11 years	The Gastrointestinal Quality of Life Index
Depression	7-17 years	Children's Depression Inventory
	≥ 18 years	Beck Depression Inventory
Mental health	> 16 years	General Health Questionnaire
Anxiety	8-12 years	State-Trait Anxiety Inventory for Children
	≥ 13 years	State-Trait Anxiety Inventory (adults)
Physical health	≥ 11 years	Pennebaker Inventory of Limbic Languidness
Personality	> 16 years	Big Five Inventory
	< 16 years	Big Five Inventory TTC (Transition to College)
Hopefulness	≥ 11 years	Hunter Opinions Personal Expectations Scale
Lie Detector	≥ 11 years	Weinberger Adjustment Inventory
Coping Mechanisms	≥ 11 years	Cognitive Emotion Regulation Questionnaire (including Cognitive Emotion Regulation Questionnaire - kids)

questionnaire contains up to 36 items, scored on a five point Likert scale (range 0-144, higher score = better quality of life), in which additional modules specified by the particular gastrointestinal disease, supplement a set of core questions. It consists of five subscales: physical well being, gastrointestinal digestion, gastrointestinal defaecation, mental well being and other which is summarized in an overall score (Table 2.5).

Table 2.5 Gastrointestinal Quality of Life Index (GIQOL) subgroups

GIQOL Subgroups	
Physical well being Enjoyed eating Fatigue Feeling unwell Appearance Endurance Feeling unfit Daily activities Leisure activities Nausea	**Gastrointestinal digestion** Pain in abdomen Fullness in abdomen Bloating Flatus Burping/belching Abdominal noises Regurgitation Eating speed Constipation Heartburn
Mental well being Coping with stress Sad about illness Nervous about illness Happy with life Frustrated by illness	**Gastrointestinal defaecation** Bowel frequency Impaired sexual life Bowel urgency Diarrhoea Blood in stool Uncontrolled stools
Other Restricted eating Wake up at night Bothered by treatment Worsened relations Dysphasia	

The GIQLI subscales have been found to have good internal reliability and the construct validity was supported by the pattern of correlations with the Rotterdam Symptom Check List and Medical Outcomes Studies (Nieveen Van Dijkum et al.,

2000). Construct validity was supported by demonstrating a reasonable correlation with the Spitzer quality of life index (r=0.53) and the Bradburn affect balance scale (r=0.42) in 204 German patients with a variety of gastrointestinal disorders (Borgaonkar and Irvine, 2000). Other studies are in agreement with the GIQOL being a valuable instrument for measuring quality of life in patients with anorectal conditions (Vordermark et al., 1999, Sailer et al., 1998, Kasparek et al., 2007)

A Finish group examined adults with FI following surgical therapy for childhood with anorectal disorders. These included 26 subjects treated surgically for benign sacrococcygeal teratoma (Rintala et al., 1993a) and 83 who had surgery for low anorectal malformations (Rintala et al., 1992). Both groups had impaired bowel function with 27-39% of the respective cohorts reporting social problems due to impaired continence. In contrast, Moore et al found that 75% of 178 patients treated surgically for Hirschsprung's disease described excellent function whereas only 6% described persistent incontinence and resultant psychosocial problems (Moore et al., 1996).

Patients with the most severe gastrointestinal disorder have shown to have a mean GIQLI score of 45 compared with healthy controls who had a mean score of 121 (Weinryb et al., 1995) or 125.8 (Guillemin et al., 1993)

2.8.2 Depression

Depression or feelings of sadness experienced in children can have a negative influence on their daily life and level of hope. Depressive symptoms have been

generally related with poor academic achievement, peer friendship/relationship problems, behaviour problems, poor self-esteem and in severe cases, suicide (Kazdin, 1990) (Worchel, 1987). As a result, medical professionals have come to appreciate how crucial it is to measure depressive symptoms in paediatrics. This provides the opportunity to identify:

1) children seriously in need of treatment
2) those indicating milder depressive symptoms that may benefit from early intervention (Crowley, 1994).

2.8.2.1 Children Depression Inventory (CDI)

Depression in children between 7-17 years of age can be assessed by using the Children's Depression Inventory (CDI) (Appendix - I). The CDI is a self-report questionnaire, which is essentially a downward extension of the Beck Depression Inventory (BDI) (Beck et al., 1985). Modifications included additional items to evaluate areas of school and social/peer relations. However, the CDI differs from the BDI mainly in its phraseology, which is more appropriate to the language of 8-13 year old children (Kovacs, 1977). The CDI comprises 27 self-rated symptom orientated scale. Each item is divided into three statements that are graded in severity and are assigned numerical values from 0 to 2, providing a total score range of 0-54. The CDI specifies a variety of depressive symptoms including (Kovacs, 1985):

- Disturbed/negative mood
- Anhedonia
- Ineffectiveness (i.e. vegetative functions)
- Self-evaluation (i.e. negative self-esteem)

- Interpersonal behaviours

Approximately half of the items begin with the choice that reflects the greatest symptom severity; for the remainder, the sequence of options is reversed.

The CDI will be chosen for this research study over similar instruments as it is commonly used and has been subjected to lengthy psychometric assessment in normal children and in the clinical setting. It has also been modified in relation to its format and items in order to improve validity and comprehension. The CDI has demonstrated to display:

1) Good reliability with reasonable valid measure of depression among children (Hepperlin et al., 1990, Ghareeb, 1989, Ollendick and Yule, 1990, Smucker et al., 1986)
2) Acceptable internal consistency and test-retest reliability (Nelson, 1990, Kaslow et al., 1984, Kazdin, 1983, Meyer et al., 1989, Saylor et al., 1984, Finch, 1987, Wierzbicki, 1987, Weiss and Weisz, 1988)
3) An index of the severity of depression (Garvin et al., 1991).
4) Diagnostically effective using different cut-points between 10 and 30 (Doerfler et al., 1988, Garvin et al., 1991, Hodges, 1990, Kazdin, 1989, Kazdin et al., 1986, Smucker et al., 1986)
5) Discriminate psychiatrically diagnosed school-aged depressed children and clinical cases whose disorders are not in the depressive domain (Hodges, 1990, Kazdin et al., 1986)

Children who score high on the CDI generally tend to have a high level of anxiety and low self-esteem. Since these two phenomena are theoretically associated with

depression and the data support the inventory/s validity (Eason et al., 1985) (Hammen and Zupan, 1984).

Funakosi et al (Funakosi et al., 2005) demonstrated that the degree of depression in children with congenital ARA. It was found that the CDI score was higher in children aged 12 to 16 years than in the children aged 7 to 11 years. During adolescence, when an individual's self-image in a society is being established, the children tried to accept the faecal dysfunction and adapt themselves to society. However, problems such as FI may cause low self-evaluation and self-esteem, resulting in a high CDI score. Ludman and Spitz interviewed children with FI on a spontaneous basis and found that children aged 12 years or older were afraid of derision and prone to be repressed.

CDI scores are reported as a T-score. T-scores are standardized scores, which have the useful characteristics that each scale will have the same mean and standard deviation. Thus, permitting the interpreter to directly compare the scores on one scale to the scores on another scale. For this research study, a child who scored a T-score above 70 (i.e. > mean of 50, SD 10) was considered to be clinically depressed.

2.8.2.2 Beck Depression Inventory

Depression in young adults aged > 17 years was assessed using the 2nd Edition Beck Depression Inventory (BDI-II) (Appendix - J) (Beck, 1996). The BDI-II is a 21-item self-report instrument for screening the severity of depression in adults. It is essentially an upward extension of the CDI (Kovacs, 1992). BDI-II was developed for diagnosing depressive disorders listed in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders- Fourth Edition (DSM-IV,

1994). For the modified version (BDI-II) four items (weight loss, body change, somatic preoccupation, and work difficulty) were replaced by four new items:

1) Agitation
2) Worthlessness
3) Concentration difficulty
4) Loss of energy.

Such modifications were performed in order to index symptoms typical of severe depression or depression warranting hospitalisation.

The BDI-II was chosen for this research study over other existing instruments for measuring depression because:

1) it is commonly used
2) it is an upward extension of the CDI
3) it reports of good reliability.
4) psychometric characteristics of the BDI-II used samples from four different psychiatric outpatient clinics and one college-student group. [It has proven to be useful with a variety of populations (Beck and Beamesderfer, 1974).
5) it correlates well with several other psychological tests. The BDI-II is positively related to both the Beck Hopelessness Scale (Beck, 1988); Scale for Suicide Ideation (SSI) (Beck et al., 1979) and Beck Anxiety Inventory (BAI) (Beck, 1990); Hamilton Psychiatric Rating Scale for Depression (HRSD) (Hamilton, 1960).
6) it is sensitive to clinical change over time (Johnson and Heather, 1974) and has been used extensively as a pre-post-outcome measure in psychotherapy studies (Rush, 1977).

For this research study, a child who scored a BDI total score above 28 (i.e. range severe depression) was considered to be clinically depressed.

2.8.3 General Health Questionnaire

The General Health Questionnaire (GHQ) (Appendix - K) is designed to identify two main classes or problem: 'inability to carry out one's normal 'healthy' functions, and the appearance of new phenomena of a distressing nature' (Goldberg 1979). It focuses on breaks in normal functioning rather than on life-long traits; therefore it only covers personality disorders or patterns of adjustment where these are associated with distress.

Psychological distress or dysfunction was measured in this research study using the General Health Questionnaire-28 (GHQ-28) (Goldberg, 1978) (Appendix - K). The GHQ is a self-administered screening instrument revealing individuals with diagnosable psychiatric disorder. Different versions of the GHQ, including GHQ-12 and GHQ-28 have been exposed to factor analysis in a variety of countries and settings. The main focus of the GHQ-28 are the following:

1) Inability to carry out one's normal 'healthy' functions
2) Appearance of new phenomena of a distressing nature

The GHQ-28 is made up of 28 items, which were originally derived from a factor analysis of the GHQ-60. It consists of four subscales:

1) Somatic symptoms
2) Anxiety and insomnia

3) Social dysfunction

4) Severe depression.

It is aimed at studies that require more information than a single severity score (Goldberg and Hillier, 1979). Factor analysis within different settings including translation into different languages basically confirmed the original structure (Iwata and Saito, 1992, Nagata et al., 1993, Riaz and Reza, 1998, Weyerer et al., 1986)

For this research purpose the GHQ-28 was chosen because:

1) it is a commonly used self-report measure, which has been validated, in an Australian population, with correlations between clinical psychiatric ratings of severity and GHQ scores (Tennant, 1977).
2) it functions well in terms of scale validity, with the four subscales contributing to 48% of the total variance (Goldberg and Hillier, 1979, Kilic et al., 1997).
3) it is valuable tool to assess general psychopathology and to screen for potential cases.
4) both versions (GHQ-12; GHQ-28) have been shown to be reliable and to have stable factor structures across cultures and across time.

The GHQ scoring method was used to assess psychiatric morbidity. This method of scoring involves a dichotomous response (i.e. 0-0-1-1) scale where only pathological deviations (1 = 'rather more than usual' and 'much more than usual') signal possession of the item ('less than usual' and 'no more than usual' are scored 0). Therefore, cut-off scores less than five is indicated as a 'probable non-case' and all those more than or equal to five as 'probable cases'.

2.8.4 Anxiety

All individuals show signs of anxiety at some point during their life, with differences existing in relation to how often and how intensely it is shown. Catell & Scheier (Cattell, 1961) suggested that anxiety has two dimensions:

1) state anxiety: one tends to feel anxiety in a particular situation
2) trait anxiety: this indicates the tendency to explain anxiety across a variety of situations.

Spielberger (1973) notes that people who have high levels of trait anxiety are more likely to view a wider range of situations as threatening or dangerous. Researchers have developed instruments to assess state and trait anxiety with different age ranges (Spielberger, 1970) (Spielberger, 1973).

The State-Trait Anxiety Inventory for Children (STAIC) (Appendix - L) (Spielberger, 1973) (Appendix L) is one of many tests used to measure anxiety in children. Primarily the STAIC was developed as a research tool for the study of anxiety in elementary school children. The STAIC is similar to the State-Trait Anxiety Inventory (STAI) (Appendix M) (Spielberger, 1970) which measures anxiety in adolescents/adults. Both the STAIC and STAI share similar items, but the format for responding to the STAIC has been simplified to cater for young children. The STAIC measures anxiety in children who are in Grades 1 through 6 (i.e. 9 to 12 years) (Spielberger, 1973). However, Spielberger et al., (Spielberger, 1973) suggested that it "may also be used with younger children who are average or above reading ability

and with older children who are below average in ability" (Spielberger, 1973) p.5). The STAIC is made up of two separate psychometric scales for measuring two distinct (yet related) anxiety concepts (as found in the STAI (Spielberger, 1973):

1) STAIC State-Anxiety: consists of 20 statements, which ask children how they feel at a *particular moment in time*. The purpose of State-Anxiety scale is to measure transitory emotional arousal or anxiety states. This includes subjective consciously perceived feelings of apprehension, tension, and worry that vary in strength and fluctuate as a function of stressful situations that occur over time.
2) STAIC Trait-Anxiety: consists of 20 item statements, yet subjects reply to these items in relation to how they *generally feel*. The Trait-Anxiety assesses relatively constant individual differences in anxiety proneness. This includes differences between children who are prone to experience anxiety states.

Children with higher Trait-Anxiety patterns are more likely to show State-Anxiety characteristics due to their inclination to look at more situations as threatening or dangerous. The STAIC was used in this research study because:

1) it is most commonly used
2) it provides reliable means to measure trait and state anxiety in children (Cross, 1993) (Finch, 1987, Dorr, 1981).

a) correlates with Children's Manifest Anxiety Scale (CMAS) (Castaneda et al., 1956)) and (General Anxiety Scale for Children) (GASC) (Sarson, 1960).

For this research study, scores at or above 35 (67^{th} percentile) were defined as high anxiety for this sample and scores at or below 30 (33^{rd} percentile) were defined as low anxiety for this sample (Emerson et al., 2005).

The STAI has been mainly used in high school and college students, working adults, military personnel, and psychiatric, psychosomatic medical, surgical, and dental patients (Spielberger, 1973). As in the STAIC, the STAI consists of 20 statements that ask respondents to report how they feel at that particular moment by rating the intensity of their subjective feelings of anxiety (such as "I feel frightened") on a four point scale:

1) 'not at all'
2) 'somewhat'
3) 'moderately so'
4) 'very much so'

For this research the STAI was chosen because:

1) it has investigated the role of anxiety in patients suffering from other chronic illnesses such asthma (Alexander, 1972, Kurata et al., 1976) colitis, dermatitis, duodenal ulcers, and infectious mononucleosis (Latimer, 1980, Rabavilas, 1980, Roark, 1971).
2) Maternal mental distress was examined as possible predisposing factor for the child's disease and/or an effect of disease (Vandvik and Eckblad, 1991).

The STAI is used to evaluate state and trait anxiety with a maximum score of 80. For this research study STAI (state anxiety), scores of 41 or less indicate normalcy, where scores of 42 to 50 imply a clinically significant state of anxiety. Furthermore, scores of higher than 50 indicate an extremely high level of anxiety (neurosis level) (Funakosi et al., 2005). For STAI (trait anxiety) scores of 44 or less represent normalcy, whereas scores of 45 to 54 indicate clinically significant characteristic

anxiety Scores higher than 55 or higher indicate extremely severe characteristic anxiety (neurosis level) (Funakosi et al., 2005).

2.8.5 Pennebaker Inventory of Limbic Languidness

The Pennebaker Inventory of Limbic Languidnes (PILL) (Appendix - N) is a 54 item scale that assesses the frequency of common physical symptoms and sensations (Pennebaker, 1993). Evidence of its validity was found in that high scores on this instrument were more likely to engage in health-related behaviours than those with lower scores (Carney et al., 2002). Previous research indicates that high scores on the PILL are significantly associated with a greater frequency of center visits, and greater number of days sick and/or work related absences. Cronbach alphas range from 0.88 to 0.91 and 2 months retest reliability ranges from 0.79 to 0.83 (Pennebaker, 1993, Carney et al., 2002).

The overall score on the PILL is obtained by summing the total number of items for which the individual endorsed experiencing the symptom at least onece every month (Pennebaker, 1993). Items include physical symptoms such as runny or congested nose, chills, headaches, fever and nausea. Subjects are asked to indicate on a 5-point scal how they experience each symptom from 1 = ‘have never or almost never experienced the symptom to 5 = ‘more than once every week. The PILL was included in this study because it is commonly used in studies of written disclosure and it is a sensitve measure of change in physical symptoms.

2.8.6 Big Five Inventory

The Big Five personality model has emerged as a widely accepted general framework for conceptualising personality traits (Digman, 1997, Digman, 1990). The Big Five Inventory (BFI) (Appendix - O) consist of 44 questions desgined to separate each patients personality into five dimentions: extroversion, agreeableness, conscientiousness, neuroticism and openess (John, 1991). The BFI uses short and simple phrase to assess the most prototypical traits associated with each of the Big Five dimensions.

Participants rate each BFI item on a 5-point scale ranging from 1 (disagree strongly) to 5 (strongly agree). Briefly, the personality dimensions encompass different traits. Extroversion describes persons who are talkaive, energetic, and assertive. Agreeableness characteristics include sympathy, kindnes and affection. Parents and teachers convey to young children that there are appropriate (good) and inappropriate (bad) ways to behave (Block et al., 2007). As articulated by Digman (Digman, 1997), in BFI terms, being a good child involves acting both agreeable (e.g. “don’t hit”, “share with your brother/sister”) and conscientiously (e.g. “do as you are told”, “pick up after yourself”). Conscientiousness describes persons who are organised, thorugh, and engage in planning. Tense, moody, and anxious persons score high in neuroticism dimensions. Finally, openness implies personality styles with wide interests, and are imaginative and insightful. The BFI scales have shown substantial internal consistency, retest reliability, and clera factor structure, as well as considerable convergent and discrimiantnt validity with longer Big Five measures

Scoring the BFI is usually done by an intuitive metric system known as percentage of maximum possible (POMP) scores (Cohen, 1999). A POMP score is a linear transformation of any raw metric into 0 to 100 scale, where 0 represents the minimum possible score and 100 represents the maximum possible score. Srivastava (Srivastava, 2003) demonstrated in a sample of adults aged 21-60 who completed the BFI, that consicientiousness and agreeableness increased throughout early and middle adulthood at varying rates; neuroticism declined among women but did not change among men.

Lounsbury et al (Lounsbury, 2003) uses the BFI - Transition to College (TTC) (Appendix - O) inventory for young adolescents, measuring *normal personality* characteristics in relation to students making the transition from high school to college. It consists of 118 items measuring personality traits, preferences, and personal style. In this thesis, the BFI-TTC was administered to young adolescents (11-16 years of age).

The BFI-TTC encompasses the "Big Five" personality traits (Table 2.6): Neuroticism (which we term here “Emotional Stability”), Extraversion, Openness, Agreeableness, and Conscientiousness. There is an emerging consensus that the Big Five represents a “grand unified theory” for personality (Digman, 1990) that is replicable for a wide range of cultures, age groups, and settings, including school and work (Digman, 1997). Consistent with an emerging literature base demonstrating that predictive validity can often be enhanced by using “Narrow” personality traits in addition to the Big Five (Ashton, 1998, Paunonen, 1998), the TTC includes the following personality dimensions Aggression, Career Decidedness, Leadership, Optimism,

Sense of Identity, Tough/Tender-Mindedness, Self-Directed Learning, and Work Drive.

Table 2.6: "Big Five" Personality Traits Measured by the Transition to College (TTC)

AGREEABLENESS	Agreeableness refers to being agreeable, participative, helpful, cooperative, and inclined to interact with others in a harmonious manner. High scorers tend to interact smoothly with other people, especially peers, and to be easygoing and accepting in group settings. Low scorers tend to be more outspoken, oppositional, contentious, argumentative, and divisive in group settings.
CONSCIENTIOUSNESS	Conscientiousness refers to being reliable, trustworthy, orderly, and rule-following. High scorers tend to dependable, disciplined, and organized as well as to have better study and work habits. They function better in structured settings. Low scorers tend to be more non-conforming and inclined to march to their own drummer, usually preferring spontaneity and a lack of structure. They function better in less structured settings.
EMOTIONAL STABILITY / RESILIENCE	Emotional Stability/Resilience (reverse of Neuroticism) reflects overall level of adjustment, resilience, and emotional stability. High scorers can function more effectively under conditions of stress and pressure, whereas low scorers are less stress-resistant, are frustrated more readily, and more subject to negative emotions.
EXTRAVERSION	Extraversion refers to being sociable, outgoing, lively, and warmhearted. High scorers tend to talk and socialize more, and they are more likely to actively participate in clubs, groups, and discussions. They tend to have extensive friendships and acquaintanceships. Low scorers tend to be introverted, quiet, focused, and reserved. They tend to have fewer but more intensive friendships.
OPENNESS TO NEW EXPERIENCE	Openness refers to receptivity to new learning, change, and novel experience. High scorers tend to be more willing to experiment and try new things, as well as to explore the world around them. Low scorers tend to prefer stability, convention, and tried-and-true ways of doing things

2.8.7 Level of hopefulness

Nunn et al (Nunn, 1996b) defines hope as the 'that general tendency to construct and respond to the perceived future positively'. The hopeful person subjectively assesses what is desired for the future to be probable or so important as to constrain believe and behaviour to the grounded upon its possibility. There are many reasons why hope should be considered to a greater degree than it has been in the past. First, the loss of hope has been shown to predict suicide as, or more powerfully, than depressive disorder (Beck et al., 1985, Wetzel et al., 1980). Second, the loss of hope and the generalisation of hopelessness has been implicated in the mediating pathway between social processes and the personal experience of depression (Nunn, 1996b). Thirdly, hope and despair contribute to therapeutic efficacy as a study factor, an outcome factor, an intervening variable and a recovering factor (Brown et al., 1992, Greene, 1989). Lastly, hope and the disorders of hope may be of central importance in mind-body interactions. The role of hope and the loss of hope in the precipitation, perpetuation and emotional burden of physical illness have been considered indirectly and qualitatively (Buehler, 1975, Schmale and Iker, 1971) and more recently directly and quantitatively (Elliott et al., 1991, Snyder et al., 1991). Considering personal hopefulness in this study, will lead to a revaluation of the significance of concepts as depression and anxiety (Nunn, 1996b).

The purpose of Hunter Opinions and Personal Expectations Scale (HO.P.E.S) (Appendix -P) was to measure personal hopefulness, focusing on essential components such as:

- Wish or desire

- Expectation and future orientation

H.O.P.E.S was the preferred instrument for this research study because:

1) it has excellent psychometric qualities.
2) Strong support for the H.O.P.E.S instrument's construct, concurrent and predictive validity (Nunn, 1996a, Nunn, 1996b, Nunn et al., 1996)
3) Correlates with other psychometric measures (e.g. STAI, BDI)

The overall score from the H.O.P.E.S measure (i.e. Hope subscale + 40 – Despair subscale) is best described as a measure of 'global personal hopefulness' (GPH) (Nunn, 1996a). Rather than defining this measure as clinical subgroups (i.e. like in the previous instruments of this chapter) it is probably more valuable to perceive this measure as a continuous index. However, in order gain a general perception of how subjects view their future; the following scoring method was applied:

- GPH score 0-36 = 'very low' or 'well below average' GPH
- GPH score 37-49 = 'low' of 'below average' GPH
- GPH score 50-62 = 'average' GPH
- GPH score 63-80 = 'high' or 'above average' GPH

Thus, a high total global personal hopefulness score indicated an excellent level of hopefulness for the future.

2.8.8 Cognitive Emotion Regulation Questionnaire (CERQ)

Cognitive emotion regulation can be understood as the cognitive way of managing the intake of emotionally arousing information (Garnefski, 2001, Garnefski, 2002,

Garnefski, 2006, Thompson, 1991). The regulation of emotions through cognitions is inextricably associated with human life and helps to manage emotions after the experience of stressful events. In all stages of life, people have to deal with a wide range of stressors and challenges to adapt to the world. As children grow older, their emotion regulation repertoire increases and shifts from primarily external, behaviourally oriented emotion regulation strategies to more internal cognitively based ones (Harris et al., 1981, Fields and Prinz, 1997, McCarty et al., 1999). By the age of eight or nine, young children have learned to regulate their emotions by means of cognitions or thoughts about themselves, their feelings or others. For example, when experiencing a negative event, some children may have thoughts of blaming themselves, while others may rather blame someone else.

The CERQ (Cognitive Emotion Regulation Questionnaire including CERQ-kids) (Appendix - Q) is a multidimenstional questionnaire constructed in order to identify the cognitive coping strategies someone uses after having experienced negative events or situations. Contrary to other coping questionnairs that do not explicity differentiate between an individual's thoughts and his or her actual actions, the present questionnaire refers exclusively to an individual's thoughts after having experienced a negative event. The CERQ is a very easy to administer, self-report questionnaire consisting of 36 items. The questionnaire has been contructed both on a theoretcal and empirical basis and measures nine different cogitive coping strategies. The CERQ makes it possible to identify individual cognitive coping strategies and compare them to norm scores from various population groups. In addition, the opportunity to investigate relationships between the use of specific cognitive coping strategies, other personality variables, psychopathology and other problems. The CERQ can be

administered in normal populations and clinical populations, both with adults and adolescents aged 12 years and over. Cognitions or cognitive processes help people regulate their emotions or feelings and not get overwhelmed by the intensity of these emotions, for example during or after experiencing a negative or stressful life event.

The CERQ is a self-report questionaire measuring cognitive coping strategies of adults and adolescents. In other words, with the help of this questionnaire it can be assessed what people 'think' after having experienced a negative or traumatic event. Cognitive coping strategies are defined here at strategies for cognitive emotion regulation, that is, regulating in a cognitive way the emotional responses to events causing the individual emotional aggravation (Thompson, 1991). Cognitive coping strategies are assumed to refer essentially to rather stable styles of dealing with negative life events, however not to such an extent that they can be compared to personality traits. It is assumed that in certain situations people may use specific cognitive strategies, which may divert from the strategies they would use in other situations. It may also be assumed that potentially cogitive coping strategies can be influenced, changed, learned and unlearned, for example through psychotherapy, intervention programmes or one's own experiences. The CERQ distinguishes nine different cognitive coping strategies, each consisting of four items measured on a 5-point Likert scale and each referring to what someone thinks after the experience of a stresssful life event. These are:

1. Self-blame - referring to thoughts of blaming yourself for what you have experienced
2. Acceptance – referring to thoughts of resigning to what has happened
3. Rumination – referring to thinking all the time about the feelings and thoughts associated with the negative event

4. Positive refocusing – which refers to thinking of other, pleasant matters instead of the actual event.
5. Refocus on planning – or thinking about what steps to take in order to deal with the event.
6. Positive reappraisal - or thinking of attaching a positive meaning to the event in terms of personal growth.
7. Putting into perspective or thoughts of playing down the seriousness of the event when compared to tother events.
8. Catastrophizing – referring to explicity emphasizing the terror of the experience.
9. Other-blame – referring to thoughts of putting the blame for what you have experienced on others.

The CERQ is suitable for use in different populations such as adolescents, adults, elderly people, students and psychiatric patients. Besides, experience has been gained in administering the questionnaire to groups of varoius educational backgronds. It has also turned out that the CERQ can be very well administered in a number of specific populations, such as chronically ill adolescents, individuals with fear of flying, groups of people characterised by having experienced similar types of traumatic events.

The psychometric properties of the CERQ have been proven to be good (Kraaij, 2006) (Garnefski, 2006). A number of previous studies have reported positively on the internal consistencies, factorial validity, construct validity and criterion-related (or predictive) validity of the CERQ scales (Garnefski, 2002) while strong relationships were found between the use of specific cognitive emotion regulation strategies of

rumination, catastrophizing and self-blame and the reporting of symptoms of depression. This might imply that by usign these strategies, people may be more vulnerable to developing symptoms of psychopathology in response to negative life events than others (Garnefski, 2002). Other outcomes suggested that people may more easily tolerate or master negative life experiences by using other cognitive styles, such as Positive Reappraisal. Internal consistency of the CERQ of the various subscales were assessed across the diverse populations which were good to very good (in most cases well over .70 and in many cases even over .80) (Garnefski, 2002). Research has shown that the subscales have good internal consistencies, with alaphas ranging from 0.67 to 081 (Garnefski, 2001, Garnefski, 2002)

2.8.9 Weinberger Adjustment Inventory

In order to demonstrate how self defning memory characteristics may reflect aspects of personality adjustment, defensiveness and distress, we selected the Weinberger Adjustment Inventory (WAI) (Appendix – R) (Weinberger, 1991). The WAI was designed to operationalize distress and self-restraint as dimension of social-emotional adjustment. It also includes scales of response and can be used as a 'lie detector' which will be use in this thesis. The two primary dimensions of self-restraint and subjective express of distress are measured in the WAI. The self-restraint includes intrapersonal (impulse control), interpersonal (suppression of aggression and consideration for others) and communal (responsability) aspects of socialisation. Low restraint is a characteristic in young children or individuals who do not regulate their impulses and affects succcessfully and is associated with problem behaviour such as durg use, delinquency and aggression (Farrell and Sullivan, 2000, Weinberger, 1998) .

Overcontrol is the result of soicalisation and can be more adaptive; however, individuals who are best socially and emotionallly adapted should show moderate self-restraint as they manage affect skillfully and do not become rigid or overly intellectualised (Asendorpf and van Aken, 1999, Hart et al., 1997) (Weinberger and Schwartz, 1990). The subjective experience to distress dimension has the subscales of trait anxiety, depression, low well being, and low self-esteem and it captures the self's own appraisal of its status in relation to personal goals as well as to external sources of threat .

Subjects are asked to complete the inventory based on ;what they are usually like' using a 5-point scale. The composite distress and restraint scale had internal consistencies of at least 0.91 and 0.85, respectively, across subsamples adolescents (Weinberger, 1991). In this thesis, the 37-item short form was used and subjects were classified as being repressors or nonrepression using the cutoff suggested by Weinberger (Weinberger, 1991).

2.9 DATA ANALYSIS

2.9.1 Software

Following database entry, data were generally exported following appropriate execution of 'queries' into a spreadsheet application (Microsoft ® Excel 97, SR-1, Microsoft Corporation, Santa Rosa, CA, USA). After manipulation within this format, further statistical analysis and graphic presentation of data were performed using a combination of computerised statistical packages including Package for the Social

Sciences (SPSS® Version 16, Chicago Illinois USA) and GraphPad Prism® 5.02 Inc (GraphPad Software 1992-2009 La Jolla, CA 92037
USA).

2.9.2 Statistical analysis

Specific statistical analyses are described within the chapters to which they refer. Deviations from a Gaussian distribution were tested using the Kolmogorov-Smirnov test. In general, most data comparison was performed with non-parametric analyses based on the distribution of data points. The Mann-Whitney U-test was used for comparison of 2 independent populations of non-parametric numeric data, and the Wilcoxon rank-sum test for paired sets of data. Contingency analyses were performed using Fisher's exact (2 rows and columns in contingency table) or chi-square tests (more than 2 rows or 2 columns in contingency table). A two-tail *p* value was calculated in all cases ($p < 0.05$ was considered significant).

Linear correlation or regression was used to compare the covariation of 2 numeric variables. In simple terms, regression was chosen when X values were controlled e.g. age. When linear regression analysis was used, 95% confidence intervals (CI), goodness of fit (r2), and residuals were calculated. When correlation was applied, parametric (Pearson correlation) or non-parametric (Spearman correlation) methods were used as appropriate. For all tests, $p < 0.05$ was considered to show a significant difference.

CHAPTER 3

RESULTS (Part I)

3.0 RESULTS - Part I

3.1 DEMOGRAPHICS FOR ALL SUBJECTS

3.1.1 Age and sex

The study population comprised 149 subjects with 91/149 males (61.1%) and 58/149 females (38.9%) (Table 3.1). There was a male predominance found overall ($p<0.01$) with higher frequency of males than females in the anorectal anomalies (ARA) and idiopathic constipation (IC) groups (Table 3.1). In each group there are 52/149 (34.9%) patients with ARA and the control groups consists of 46/149 (30.9%) patients with IC and 51/149 (34.2%) subjects who have undergone an appendectomy (healthy controls).

Table 3.1: Distribution of sex in all groups

Group	**Male**	**Female**	*Total*
Anorectal Anomalies	33 (63.5%)	19 (36.5%)	*52*
Idiopathic Constipation	33 (71.7%)	13 (28.3%)	*46*
Healthy controls	25 (49.0%)	26 (51.1%)	*51*
Total	*91*	*58*	*149*

$\chi 2 = 5.44$; df 2; $p = 0.066$

Age groups for the entire sample consisted of two groups i) 103/149 subjects between the ages of 11-18 (69.1%) and ii) 46 subjects > 18 years of age (30.9%) (Table 3.2,

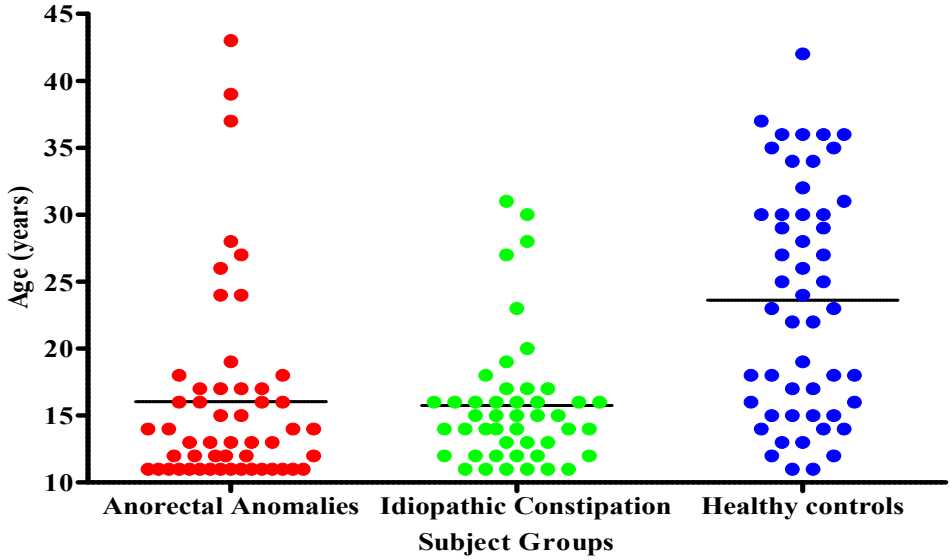
Figure 3.1). There was significantly a higher number of the second age group (>18 years) in the healthy controls (p<0.0001) in comparison to ARA and IC groups (Table 3.2). There was a significance between age and gender (p = 0.009) with a higher frequency of males between the ages 11-18 years (70 males; 33 females) than subjects > 18 years of age (21 males; 25 females).

Table 3.2: Distribution of age groups in all groups

Groups	**11-18 years**	**> 18 years**	*Total*	Mean (+/- SD)
Anorectal Anomalies	43 (82.7%)	9 (17.3%)	*52*	16.04 (+/- 7.37)
Idiopathic Constipation	39 (84.8%)	7 (15.2%)	*46*	15.76 (+/-4.89)
Healthy controls	21 (41.2%)	30 (58.8%)	*51*	23.63 (+/-8.66)
Total	*103*	*46*	*149*	*18.55(+/-8.05)*

$\chi 2 = 28.44$; df 2; p <0.0001

Figure 3.1: Age Distribution of all Groups



3.1.2 Ethnicity

Ethnicity was divided into the following groups: Caucasian, Asian, African-Caribbean or those who did not wish to state their ethnicity ('not stated'). Overall, the majority of our population were Caucasian in the total study population (73/149) (49.0%) (Table 3.3). There was significantly a higher distribution of Asian ethnicity (16/23) (69.6%) in healthy controls, in comparison to IC (1/23) (4.31%) and ARA (6/23) (2.61%) ($p = 0.005$) (Table 3.3).

Table 3.3: Distribution of ethnicity in all groups

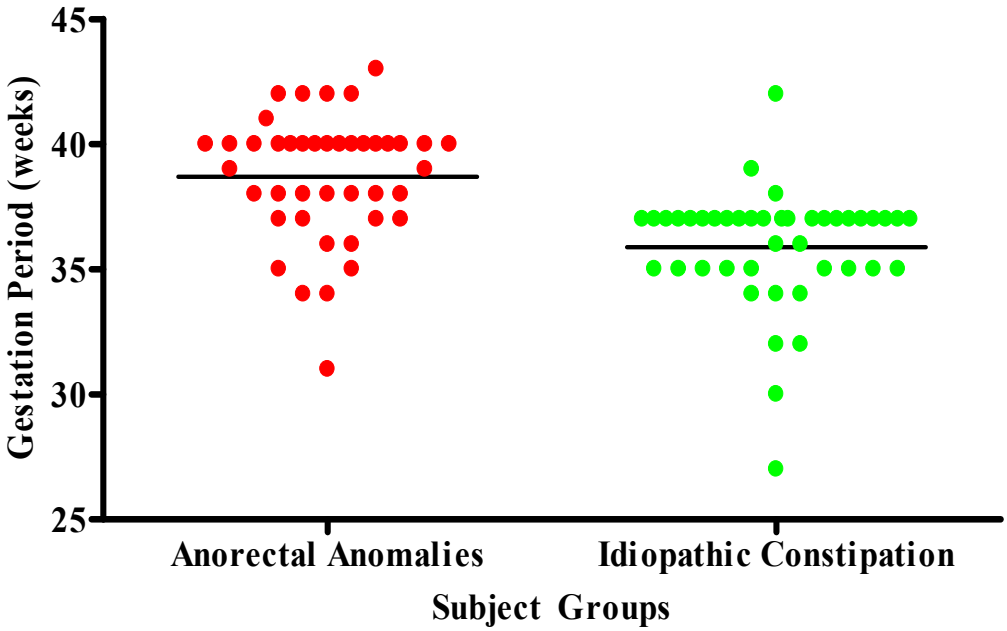
Group	**Caucasian**	**Asian**	**African-Caribbean**	**Not-stated**	*Total*
Anorectal Anomalies	28 (53.8%)	6 (11.5%)	3 (5.8%)	15 (28.8%)	*52*
Idiopathic Constipation	23 (50.0%)	1 (2.2%)	3 (6.5%)	19 (41.3%)	*46*
Healthy controls	22 (43.1%)	16 (31.4%)	1 (2.0%)	12 (23.5%)	*51*
Total	*73*	*23*	*7*	*46*	*149*

$\chi 2 = 18.61$; df 6; $p < 0.005$

3.1.3 Gestation

The gestation period ranged from 27 to 43 weeks gestation (Mean 37.3 +/- 2.81) (Figure 3.2). There was a significantly longer gestation period found in ARA than IC ($p<0.0001$, Mann Whitney test) in the study population.

Figure 3.2: Distribution of Gestation Period



3.2 ANORECTAL ANOMALY GROUP

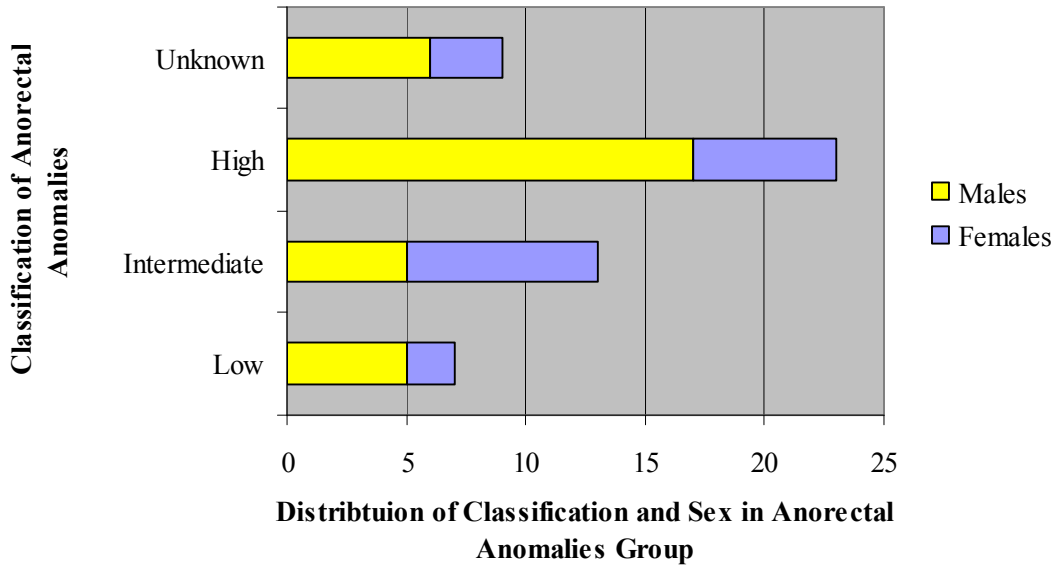
As discussed in Chapter 1, in this thesis we will be using the Wingspread International Classification in order to analyse the results. In the ARA sample, there were 7 patients with a low defect, 13 with intermediate and 23 with a high defect and 9 patients unknown (Table 3.4). Classifying them in terms of type of anorectal anomalies can be difficult due to the lack of documentation, however in our population 29/52 were specified: 4 cloaca, 6 anorectal agenesis, 4 rectovesical fistula, 3 rectourethral fistula, 2 rectovulvar fistula, 1 sacral agenesis, 1 anal stenosis, 1 rectovaginal, 4 rectovestibular fistula and 3 no fistula. There was a male predominance found in each classification which was significant ($p<0.03$) (Figure 3.3).

Table 3.4: Wingspread international classification for anorectal anomalies

Group	Male	Female	*Total*
High	17 (73.9%)	6 (26.1%)	*23*
Intermediate	5 (38.5%)	8 (61.5%)	*13*
Low	5 (71.4%)	2 (28.6%)	*7*
Unknown	6 (66.7%)	3 (33.3%)	*9*
Total	*33*	*19*	*52*

$\chi 2 = 4.82$; df 3; $p = 0.19$

Figure 3.3 Distribution of Wingspread Classification and Sex in Anorectal anomalies



3.2.1 Type of Reconstructive Surgery

The most common type of reconstructive surgical approach used in our ARA population sample was the posterior sagittal anorectoplasty (PSARP) including the modified version (Table 3.5).

Table 3.5: Type of Reconstructive Surgery for anorectal anomalies

Type of reconstructive surgery	**Number (%)**
Posterior sagittal anorectoplasty (PSARP)	32 (62)
Abdominal perineal pull through (ABpt)	2 (4)
Combination of PSARP and ABpt	3 (6)
* Other	7 (14
Unknown	8 (15)

* These included: anal transposition and other perineal pull through

3.2.2 Associated conditions

As mentioned in Chapter 1, ARA occur commonly in multi-anomaly sequences, such as the VACTERL (vertebral, anorectal, cardiac, trachea-oesophageal, renal and limb (radius). In our population sample, 24/52 (46%) of patients with ARA had associated VACTERL conditions. Other conditions not associated with the VACTERL list were found in 8 patients such as: asthma, eczema, ophthalmologic problems, deafness, epilepsy, spina bifida and diabetes. There is a higher incidence of VACTERL in patients with a high defect (13/24) (54.2%) in comparison to low (1/24) (4.2%). One patient in our ARA population sample had a history of child physical abuse (Table 3.6).

Table 3.6: Distribution of VACTERL/Other conditions with anorectal anomalies classification

Anorectal Anomalies	High	Intermediate	Low	Unknown
VACTERL	13	8	1	2
Other Conditions	5	1	1	1
Total	*18*	*9*	*2*	*3*

3.3 REPRESENTATION OF OUR CONTROL GROUPS

3.3.1 Idiopathic Constipation

The study sample comprised 46 subjects with IC with 33 males (72%) and 13 females (28%) (Table 3.1) diagnosed ≥ 5 years of age. As discussed in Chapter 1, there is a subgroup of patients with functional constipation which have persistent dilation of the rectum and/or colon, termed idiopathic megarectum (Holdstock et al., 1970) (Gladman et al., 2007). In our patients with IC, 13/46 (28%) were diagnosed soley with a megarectum, 13/46 (28%) with a slow transit and 11/46 (24%) with both a megarectum and slow transit.

In our IC population sample, 8/46 (17%) had VACTERL conditions (i.e. not related to bowel habit). Other conditions not associated with the VACTERL list were also found which included: asthma, eczema, dyslexia, diabetes, obesity, hearing difficulties, hypothyroidism, autism, Perthes disease, dysprexia and Ehlers-Danlos syndrome.

3.3.2 Appendectomy (Healthy Controls)

In this thesis, the negative disease control group included patients who have been diagnosed with appendicitis and have had surgery (appendectomy). Thus they are categorised as our 'healthy control' group. They have been treated for a condition entirely separate from the area that our patients ARA and IC individuals share in common. The study sample comprised 51 subjects who have had an appendectomy with 25 males (49%) and 26 females (51%) (Table 3.1). All subjects had their appendectomy more than 1 year ago (1980-2006), prior to taking part in this research. Other conditions noted in this group included a variety of symptoms/diseases such as: hard of hearing (temporary deafness), asthma, insomnia and three patients had a history of haemorrhoids. As discussed in Chapter 2, all groups filled out the Pennebaker Inventory of Limbic Languidnes (PILL) which is a 54 item scale that assesses the frequency of common physical symptoms and sensations. This will be discussed in Chapter 4 (Part II).

3.4 OTHER TREATMENT MODALITIES

3.4.1 Antegrade Continence Enema

As discussed in Chapter 1, a surgical treatment offered to children suffering from chronic constipation and FI is the antegrade continence enema (ACE), also known as the Malone antegrade continence enema. In our population sample, 40/98 (40.8%) patients had an ACE stoma comprising 25 males and 15 females (Table 3.7) with a

mean age of 14 years old (age range 11-19 years old). In the ACE population, 21/40 (41%) were ARA (Table 3.7) including 12 with a high, 4 with an intermediate and 1 with a low defect anomaly. Additionally, 19/40 (48%) patients with IC have had the ACE stoma (Table 3.7), 11 of which have a megarectum.

Table 3.7: Wingspread International Classification in ACE population

Group	**Male**	**Female**	*Total*
Anorectal anomalies	12 (57.1%)	9 (42.9%)	*21*
Idiopathic Constipation	13 (68.4%)	6 (31.6%)	*19*
Total	*25*	*15*	*40*

Fisher's exact test p = 0.527

In this ACE population, 10/40 (25%) of patients had their ACE stoma closed (Table 3.8). Reasons for closing the ACE stoma were due to i) success of treatment (improved symptoms); ii) non-compliance; iii) no improvement to the patient's symptoms and opted for other treatment modalities; iv) didn't like the ACE (physically and psychologically) and/or v) time consuming to fit in their daily lifestyle.

Table 3.8: ACE distribution in patients with anorectal anomalies and idiopathic constipation

Patient Groups	**Open ACE**	**Closed ACE**	*Total*
Anorectal anomalies	15 (71.4%)	6 (28.6%)	*21*
Idiopathic constipation	15 (78.9%)	4 (21.1%)	*19*
Total	*30*	*10*	*40*

3.4.2 Medication

As discussed in Chapter 1, patients use a variety of medications to resolve their ongoing symptoms such as FI and constipation (Table 3.9). Both stimulant and osmotic laxative are the most common type of medication used in our population. In our population sample, 33/52 (63.5%) patients with ARA and 41/46 (89.1%) in IC have used or are using more than one type of medication to resolve their symptoms. There are 6 in ARA and 3 in IC, who currently don't use any form of medication.

Table 3.9: Use of medication in anorectal anomalies and idiopathic constipation

Medication	**Anorectal Anomalies**	**Idiopathic Constipation**	*Total*
Bulk forming laxatives	4 (28.6%)	10 (71.4%)	*14*
Stimulant laxatives	39 (48.8%)	41 (51.3%)	*80*
Faecal softeners	4 (44.4%)	5 (55.6%)	*9*
Osmotic laxatives	33 (47.1%)	37 (52.9%)	*70*
Bowel cleansing solutions	6 (25.0%)	18 (75.0%)	*24*

Pearson $\chi 2 = 5.88$; df 4; $p = 0.208$

3.5 SYMPTOM SCORES

3.5.1 Knowles-Eccersley-Scott-Symptom (KESS) - Constipation

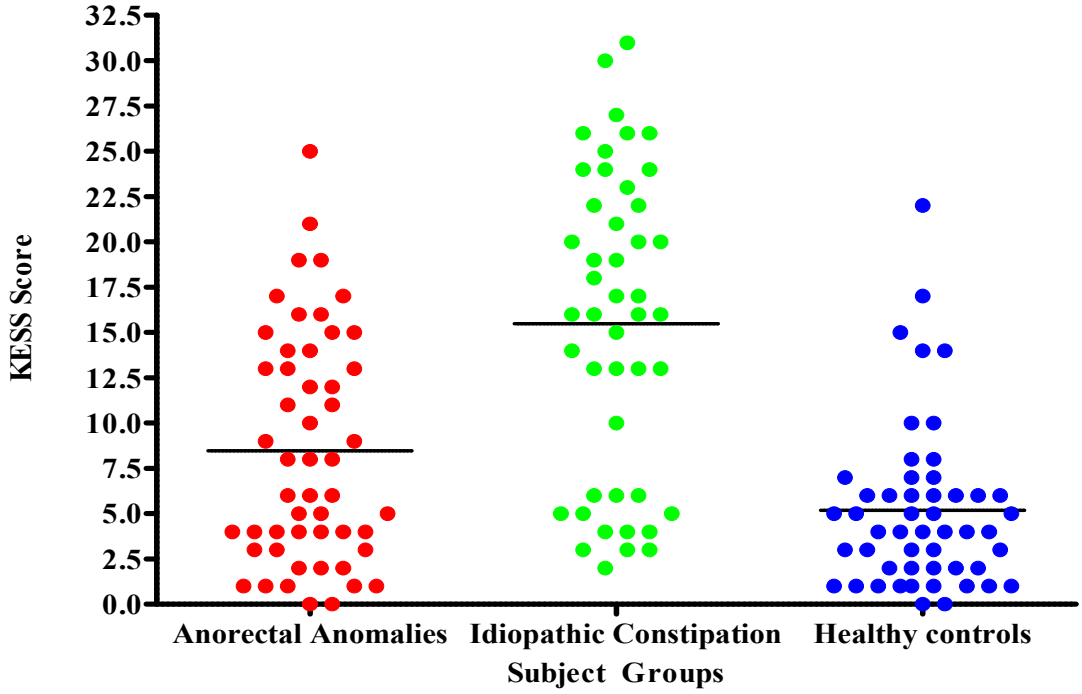
The Knowles-Eccersley-Scott-Symptom (KESS) questionnaire (Appendix) was used to assess for ongoing symptoms of constipation. The total KESS score is the sum of all scores gained on individual questions with a maximum possible of 39 points. The answers to each question were worded such that any patient who fitted agreed criteria (Whitehead, 1991) for constipation would be likely to score at least one point per question. A score of ≥ 5 points was considered abnormal in this thesis and a score of >12 were considered severe ongoing symptoms of constipation. The highest mean score was found in the IC group (15.48 +/-8.43) in comparison to ARA and healthy controls (Table 3.10, Figure 3.4). Statistical analysis included a 1-way ANOVA, with a significantly higher KESS score found in patients with IC (<0.0001) compared to ARA and healthy controls (Adjusted r^2 0.2874). Overall a total of 53/149 (36%) had severe constipation according to the KESS score (Table 3.10), with IC having the highest number (32/149) (21.5%) (Table 3.10).

Table 3.10: Summary of KESS scores in all groups

Groups	**Score < 5**	**Score 5-12**	**Score > 12**	**Mean (+/-SD)** * ***CI of mean***
Anorectal anomalies	20 (37.0%)	16 (38.1%)	16 (30.2%)	8.48 (+/-6.317) *(6.722-10.24)*
Idiopathic constipation	7 (13.0%)	7 (16.7%)	32 (60.4%)	15.48 (+/-8.427) *(12.98-17.98)*
Healthy controls	27 (50.0%)	19 (45.2%)	5 (9.4%)	5.176 (+/-4.573) *(3.890-6.463)*
Total	*54*	*42*	*53*	

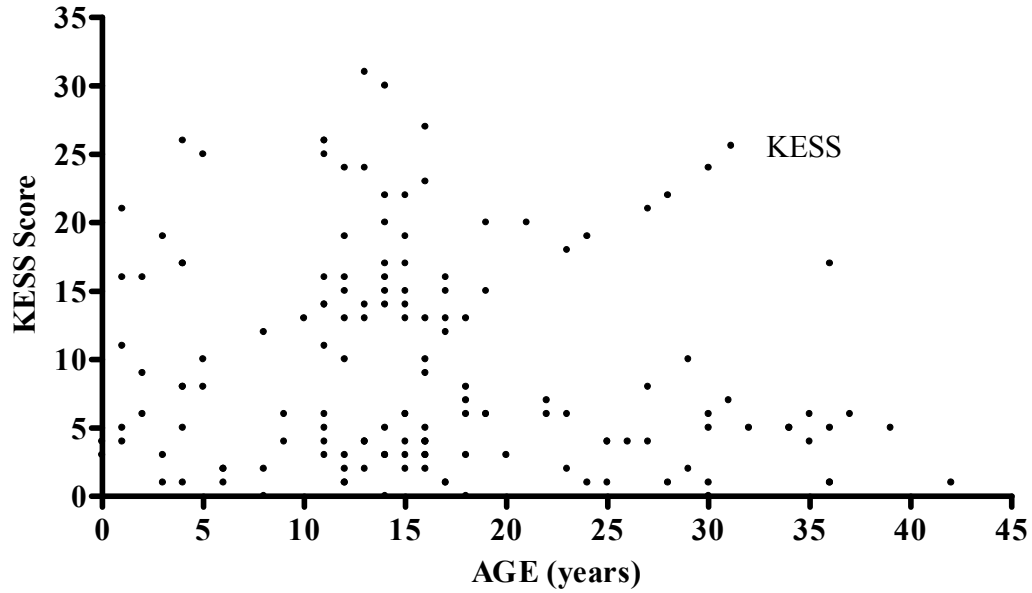
*** CI of mean (Lower - Upper 95%)**

Figure 3.4: The KESS Score (Constipation) in all groups



There was no significant relationship between age of subject and KESS score (Figure 3.5). Linear regression analysis can be demonstrated in Figure 3.5 ($r^2 = 0.028$).

Figure 3.5: Linear regression of age and KESS scores in all groups



3.5.2 Vaizey Incontinence Score

The 'Vaizey Incontinence Questionnaire' consists of seven questions. A score of 0 suggests no problems with bowel continence (complete continence), and a score of 24 suggests very severe problems with incontinence (complete incontinence). A Vaizey Incontinence score of at least 12 is considered poor (Deutekom et al., 2007, Deutekom et al., 2005) (Dobben et al., 2007) (Terra et al., 2006a, Terra et al., 2006b) (Terra et al., 2008) (Felt-Bersma et al., 2007). The IC had a higher mean Vaizey Incontinence score (7.26 SD +/- 7.01) in comparison to ARA and healthy controls (Table 3.11, Figure 3.6). Partial to full incontinence was evident in 11/13 and 12/13 patients with a megarectum and slow transit respectively (Table 3.12)

Statistical analysis included a 1-way ANOVA (Kruskal Wallis), with a significantly higher Vaizey score found in patients with ARA (<0.0001) and IC (0.0002) compared healthy controls (Adjusted r^2 0.1989).

Table 3.11: Summary of Vaizey Incontinence scores in all groups

Groups	**Perfect Continence**	**Partial Incontinence**	**Full Incontinence**	**Mean (+/-SD)** ^{N} ***CI of mean***
Anorectal anomalies	20 (27.0%)	21 (58.3%)	11 (44.0%)	5.87 (+/-6.639) *(4.017-7.714)*
Idiopathic constipation	14 (18.9%)	16 (44.4%)	16 (64.0%)	7.26 (+/-7.006) *5.180-9.341)*
Healthy controls	41 (55.4%)	10 (27.8%)	0 (0.0%)	0.63 (+/1.496) *(0.2067-1.048)*
Total	*74*	*36*	*25*	

***N* CI of mean (Lower - Upper 95%)**

Figure 3.6: Vaizey Incontinence scores for patient groups

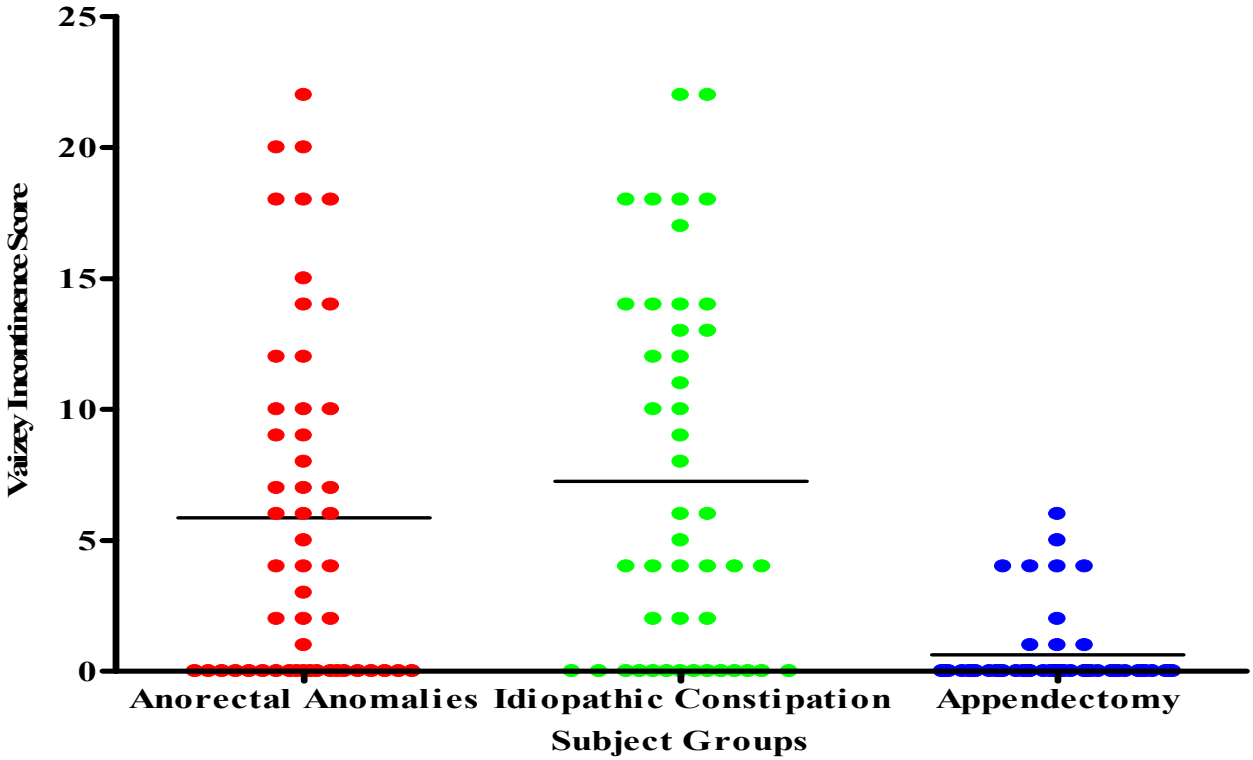


Table 3.12: Vaizey incontinence score in patients with IC and megarectum

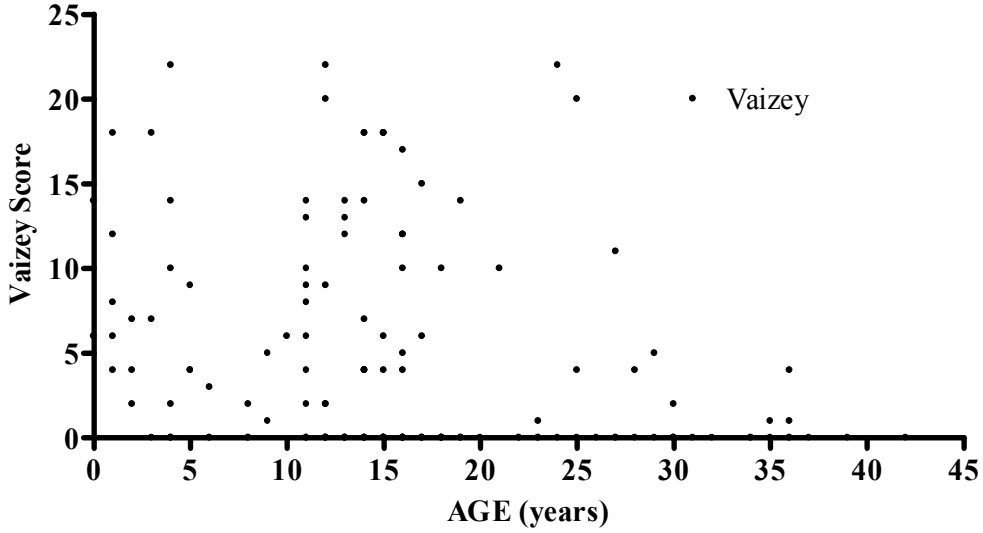
	Perfect Continence	**Partial continence**	**Full incontinence**	**TOTAL**
Megarectum	2	4	7	13
Slow transit	1	6	6	13
Megarectum & slow transit	7	3	1	11
* Unknown	4	3	2	9

* Absence of information within medical notes

There was no significant relationship between age of subject and KESS score (Figure 3.7). Linear regression analysis can be demonstrated in Figure 3.7 ($r^2 = 0.076$).

3.5.3 Symptom scores and ACE

Figure 3.7: Linear regression of age and Vaizey Incontinence score in all groups



On the KESS score, IC had significantly a higher KESS mean score of 18.79 (+/-8.08) compared to ARA 10.19 (+/-8.08) ($p<0.001$ Mann Whitney t test) (Table 3.13). A score of >12 is considered severe constipation, which was found mostly in the IC group (16/19) (84.2%) compared to ARA (8/21) (38.1%).

On the Vaizey Incontinence Score, IC had a higher total mean score 9.74 (+/-6.95) compared to ARA 5.86 (+/-5.42), yet there was no statistical significance (Table 3.14). In IC, there are a higher number of patients who are fully incontinent (10/19)

(52.6%) compared to perfectly clean (3/19) (15.8%) compared to ARA group (5/21, 3/21 respectively) (Table 3.13).

Table 3.13: Distribution of KESS Score in the ACE population

Groups	**Score < 5**	**Score > 5**	**Mean (+/-SD) (Range) * *CI of mean***
Anorectal anomalies	6 (75.0%)	15 (46.9%)	10.19 (+/-18.79) (1-25) *7.15-13.24*
Idiopathic constipation	2 (25.0%)	17 (53.1%)	18.79 (+/-8.08) (3-30) *14.90-22.68*
Total	*8*	*32*	

*** CI of mean (Lower - Upper 95%)** Fisher's exact test p = 0.241

Table 3.14: Distribution of Vaizey Incontinence scores in the ACE population

Groups	**Perfect Continence**	**Partial Incontinence**	**Full Incontinence**	**Mean (+/-SD) (Range) * *CI of mean***
Anorectal anomalies	5 (62.5%)	13 (68.4%)	3 (23.1%)	5.86 (+/-5.42) (0-20) *3.39-8.32*
Idiopathic constipation	3 (37.5%)	6 (31.6%)	10 (90.9%)	9.74 (+/-6.95) (0-22) *6.39-13.09*
Total	*8*	*19*	*13*	

*** CI of mean (Lower - Upper 95%)**

CHAPTER 4

RESULTS (Part II)

4.0 RESULTS Part II

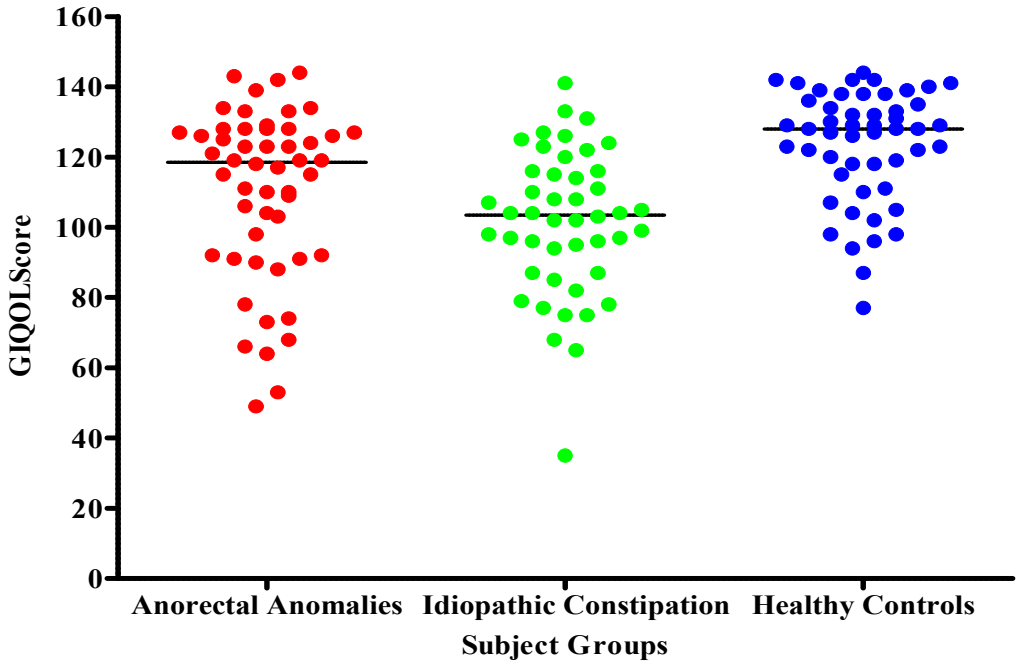
4.1 PSYCHOSOCIAL AND QOL MEASURES

As discussed in Chapter 2, psychosocial measures for this thesis included specific measures of quality of life (specific to gastrointestinal symptoms), coping mechanisms, depression, anxiety, personality, general health and level of hopefulness (Table 2.4). This chapter will provide a detailed analysis for each psychosocial measure, correlating it with symptom scores as discussed in Chapter 3. Lastly, an overview of the psychosocial measures in the ACE population will be presented separately.

4.1.1 The Gastrointestinal Quality of Life Index Questionnaire (GIQOL)

As discussed in Chapter 2, the gastrointestinal quality of life index (GIQLI) contains up to 36 items, scored on a five point Likert scale (range 0-144, higher score = better quality of life), in which additional modules specified by the particular gastrointestinal disease, supplement a set of core questions. It consists of five subscales: physical well being, gastrointestinal digestion, gastrointestinal defecation, mental well being and other which is summarized in an overall score. The lowest total GIQOL mean score was found in the IC group (101.4 SD+/-20.69) in comparison to ARA and healthy controls (Table 4.1, Figure 4.1). In addition to the total GIQOL score, IC had the lowest mean score in the majority of the GIQOL subgroups in comparison to ARA and healthy controls (Table 4.1)

Figure 4.1: Gastrointestinal Quality of Life (GIQOL) Scores



Statistical analysis included a 1-way ANOVA (Krushkal-Wallis test, Dunn's Multiple Comparison test), indicating significance between the three groups (Adjusted r^2 = 0.152). There is a significantly poorer total GIQOL score found in patients with IC compared to healthy controls ($p<0.001$) and ARA compared to healthy controls ($p<0.01$) (Figure 4.1). There was no significant difference found between ARA and IC ($p>0.05$). The poorest GIQOL scores for physical well being was significantly poorer in patients with IC compared to ARA ($p<0.01$) and IC compared to healthy controls ($p<0.001$) (Table 4.1) (Figure 4.2 A). Additionally, ARA had significantly poorer GIQOL scores for physical well being compared to healthy controls ($p<0.01$). IC had significantly poorer GIQOL scores for gastrointestinal digestion symptoms compared to healthy controls ($p<0.01$) (Table 4.1) (Figure 4.2 B). ARA had significantly poorer GIQOL life scores for gastrointestinal defaecation symptoms compared to healthy controls ($p<0.001$) and IC also had poorer GIOQL scores for gastrointestinal symptoms compared to healthy controls ($p<0.01$) (Table 4.1) (Figure

4.2 C). In terms of mental state, ARA had significantly poorer GIOQL score to healthy controls (<0.05) and IC had significantly poorer mental state to healthy controls (p<0.001). Items not included in a subscale ('other') included questions on restricted eating, wake up at night, bothered by treatment, worsened relations and dysphasia. ARA had poorer GIQOL 'other' scores, compared to healthy controls (p<0.01) and IC had also poorer GIQOL scores for 'other' compared to healthy controls (p<0.01).

Table: 4.1: Statistical Analysis for GIQOL scores for all Groups

Subject Groups **(Score range)**	**Anorectal Anomalies** Mean (+/-SD) (Range) * *CI of mean*	**Idiopathic Constipation** Mean (+/-SD) Range *CI of mean*	**Healthy controls** Mean (+/-SD) Range *CI of mean*
GIQOL Total **(0-144)**	110.2 (+/-24.05) (49-144) *103.5-116.9*	101.4 (+/-3.05) (35-141) *95.29-107.6*	123.5 (+/-5.58) (77-144) *119.0-127.9*
Subgroups			
Physical well being (0-40)	30.44 (+/-7.14) (10-40) *28.46-32.43*	26.04 (+/-6.68) (7-40) *24.06-28.03*	34.12 (+/-5.58) (13-40) *32.55-35.69*
Gastrointestinal digestion (0-40)	30.60 (+/-7.02) (11-40) *28.64-32.55*	28.17 (+/-7.01) (15-40) *26.09-30.26*	33.08 (+/-5.43) (20-40) *31.55-34.61*
Gastrointestinal defaecation (0-24)	19.31 (+/-4.27) (6-24) *18.12-20.50*	19.54 (+/4.34) (6-24) *18.25-20.83*	21.92 (+/-3.3) (7-24) *20.99-22.86*
Mental well being (0-20)	14.13(+/-4.77) (3-20) *12.81-15.46*	13.35 (+/-4.25) (4-20) *12.08-14.61*	16.41 (+/-3.52) (6-20) *15.42-17.40*
Other (0-20)	15.50 (+/-4.02) (4-20) *14.38-16.62*	15.24 (+/-4.13) (1-20) *14.01-16.47*	17.75 (+/-2.73) (10-20) *16.98-18/51*

* Lower –Upper 95% CI of mean

Figure 4.2 GIQOL Subgroup Scores for all groups (A: Physical well being; B: Gastrointestinal digestion; C: Gastrointestinal defaecation; D: Mental well being)

Figure 4.2 (A) Physical well being

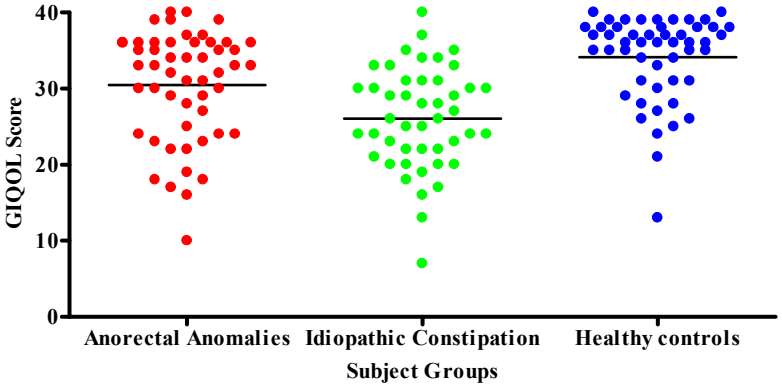


Figure 4.2 (B) Gastrointestinal Digestion

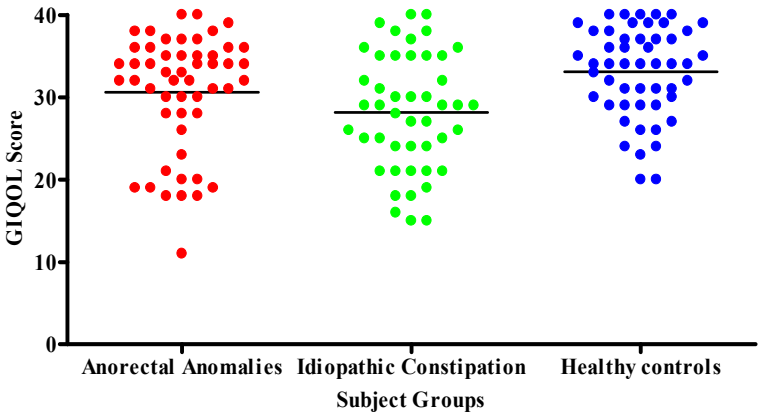


Figure 4.2 (C) Gastrointestinal Defaecation

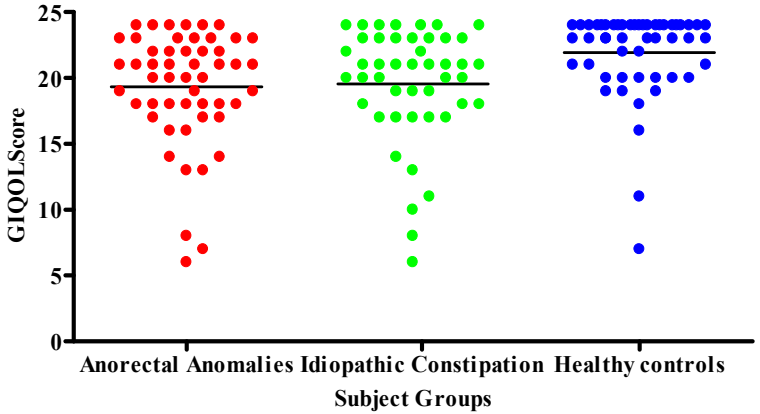
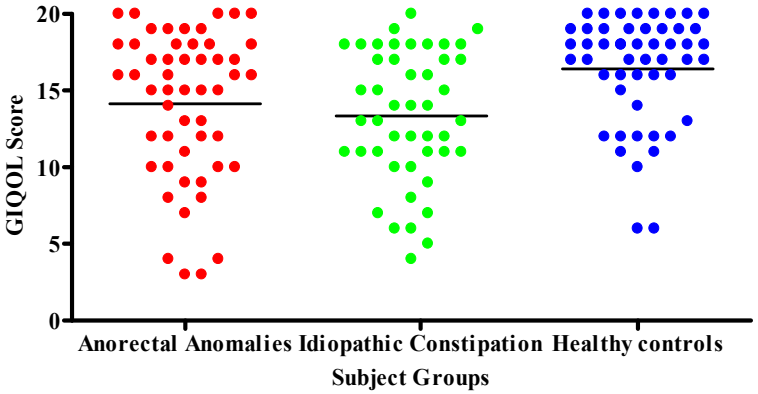


Figure 4.2 (D) Mental well being



4.1.1.1 Relationship with GIQOL and Symptoms Scores

Statistical analysis included a Fisher's exact test to evaluate the relationship between GIQOL and symptoms scores. Subjects who had a higher KESS score, significantly had poorer GIQOL scores (65/81) compared to those with normal KESS scores (16/81) ($p<0.0001$) (Table 4.2, 4.4, Figure 4.3). There was a significant difference with GIQOL and Vaizey Incontinence Scores, whereby subjects with full incontinence significantly had poorer GIQOL compared to good GIQOL ($p<0.0001$ $\chi 2$ 22.16, df 2) (Table 4.3, 4.4, Figure 4.4)

Table 4.2: Relationship between GIQOL and KESS scores

GIQOL	**Poor GIQOL**	**Good GIQOL**	*Total*
*** KESS <5**	16 (29.1%)	39 (40.1%)	*55*
KESS ≥ 5	65 (69.1%)	29 (30.9%)	*94*
Total	*81*	*68*	*149*

* KESS < 5 (normal); ≥ 5 (abnormal); Fisher's exact test $p<0.0001$

Table 4.3: Relationship between GIQOL and Vaizey Incontinence scores

GIQOL	**Poor GIQOL**	**Good GIQOL**	*Total*
Full continence	30 (40.0%)	45 (60.0%)	*75*
Partial Incontinence	26 (55.3%)	21 (44.7%)	*47*
Full Incontinence	25 (92.6%)	2 (7.4%)	*27*
Total	*81*	*68*	*149*

$\chi 2 = 22.16$; df 2; $p < 0.0001$

Additionally, there was a significant relationship between poor quality of life and high KESS score ($p < 0.003$) and high Vaizey incontinence score ($p<0.02$) in patients with ARA (Table 4.4). There was no significant relationship between type of anorectal defect and GIQOL score. Healthy controls who had abnormal KESS scores (24/51) (47.1%), had significantly poorer GIQOL scores (12/24) (50.0%) than those with normal KESS score with poor GIQOL score 3/27) (11.1%) ($p<0.005$) (Table 4.4).

Figure 4.3: Relationship between GIQOL and KESS

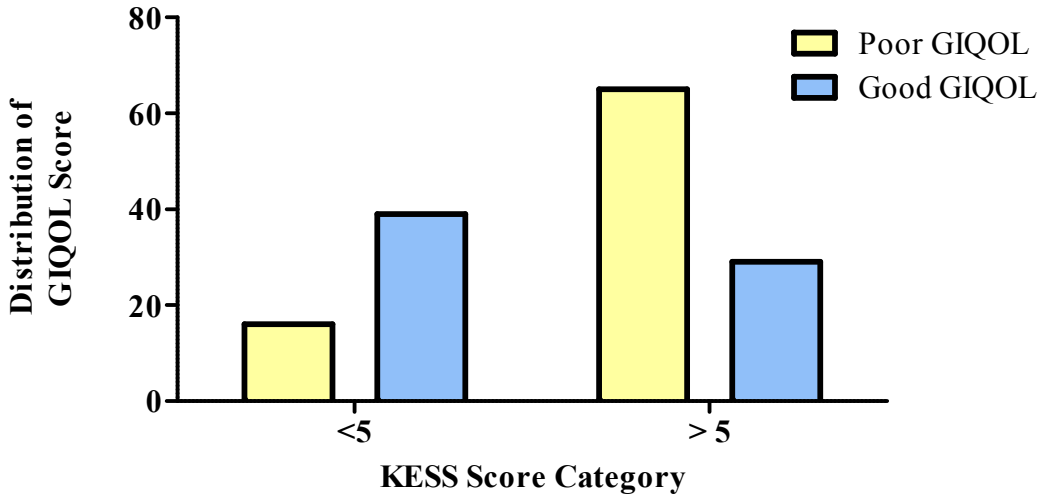


Figure 4.4: Relationsihp between GIQOL and Vaizey Score

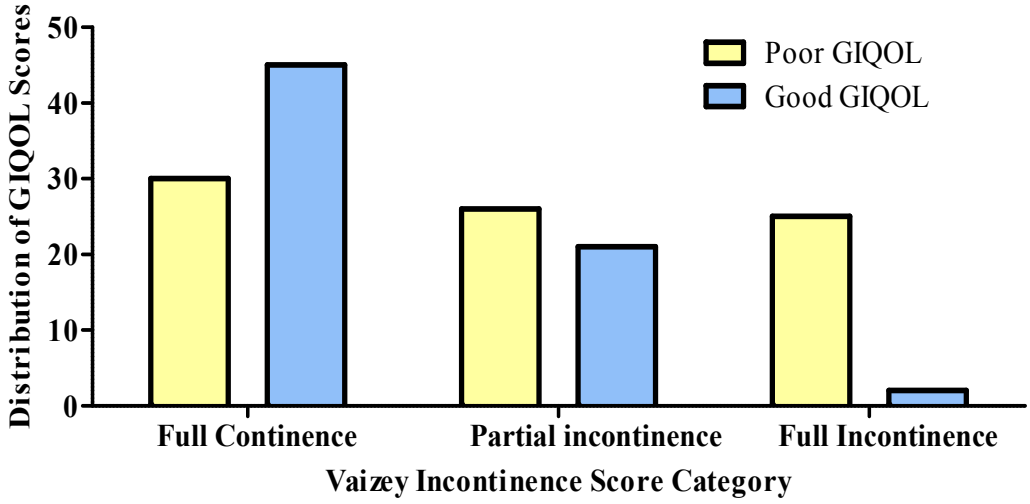


Table 4.4: GIQOL with symptoms scores

GIQOL	Good GIQOL			Poor GIQOL			
	ARA (%/Total)	*IC (%/Total)*	*HC (%/Total)*	*ARA (%/Total)*	*IC (%/Total)*	*HC (%/Total)*	*Total*
Symptom Scores							
KESS							
< 5 (normal)	15 (65%)	0	24 (67%)	6 (21%)	7 (19%)	3 (20%)	
> 5 (abnormal)	8 (35%)	9 (100%)	12 (33%)	23 (79%)	30 (81%)	12 (80%)	
Total	*23*	*9*	*36*	*29*	*37*	*15*	*149*
VAIZEY							
Full continence	12 (52%)	2 (2%)	31 (86%)	8 (28%)	12 (32%)	10 (67%)	
Partial Incontinence	10 (43%)	6 (66%)	5 14%)	11 (38%)	10 ((27%)	5 (33%)	
Full Incontinence	1 (4%)	1 (1%)	0	10 (34%)	15 (41%)	0	
Total	*23*	*9*	*36*	*29*	*37*	*15*	*149*

Legend: ARA (anorectal anomalies); IC (idiopathic constipation); HC (healthy controls)

4.1.2 Hunter Opinions and Personal Expectations Scale (HO.P.E.S)

The purpose of Hunter Opinions and Personal Expectations Scale (HO.P.E.S) was to measure personal hopefulness, focusing on essential components such as wish or desire and/or expectation and future orientation. As discussed in Chapter 2, the overall score from the H.O.P.E.S measure (i.e. Hope subscale + 40 – Despair subscale) is best described as a measure of 'global personal hopefulness' (GPH) (Nunn, 1996a).

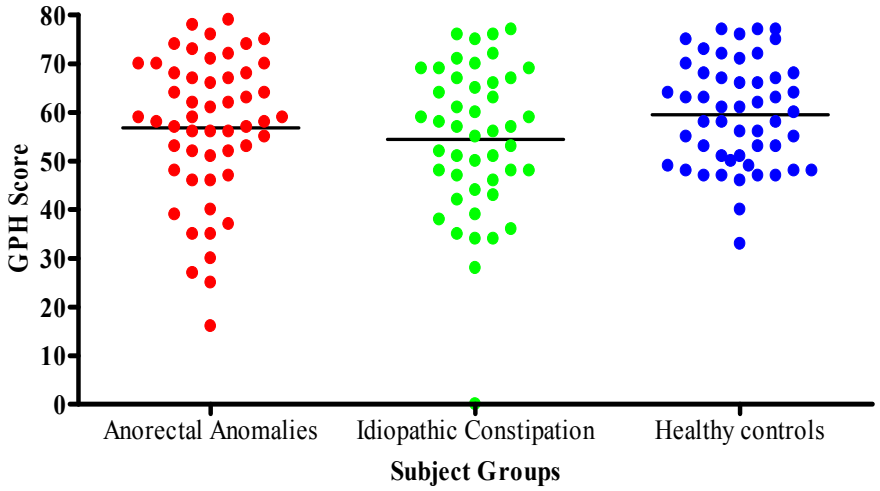
The highest GPH score was found in healthy controls compared to ARA and IC (Table 4.2, Figure 4.5), however there was no significance relationship between these groups ($p > 0.05$; Adjusted $r^2 = 0.002$). Additionally, there was no significant differences between the three groups for the hopes and despair subgroups (p>0/05) (Table 4.5)

Table 4.5: Mean scores for Global Personal Hopefulness in all groups

Groups	**Anorectal Anomalies**	**Idiopathic constipation**	**Healthy controls**
GPH (Mean (+/-SD)	56.85 (+/-14.67)	54.46 (+/-15.36)	59.49 (+/-10.75)
* CI of mean	52.8-60.9	49.9-59.0	56.5-62.5
Hopes Subgroup	27.1 (+/-9.26)	25.13 (+/-8.60)	29.3(+/-6.53)
Despair subgroup	10.3 (+/-9.32)	9.28 (+/-8.28)	9.82 (+/-6.12)

* Lower –Upper 95% CI of mean

Figure 4.5: Global Personal Hopefulness (GPH) in all groups



Statistical analysis included Fisher's exact test to evaluate the relationship between GPH and GIQOL measure. Subjects with good GIQOL score correlated significantly with normal GPH ($p<0.005$) (Table 4.6). Additionally, there was no significant relationship between GPH score and symptom scores in the population sample.

Table 4.6: Relationship between GIQOL and Global Personal Hopefulness

	Poor GIQOL	**Good GIQOL**	*Total*
Normal GPH	52 (47.3%)	58 (52.7%)	*110*
Low GPH	29 (74.4%)	10 (25.6%)	*39*
Total	*81*	*68*	*149*

Fisher's exact test $p<0.005$

4.1.3 Pennebaker Inventory of Limbic Languidness (PILL)

The Pennebaker Inventory of Limbic Languidnes (PILL) (Appendix) is a 54 item scale that assesses the frequency of common physical symptoms and sensations (Pennebaker, 1993).

Table 4.7: Mean scores for PILL in all groups

Groups	Anorectal Anomalies	Idiopathic constipation	Healthy controls
Mean (+/-SD)	45.35 (31.1+/-)	12.72 (12.26+/-)	40.55 (26.96+/-)
* *CI of mean*	36.6-54.1	9.08-16.36	33.0-48.1

Idiopathic constipation had the lowest mean PILL score compared to ARA and healthy controls (Table 4.7, Figure 4.6). Statistical analysis included a 1-way ANOVA (Krushkal-Wallis test), indicating a significance between the three groups (Adjusted $r^2 = 0.2341$). There was significantly lower PILL score in the IC group compared to healthy controls ($p<0.0001$) and ARA ($p<0.001$). There was no significant relationship between PILL and GIQOL and symptom scores.

4.1.4 Cognitive Emotion Regulation Questionnaire (CERQ)

The CERQ distinguishes nine different cognitive coping strategies, each consisting of four items measured on a 5-point Likert scale and each referring to what someone thinks after the experience of a stresssful life event (Refer to Chapter 2).

Means, standard deviations and confidence intervals for the total CERQ score and subgroups are presented in Table 4.8. Statistical analysis included a 1-way ANOVA (Krushkal-Wallis test, Dunn's Multiple Comparison test), indicating a significance difference in overall coping mechanisms between ARA and healthy controls ($p<0.05$) (Figure 4.7). Reasons for this comparison can be shown by observing the different coping mechanisms used mostly by that group (Table 4.8). ARA significantly used

significantly more positive reappraisal ($p<0.05$) and putting into perspective ($p<0.01$) as a way of coping under stressful situations in comparison to healthy controls (Table 4.8).

Figure 4.6: Pennebaker Inventory of Limbic Languidnes (PILL) scores in all groups

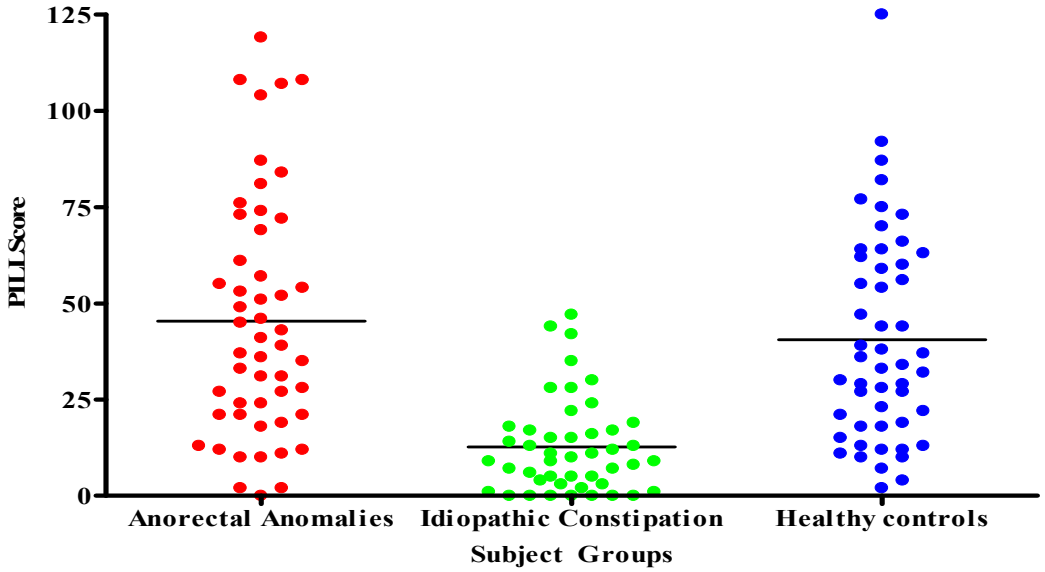


Figure 4.7: Cognitive Emotion Regulation Questionnaire (CERQ) scores in all groups

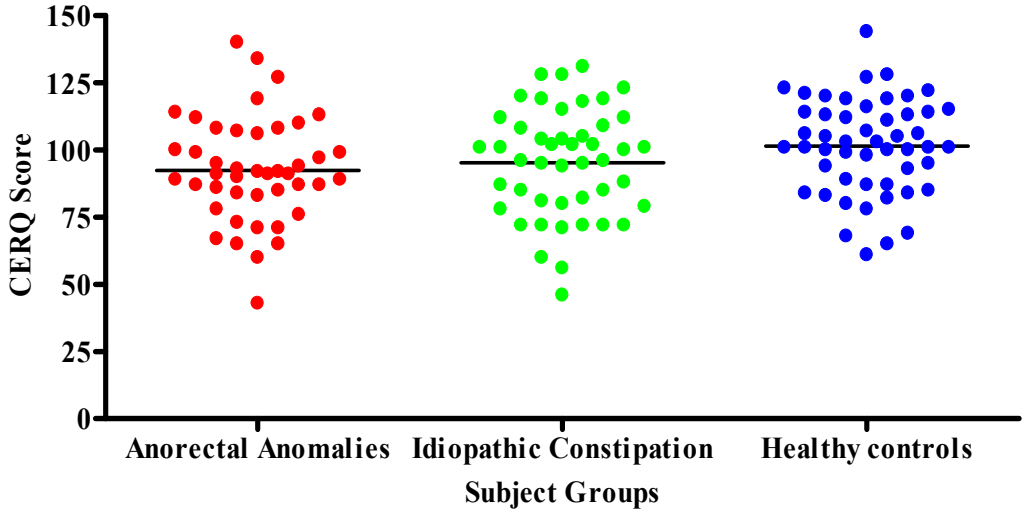


Table 4.8: The Cognitive Emotion Regulation Questionnaire (CERQ) scores for all groups

Groups	Anorectal Anomalies		Idiopathic Constipation		Healthy controls	
	Mean (+/-SD)	* *CI of mean*	Mean (+/-SD)	*CI of mean*	(Mean (+/-SD)	* *CI of mean*
Total CERQ Score	92.45 (+/-19.49)	86.5-98.4	95.17 (+/-20.15)	89.2-101.2	101.4 (+/-17.63)	96.4-106.3
Subgroups						
Self-blame	9.09 (+/-3.46)	8.0-10.1	9.17 (+/-3.68)	8.0-10.3	9.37 (+/-3.39)	8.2-10.3
Acceptance	11.30 (+/-3.88)	10.1-12.5	11.87 (+/-4.26)	10.6-13.1	12.43 (+/-3.18)	11.5-13.3
Rumination	9.71 (+/-3.81)	8.5-10.9	11.30 (+/-3.86)	10.2-12.5	11.25 (+/-3.85)	10.2-12.3
Positive Refocusing	10.5 (+/-3.63)	9.4-11.6	11.2 (+/-4.37)	9.9-12.5	10.75 (+/-4.02)	9.6-11.9
Planning	11.25 (+/-3.55)	10.2-12.3	11.50 (+/-3.45)	10.5-12.5	13.61 (+/-3.05)	12.8-14.5
Positive Reappraisal	11.05 (+/-3.33)	10.0-12.1	12.04 (+/-4.20)	10.8-13.3	13.06 (+/-3.36)	12.1-14.0
Putting into Perspective	11.20 (+/-3.53)	10.1-12.3	11.93 (+/-3.97)	10.8-13.1	13.55 (+/-3.21)	12.7-14.5
Catastrophising	8.80 (+/-3.57)	7.7-9.9	9.20 (+/-3.36)	8.2-10.2	8.71 (+/-2.94)	7.9-9.5

* Lower –Upper 95% CI of mean

4.1.5 Depression

Depression in children between 7-17 years of age was assessed by using the Children's Depression Inventory (CDI) and the Beck Depression Inventory (BDI-II) instrument was used for screening the severity of depression in adults (Refer to Chapter 2). Means and standard deviations for both CDI and BDI scores are presented in Table 4.9.

Table 4.9: Mean and standard deviation scores for CDI and BDI

Depression Scores	**CDI** Mean (+/-SD)	**BDI** Mean (+/-SD)
Anorectal Anomalies	7.36 (+/-8.22)	26.0 (+/-22.63)
Idiopathic Constipation	10.12 (+/-9.56)	23.0 (+/-14.14)
Healthy controls	9.14 (+/-7.26)	25.5 (+/-30.41)

Table 4.10: Distribution of depression in all Groups

Depression Scores	**Depressed**	**Normal**	*Total*
Anorectal Anomalies	10 (19.2%)	42 (80.8%)	*52*
Idiopathic Constipation	13 (28.3%)	33 (71.7%)	*46*
Healthy controls	4 (7.8%)	47 (92.2%)	*51*
Total	*27*	*122*	*149*

$\chi 2 = 6.86$; df 2; $p < 0.03$

Overall, 27/149 (18%) of our population sample were diagnosed to have clinical depression. Statistical analysis using $\chi 2$ indicated a higher number of depressed

subjects in groups ARA (10/52) (19.2%) and IC (13/46) (28.3%) ($p<0.03$ $\chi 2 = 6.86$; df 2) in comparison to healthy controls (4/51) (7.8%) (Table 4.10). There was no significant relationship with symptom scores and depression measures. Subjects who are depressed significantly had poorer GIQOL scores in comparison to those not depressed using Fisher's exact test ($p<0.0005$) (Table 4.11).

Table 4.11: Relationship between GIQOL and depression

	Normal	**Depressed**	*Total*
Poor GIQOL	58 (71.6%)	23 (28.4%)	*81*
Good GIQOL	64 (94.1%)	4 (5.9%)	*68*
Total	*122*	*27*	*149*

Fisher's exact test $p < 0.0005$

Subjects who score normal on the global personal hopefulness (GPH) are significantly less likely to be depressed in comparison to those who have a low GPH ($p<0.0001$) (Table 4.12).

Table 4.12: Relationship between depression and Global Personal Hopefulness

	Normal	**Depressed**	*Total*
Normal GPH*	100 (90.9%)	10 (9.1%)	*110*
Low GPH	22 (56.4%)	17 (43.6%)	*39*
Total	*122*	*27*	*149*

* GPH (global personal hopefulness) Fisher's exact test $p < 0.0001$

4.1.6 Anxiety

The State-Trait Anxiety Inventory for Children (STAIC) and the State-Trait Anxiety Inventory (STAI) (Spielberger, 1970) (Appendix) which measures anxiety in adolescents/adults were used in this thesis (Refer to Chapter 2). Means and standard deviations for both STAIC and STAI scores are presented in Table 4.13.

Table 4.13: Mean and standard deviation scores for STAIC and STAI

Anxiety Scores	**STAIC** Mean (+/-SD)		**STAI** Mean (+/-SD)	
	State	Trait	State	Trait
Anorectal Anomalies	28.95 (+/-4.35)	34.18 (+/-8.89)	34.23 (+/-11.35)	40.97 (+/-14.21)
Idiopathic Constipation	34.80 (+/-9.20)	34.20 (+/-6.83)	40.78 (+/-13.01)	43.05 (+/-13.24)
Healthy controls	32.67 (+/-11.72)	37.00 (+/-3.61)	35.29 (+/-11.26)	38.54 (+/-10.38)

Table 4.14: Distribution of High State/Trait anxiety in all groups

Anxiety scores	**High Trait Anxiety**	**High State Anxiety**
Anorectal Anomalies	22 (35.5%)	10 (19.6%)
Idiopathic Constipation	23 (37.1%)	24 (47.1%)
Healthy controls	17 (27.4%)	17 (33.3%)
Total	*62*	*51*

$\chi 2 = 3.48$; df 2; $p = 0.175$

Overall, 62/149 (42%) of our population sample were diagnosed to have high trait anxiety and 51/149 (34%) with high state anxiety. Statistical analysis using $\chi 2$ indicated no significance difference between the three groups (Table 4.14). Subjects with perfect continence significantly indicate normal 'state' anxiety levels in comparison to those with partial and full incontinence ($p<0.0005$ $\chi 2 = 15.11$; df 2) (Table 4.15). There was no significant association with 'trait' anxiety and Vaizey Incontinence scores (Table 4.15). There was no significant association between anxiety scores and KESS scores.

Table 4.15: Relationship between Vaizey Incontinence scores and anxiety

Anxiety scores	**State Anxiety**		**Trait Anxiety**	
	Normal	High	Normal	High
Perfect continence	57 (55.9%)	18 (38.3%)	47 (54.0%)	28 (45.2%)
Partial incontinence	35 (34.3%)	12 (25.5%)	30 (34.5%)	17 (27.4%)
Full incontinence	10 (9.8%)	17 (36.2%)	10 (11.5%)	17 (27.4%)
Total	*102*	*47*	*87*	*62*

State anxiety: $\chi 2 = 15.11$; df 2; $p < 0.0005$; Trait anxiety: $\chi 2 = 6.20$; df 2; $p = 0.05$

Subjects with poor GIQOL score significantly have higher state ($p<0.001$) and trait ($p<0.0001$) anxiety compared to subjects with good GIQOL scores (Fisher's exact test) (Table 4.16).

Table 4.16: Relationship between GIQOL and anxiety

Anxiety scores	**State Anxiety**		**Trait Anxiety**	
	Normal	High	Normal	High
Poor GIQOL	46 (45.1%)	35 (74.5%)	35 (40.2%)	46 (74.2%)
Good GIQOL	56 (54.9%)	12 (25.5%)	52 (59.8%)	16 (25.8%)
Total	*102*	*47*	*87*	*62*

State anxiety: Fisher's exact test $p< 0.001$ Trait anxiety: Fisher's exact test $p< 0.0001$

Subjects with poor global personal hopefulness (GPH) scores significantly have higher state ($p<0.0002$) and trait ($p<0.0001$) anxiety compared to subjects with good GPH scores (Fisher's exact test) (Table 4.17).

Table 4.17: Relationship between Global Personal Hopefulness and anxiety

Anxiety scores	**State Anxiety**		**Trait Anxiety**	
	Normal	High	Normal	High
Normal GPH*	85 (83.3%)	25 (53.2%)	73 (83.9%)	37 (59.7%)
Low GPH	17 (16.7%)	22 (46.8%)	14 (16.1%)	25 (40.3%)
Total	*102*	*47*	*87*	*62*

* GPH (global personal hopefulness); State anxiety: Fisher's exact test $p< 0.0002$ Trait anxiety: Fisher's exact test $p< 0.0001$

Subjects who are depressed, significantly have higher state ($p<0.0001$) and trait ($p<0.0001$) anxiety compared to subjects who are not depressed (Fisher's exact test) (Table 4.18).

Table 4.18: Relationship between depression and anxiety

Anxiety scores	**State Anxiety**		**Trait Anxiety**	
	Normal	High	Normal	High
Normal	97 (95.1%)	25 (53.2%)	86 (98.9%)	36 (58.1%)
Depressed	5 (4.9%)	22 (46.8%)	1 (1.15%)	26 (41.9%)
Total	*102*	*47*	*87*	*62*

State anxiety: Fisher's exact test $p< 0.0001$ Trait anxiety: Fisher's exact test $p< 0.0001$

4.1.7 Big Five Inventory

The Big Five Inventory (BFI) consist of 44 questions desgined to separate each patients personality into five dimentions: extroversion, agreeableness, conscientiousness, neuroticism and openess as discussed in Chapter 2 (John, 1991). The BFI - Transition to College (BFI-TTC) was administered to young adolescents (11-16 years of age). Means and standard deviations for both BFI and BFI-TTC scores are presented in Table 4.20. Overall, in our population sample 83/142 (58%) are extroverts, 84/142 (59%) agreeable, 88/142 (62%) conscientious, 79/142 (56%) neurotic and 90/142 (63%) openness (Table 4.19). Figure 4.8 demonstrates the distribution of personality traits within in each group. Statistical analysis using $\chi 2$ indicated no significant difference between the three groups.

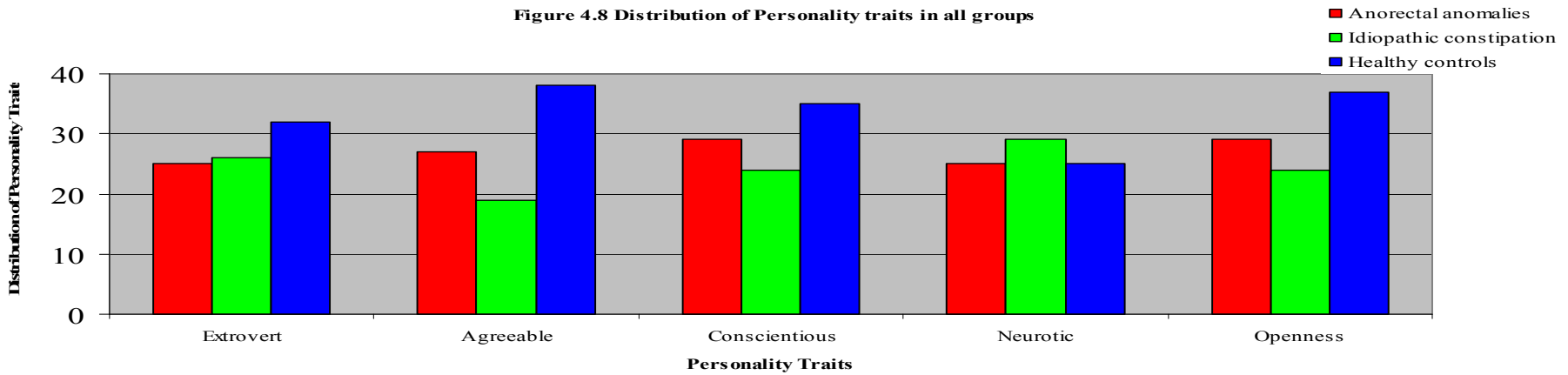
Table 4.19: Distribution of Personality traits in all groups

Groups	**Anorectal Anomalies**	**Idiopathic constipation**	**Healthy controls**	*Total*
Extroversion	25 (30.1%)	26 (31.3%)	32 (38.6%)	*83*
Agreeableness	27 (32.1%)	19 (22.6%)	38 (45.2%)	*84*
Conscientiousness	29 (33.0%)	24 (27.6%)	35 (39.8%)	*88*
Neuroticism	25 (31.6%)	29 (36.7%)	25 (31.6%)	*79*
Openess	29 (32.2%)	24 (26.7%)	37 (41.1%)	*90*

Table 4.20: The Big Five Inventory scores for all groups

Groups	Anorectal Anomalies Mean (+/-SD)		Idiopathic Constipation Mean (+/-SD)		Healthy controls Mean (+/-SD)	
	BFI	**BFI-TTC**	**BFI**	**BFI-TTC**	**BFI**	**BFI-TTC**
Extroversion	3.28 (+/-1.00)	3.57 (+/-0.64)	3.48 (+/-1.06)	3.71 (+/-0.56)	3.58 (+/-0.77)	3.83 (+/-0.55)
Agreeableness	4.01 (+/-0.61)	3.31 (+/-0.72)	3.71 (+/-0.91)	3.15 (+/-0.59)	3.96 (+/-0.55)	3.60 (+/-0.714)
Conscientiousness	3.49 (+/-0.822)	3.16 (+/-0.77)	3.42 (+/-1.05)	3.35 (+/-0.70)	3.78 (+/-0.59)	3.28 (+/-0.91)
Neuroticism	3.14 (+/-1.16)	3.37 (+/-0.58)	3.30 (+/-1.49)	3.36 (+/-0.66)	2.72 (+/-0.78)	3.51 (+/-0.54)
Openness	3.69 (+/-0.75)	3.54 (+/-0.80)	3.70 (+/-0.78)	3.36 (+/-0.72)	3.56 (+/-0.67)	3.70 (+/-0.614)

Figure 4.8 Distribution of Personality traits in all groups



Extroversion significantly correlated to lower global personal hopefulness (GPH) scores (24/38) (63.2%) in comparison to introversion (14/38) (36.9%) (Fisher's exact test $p<0.002$). Higher PILL scores significantly correlated with extroversion (27/32) compared to introversion (5/32) (15.6%) ($p<0.0001$). Neuroticism significantly correlated with lower GPH scores (28/38) (73.7%) compared to normal GPH scores (10/38) (26.3%) ($p<0.01$). Additionally, neuroticism significantly correlated with high state (33/46) (71.8%) and high trait anxiety (42/62) (67.7%) compared to subjects who were not identified to have neurotic personality traits ($p<0.01$).

4.1.8 General Health Questionnaire-28 (GHQ-28)

General Health Questionnaire-28 (GHQ-28) (Goldberg, 1978) is a self-administered screening instrument revealing individuals with diagnosable psychiatric disorder. As discussed in Chapter 2, a cut-off scores less than five is indicated as a 'probable non-case' and all those more than or equal to five as 'probable cases'. Means and standard deviations for GHQ scores are presented in Table 4.21. Overall, 21/91 (23%) of our population sample, have a probable case of a psychiatric illness. Statistical analysis using $\chi 2$ indicated no significance difference between the three groups (Table 4.22).

Subjects with probable case of psychiatric illness significantly correlated with poorer GIQOL scores ($p<0.001$), lower global personal hopefulness ($p<0.0007$), depression ($p<0.001$), high state and trait anxiety ($p<0.0002$), neuroticism ($p<0.0001$) and place more emphasis on their physical health ($p<0.006$) compared to subjects who are not a probable case.

Table 4.21: Mean and standard deviation scores for GHQ-28

	GHQ-28 Mean (+/-SD)
Anorectal Anomalies	4.59 (+/-6.49)
Idiopathic Constipation	8.47 (+/-9.13)
Healthy controls	3.47 (+/-5.70)

Table 4.22: Distribution of probable psychiatric cases in all groups

GHQ-28	**Probable case**	**Non Probable case**	*Total*
Anorectal Anomalies	4 (19.0%)	17 (81.0%)	*21*
Idiopathic Constipation	7 (29.2%)	17 (70.8%)	*24*
Healthy controls	10 (21.7%)	36 (78.3%)	*46*
Total	*21*	*70*	*91*

$\chi 2 = 0.74$; df 2; $p = 0.691$

4.1.9 Weinberger Adjustment Inventory (WAI)

The Weinberger Adjustment Inventory (WAI) (Weinberger, 1991) was designed to perationalize distress and self-restraint as dimension of social-emotional adjustment. It also includes scales of response and can be used as a 'lie detector' which will be use in this thesis. Means and standard deviations for WAI scores are presented in Table 4.23. Statistical analysis using $\chi 2$ indicated no significance difference between the three groups. Lie detection was included to see how truthfully our subjects were answering the questions. There were 140/149 (94%) who completed the WAI questionnaire, with 14/140 (10%) detected of lying (Table 4.23).

Table 4.23: Mean scores for Weinberger Adjustment Inventory (WAI) in all groups

Groups	Anorectal Anomalies (Mean (+/-SD)	Idiopathic constipation (Mean (+/-SD)	Healthy controls (Mean (+/-SD)
Restraint	3.64 (+/-0.73)	3.47 (+/-0.75)	3.79 (+/-0.68)
Distress	2.58 (+/- 0.89)	2.77 (+/-1.34)	2.39 (+/-0.70)
Defensive	2.60 (+/-0.92)	2.74 (+/-0.80)	2.81 (+/-0.69)
Lie Detector	*3 detected*	*7 detected*	*4 detected*

4.2 ACE POPULATION AND QUALITY OF LIFE AND PSYCHIATRIC MEASURES

4.2.1 Gastrointestinal Quality of Life

In the ACE population, the GIQOL mean score for ARA was 100.5 (+/-27.07) and 99.79 (+/-19.02) in IC (Figure 4.9, Table 4.24). There was no significant difference between ARA and IC in terms of GIQOL total and subgroup means (Table 4.23).

Figure 4.9: Gastrointestinal Quality of Life (GIQOL) in ACE patients

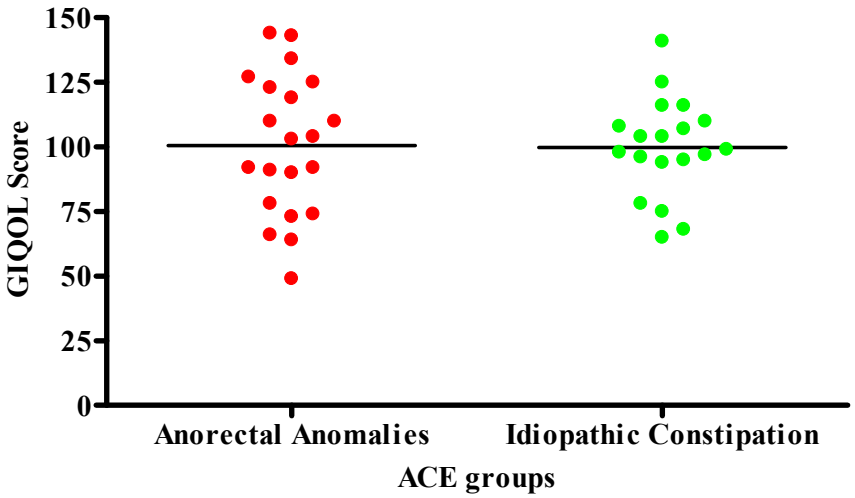


Table 4.24: Statistical Analysis for GIQOL scores in ACE population

Subject Groups **(Score range)**	**Anorectal Anomalies** Mean (+/-SD) (Range) ** CI of mean*	**Idiopathic Constipation** Mean (+/-SD) (Range) ** CI of mean*	*** Significance between ARA and IC (p value)**
GIQOL Total **(0-144)**	100.5 (+/-27.07) (29-144) *(88.20-112.8)*	99.79 (+/-19.02) (65-141) *(90.62-109.0)*	ns
Subgroups			
Physical well being (0-40)	27.00 (+/-7.24) (16-40) *23.70-30.30*	24.05 (+/-6.61) (13-40) *20.87-27.24*	ns
Gastrointestinal digestion (0-40)	28.19 (+/-28.32) (18-39) *23.94-31.44*	28.32 (+/-6.86) (15-40) *25.01-31.62*	ns
Gastrointestinal defaecation (0-24)	18.90 (+/-4.92) (6-24) *16.67-21.14*	20.00 (+/-4.37) (6-24) *17.89-22.11*	ns
Mental well being (0-20)	11.90 (+/-5.59) (3-20) *9.36-14.45*	13.37 (+/-4.11) (5-20) *11.39-15.35*	ns
Other (0-20)	13.33 (+/-4.31) (4-20) *(11.37-15.29)*	14.05 (+/-3.95) (7-20) *(12.15-15.96)*	ns

* Mann Whitney t test (ns = not significant)

The majority of patients with poor GIQOL score, also have a high KESS score (27/40) (67.5%) compared to those with good GIQOL score 5/40 (12.5%) (Table 4.24), however, the sample is too small to have any statistical significance. In the ACE population 32/40 (80.0%) had a poor GIQOL score, 7/40 (17.5%) of which were fully clean and 25/40 (62.5%) partially to fully incontinent (Table 4.25). Being partially or fully incontinent significantly correlates with poor GIQOL score (Fisher's exact test $p<0.05$).

Table 4.25: Relationship between GIQOL and KESS scores in ACE population

GIQOL	**Poor GIQOL**	**Good GIQOL**	*Total*
*** KESS <5**	5 (62.5%)	3 (37.5%)	*8*
KESS > 5	27 (84.3%)	5 (15.6%)	*32*
Total	*32*	*8*	*40*

* KESS < 5 (normal); > 5 (abnormal); Fisher's exact test p= 0.320

Table 4.26: Relationship between GIQOL and Vaizey Incontinence scores in ACE population

GIQOL	**Poor GIQOL**	**Good GIQOL**	*Total*
Full continence	7 (87.5%)	1 (12.5%)	*8*
Partial Incontinence	13 (68.4%)	6 (31.6%)	*19*
Full Incontinence	12 (92.3%)	1 (7.7%)	*13*
Total	*32*	*8*	*40*

$\chi 2$ 3.10; df 2; p = 0.212

4.2.2 Other Psychosocial Measures in the ACE population

Global personal hopefulness (GPH) mean scores were similar between ARA (51.10 +/-17.25) and IC (54.63 +/- 18.46) (Table 4.27) with no significant differences. Overall, ARA had higher number of patients with low GPH (8/21) (38.1%) compared to IC (3/19) (15.8%). Table 4.27 demonstrates mean and standard deviations for hope and despair subgroups, with no significant differences found between ARA and IC, yet a higher mean despair mean score in ARA compared to IC is evident (Table 4.27). There was no significant relationship between global personal hopefulness (GPH) and GIQOL scores in the ACE population.

Table 4.27: Mean scores for Global Personal Hopefulness in ACE population

Groups	**Anorectal Anomalies**	**Idiopathic constipation**
GPH (Mean (+/-SD) (Range)	51.10 +/-17.25 (16-79)	54.63 +/- 18.46 (0-77)
** CI of mean*	*43.24-58.95*	*45.74-63.53*
Hopes Subgroup	22.43 (+/-10.66)	25.47 (+/-10.28)
Despair subgroup	11.33 (+/-9.68)	8.74 (+/-8.09)

* Lower –Upper 95% CI of mean

In terms of the Pennebaker Inventory of Limbic Languidnes (PILL), the total mean score in ARA was 54.00 (+/- 32.66) and 52.00 (+/-43.34) in IC, with no significant differences between the groups. General Health Questionnaire-28 (GHQ-28) was filled out by patients > 16 years of age, thus 13/40 patients with an ACE completed this questionnaire. Overall, 6/13 had probable case of psychiatric diagnosis, 4 in ARA

and 2 in IC respectively. In the ACE population, there was no significant differences evident between ARA and IC in terms of personality traits (Table 4.28).

Table 4.28: Distribution of Personality traits in ACE Population

Groups	**Anorectal Anomalies**	**Idiopathic constipation**	*Total*
Extroversion	12 (52.2%)	11 (47.8%)	*23*
Agreeableness	11 (64.7%)	6 (35.3%)	*17*
Conscientiousness	13 (61.9%)	8 (38.1%)	*21*
Neuroticism	12 (52.2%)	11 (47.8%)	*23*
Openess	14 (60.9%)	9 (39.1%)	*23*

$\chi 2$ 1.16; df 4; p = 0.884

Means, standard deviations and confidence intervals for the total CERQ score and subgroups are presented in Table 4.29. There was no significant difference, between ARA and IC in the ACE population for CERQ total and subgroups.

As indicated in Table 4.30, there is no significant difference between ARA and IC in our population sample in terms of distribution of patients who are clinically depressed. Overall, 14/40 (35.0%) patients are clinically depressed, with 8 patients in ARA and 6 in IC respectively (Table 4.30). As indicated in Table 4.30, there is no significant difference between ARA and IC in our population sample in terms of distribution of patients who are clinically anxious. Overall, 17/40 (42.5%) patients have high trait anxiety and 26/40 (65.0%) high state anxiety (Table 4.30).

Table 4.29: The Cognitive Emotion Regulation Questionnaire (CERQ) scores in ACE population

Groups	**Anorectal Anomalies**		**Idiopathic Constipation**	
	Mean (+/-SD)	* *CI of mean*	Mean (+/-SD)	*CI of mean*
Total CERQ Score (Range)	93.85 (+/-22.15) (43-140)	*83.48-104.2*	99.00 (+/-18.26) (72-128)	*90.20-107.8*
Subgroups				
Self-blame	9.05 (+/-3.63)	*7.30-10.80*	9.11 (+/-3.30)	*7.52-10.69*
Acceptance	10.42 (+/-3.72)	*8.63-12.21*	12.00 (+/-4.11)	*10.02-13.98*
Rumination	9.90 (+/-4.25)	*7.84-11.95*	10.95 (+/-3.70)	*9.16-12.73*
Positive Refocusing	11.16 (+/-3.15)	*9.64-12.68*	12.84 (+/-4.54)	*10.66-15.03*
Planning	11.37 (+/-3.32)	*9.77-12.97*	11.89 (+/-3.89)	*10.02-13.77*
Positive Reappraisal	11.16 (+/-3.27)	*9.58-12.73*	13.53 (+/-4.39)	*11.41-15.64*
Putting into Perspective	11.26 (+/-4.23)	*9.23-13.30*	12.68 (+/-4.20)	*10.66-14.71*
Catastrophising	8.63 (+/-3.44)	*6.98-10.29*	9.32 (+/-3.61)	*7.58-11.05*

Table 4.30: Distribution of depression in ACE population

Depression Scores	**Depressed**	**Normal**	*Total*
Anorectal Anomalies	8 (38.1%)	13 (61.9%)	*21*
Idiopathic Constipation	6 (31.6%)	13 (68.4%)	*19*
Total	*14*	*26*	*40*

Fisher's exact test p = 0.746

Table 4.31: Distribution of State/Trait anxiety in ACE population

Anxiety scores	High Trait Anxiety	High State Anxiety
Anorectal Anomalies	8 (47.1%)	16 (61.5%)
Idiopathic Constipation	9 (52.9%)	10 (38.5%)
Total	*17*	*26*

Fisher's exact test p = 0.531

Means and standard deviations for Weinberger Adjustment Inventory (WAI) scores are presented in Table 4.32. There was no significance difference between ARA and IC. Lie detection was included to see how truthfully our subjects were answering the questions with 6/40 (15.0%) subjects detected of lying in the ACE population (Table 4.32).

Table 4.32: Mean scores for Weinberger Adjustment Inventory (WAI) in ACE population.

Groups	Anorectal Anomalies (Mean (+/-SD)	Idiopathic constipation (Mean (+/-SD)
Restraint	3.76 (+/-0.63)	3.59 (+/-0.82)
Distress	2.61 (+/-0.86)	2.40 (+/-0.93)
Defensive	2.63 (+/-1.21)	2.73 (+/-0.87)
Lie Detector	*2 detected*	*4 detected*

CHAPTER 5

RESULTS (Part III)

5.0 RESULTS Part III

5.1 PATHOPHYSIOLOGY OF ANORECTAL ANOMALIES

5.1.1 Introduction

As discussed in Chapter 1, currently, our knowledge of the pathophysiology of FI relates almost exclusively to information gained in adults with acquired symptoms (i.e. usually post-obstetric or following anal surgery) (Lunniss, 2007). The pathophysiology of incontinence in congenital anorectal anomalies (ARA), however, remains unclear and our understanding rudimentary. Notably, the importance of extra-sphincteric mechanisms has not been adequately addressed.

The aim of this chapter is to present the results of a retrospective study of adults with anorectal anomalies (ARA), presenting to our tertiary GIPU (Barts and The London, The Royal London Hospital NHS Trust) with a history of previous surgery for ARA. This will be achieved by comprehensive evaluation of those measurable components contributing to continence (as discussed in Chapter 2) and the pathophysiological mechanisms which might contribute to poor bowel function.

Preliminary results to this chapter have been published (Athanasakos EP et al. (2008). *British Journal of Surgery* 95 (11): 1394-400).

5.1.2 Demographics and General Background of the population sample

The study population comprised 32 consecutive patients comprised 15 females and 17 males. Age range of the population sample was 11-42 years of age and mean of 24 (+/- 9). All patients who have all underwent surgery for ARA as infants and were referred for investigation of their symptoms of FI between 1998- 2006. All patients had a detailed clinical history taken and underwent anorectal physiological assessment. All patients reported life long FI; the nature of which was urge in 16, passive in 6 and combined urge and passive FI 10. Eighteen patients had associated symptoms of intractable constipation that met with the Rome III diagnostic criteria.

Using the Wingspread Classification Score, ARA were classified as: high in 16 (females: cloacal; males: rectoprostatic); intermediate in 8 (females: rectovestibular; males: rectourethral); and low in 7 (perineal in both females and males); in one patient, the abnormality was unknown (Table 5.1). One patient also had Klippel-Fiel syndrome and another neuropathic bladder. Surgery included a variety of techniques including 8 posterior sagittal anorectoplasty (PSARP), 8 anal transposition, 5 abdominal perineal pull through, 2 combined PSARP and abdominal perineal pull through and 7 others (Stephens, cut-back and anoplasty) (Table 5.1).

Out of 32 patients, 7 had an Antegrade Continence Enema (ACE), 2 of which were intermediate and 5 high ARA. Patients with an ACE presented with 5/7 with urge FI, 1 passive FI and 1 with a combination of urge and passive FI.

5.1.3 Summary of Physiological Measures

As discussed in detail in Chapter 2, subjects underwent station pull through manometry of the anal canal, assessment of pudendal nerve terminal motor latencies and endoanal ultrasonography. Rectal sensory thresholds were determined using a volumetric-based balloon distension technique. In patients with symptoms of constipation and incontinence, colonic transit studies using radio-opaque markers, were performed to distinguish between normal and slow colonic transit. Evacuation proctography was performed where indicated in those patients with symptoms of obstructed defaecation.

Table 5.1: Summary of classification and surgery in anorectal anomalies

Grade of Anorectal Anomaly (Frequency)	Surgical Technique	Male	Female
Low (7)	Unknown		1
	Cut-back procedure	1	1
	Anorectoplasty		1
	Anoplasty	1	
	Anal Transposition		1
	Abdominal perineal + revised PSARP	1	
Intermediate (8)	Posterior sagittal anorectoplasty		2
	Unknown		1
	Abdominal perineal pull through	1	
	Anal Transposition		4
High (16)	Posterior sagittal anorectoplasty	6	
	Anal Transposition		3
	Stephens sacro-perineal	3	
	Abdominal perineal pull through	3	
	Abdominal perineal pull through + PSARP	1	
*** Unknown (1)**	Abdominal perineal pull through		1

*** Unknown information was due to destroyed medical records**

5.1.4 Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Version 12.0.01, Chicago, USA). Fisher's exact test was used to analyse contingency tables. For this test, $p<0.050$ was considered to show a significant difference

5.2 RESULTS

5.2.1 Anorectal physiology

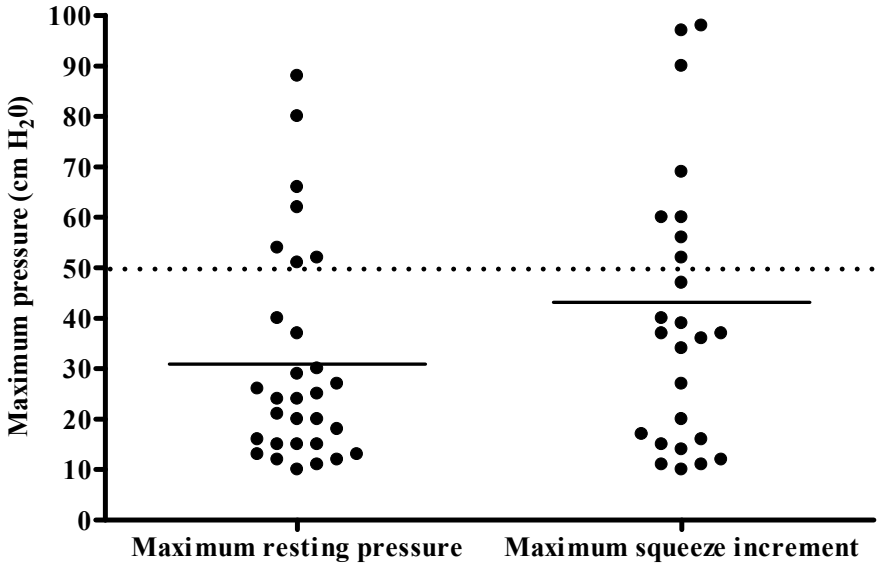
All tests could not be performed in all patients due to subject preference or intolerance. However, anorectal physiology was demonstrated to be abnormal in all subjects, which involved multiple mechanisms in every individual (Table 5.2).

5.2.1.1 Sphincter function and morphology

Anal resting tone and squeeze increments were attenuated in 23/32 and 17/32 patients respectively (4 of which could not be elicited) (Figure 5.1). The mean for maximum resting pressure (MRP) was 30.9 (+/- 21.4) ranging from 10.0-88.0 cm H_2O and the mean for maximum squeeze increment (MSI) was 43.2 (+/-30.7) ranging from 10.0 to 118.0 cm H_2O.

Note (Figure 5.1): The dotted line shows the lower limit of normal; bars represent means.

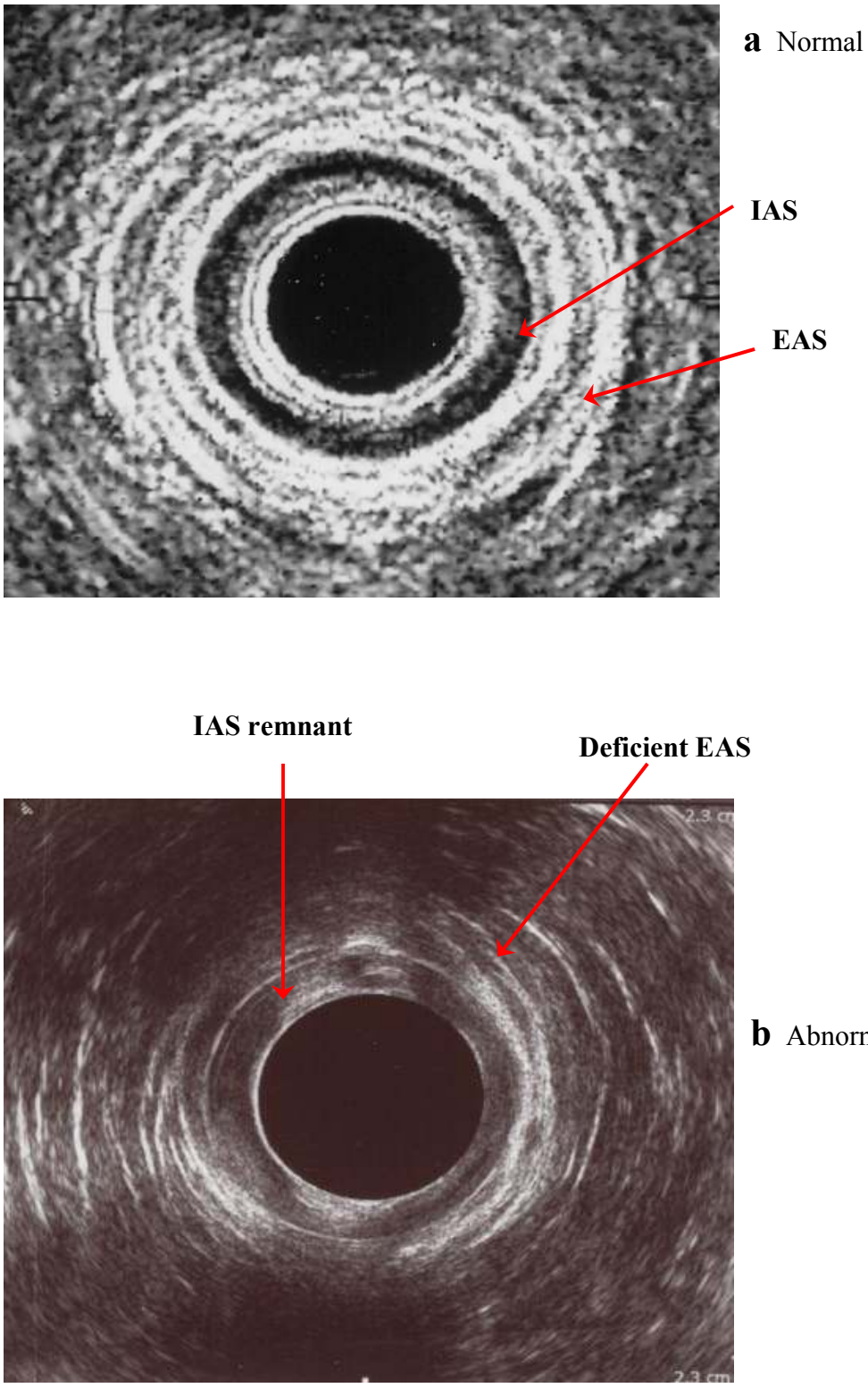
Figure 5.1: Anal manometry in anorectal anomalies



Endosonography was performed in 29/32 patients, with only three patients having at least one anal sphincter completely present including 2 low and 1 high ARA (Table 5.2). Eight patients had almost incomplete or 'absent' sphincters in both IAS and EAS, all had abnormal MRP and MSI and all presented with urge FI and 3 having a combination of both urge and passive FI. In Figure 5.2a demonstrates a healthy control without ARA compared to 5.2b with an ARA (Figure 5.2).

Evidence of pudendal neuropathy was found in 11/13 patients studied; this was unilateral in 5 and bilateral in 6 (Table 5.2). Patients with neuropathy presented with urge FI, either in isolation (n = 4) or passive FI (n =2) or in combination of urge and passive (n = 5) and all patients had fragmented to incomplete sphincters.

Figure 5.2: Endosonography of (a) normal and (b) abnormal sphincteric mechanism (IAS, internal anal sphincter; EAS, external anal sphincter).



5.2.1.1 Extra-sphincteric function

Abnormal rectal sensation was demonstrated in 18/22 (82%) patients, with 10/22 (45%) being hypersensitive, 4/22 (18%) hyposensitive and normal in 4/22 (18%) (Table 5.2). In the 8 patients tested with a high anorectal anomaly, 5 had sensory dysfunction, all of whom were hypersensate and 3 normal rectal sensation (Table 5.2). There was a mixed picture in the other two groups: in low anomalies, all 5 patients tested had sensory dysfunction, 3 of whom were hypersensate and 2 were hyposensate; in the intermediate anomaly group, of the 5 patients tested, 2 were hyposensate, 2 were hypersensate and 1 had normal rectal sensation (Table 5.2). The patient in whom the anomaly was unknown was hypersensitive. Six of ten patients with rectal hypersensitivity presented with symptoms of urge FI, followed by 1 passive FI and 3 a combination of urge and passive FI (Table 5.2). All patients found to have rectal hyposensitivity had delayed colonic transit and concomitant symptoms of constipation (Table 5.2).

The recto-anal inhibitory reflex (RAIR) was absent in 4/22 patients tested, all of whom had a pudendal neuropathy (unilateral in 1 and bilateral in 3); 3 of these 4 had co-existent constipation. The RAIR was absent in 2 patients with an intermediate anomaly, 1 with a low anorectal anomaly and the patient in whom anomaly grade was unknown (Table 5.2).

Overall rectal emptying was abnormal in 9/14 patients tested, which was secondary to ‘outlet dysfunction’ (poor defecation dynamics pelvic floor dyssynergia) in the majority (7), mechanical obstruction in 1, and a combined functional / mechanical problem in 1. Patients with a ‘functional’ problem included those with all grades of

anomaly: 2 of 3 low anomalies tested, 3 of 5 intermediate and 3 of 6 high anorectal anomalies. In the 18 patients with co-existent constipation, 5 had abnormal parameters of evacuation and 8 had delayed colonic transit. Only 1 patient with combined FI and constipation had normal rectal emptying on proctography and normal colonic transit. In those patients with combined symptoms of incontinence and constipation, colonic transit was delayed in 5/18 (28%). All 4 hyposensate patients were within this group, and the other was hypersensitive (Table 5.2). Patients with delayed colonic transit had either a low (n = 2) or intermediate anorectal anomaly (n = 4) or high (n = 2). There were no statistical relationship with the type of anorectal defect and type of reconstructive surgery and physiological outcomes in this selected population group.

5. 3 PSYCHOSOCIAL MEASURES

Chapters 3 and 4 were studies completed independently from the pathophysiology component study. However, 14/32 (43.8%) patients were involved in all studies. In these 14 patients, 10/14 (71.4%) had a KESS score > 5 and 9/14 (64.3%) had partial to full FI (5 of whom denied FI in their questionnaire), 11/14 (78.6%) had poor GIQOL scores, 5/14 (35.7%) had low level of global personal hopefulness, 3/14 (21.4%) clinically depressed, 8/14 (57.1%) clinically anxious in which was mainly trait anxiety (n = 5) and both trait and state in the remaining, 3/14 (21.4%) probable cases of psychiatric diagnosis and 2/14 (14.3%) with high PILL scores. In terms of personality traits, 9/14 (64.3%) extroverts, 9/14 (64.3%) agreeable, 7/14 (50.0%) concientious, 6/14 (42.9%) neurotic and 7/14 (50.0%) open minded.

Table 5.2: History and test results of 32 patients with faecal incontinence after surgery for congenital anorectal anomalies

Anorectal Anomaly Grade	Surgical Procedure	Type of FI	Constipation	Anal Pressures		PNTML	Endosonography		RAIR	Rectal Sensation	Colonic Transit	Proctography
				MRP	MSP		IAS	EAS				
Low	Unknown	Urge	NO	N	A	Unilateral	Fragmented	Absent	Present	*Hyper*sensitive	-	-
Low	Cut-back	Both	YES	A	N	Bilateral	Fragmented	Fragmented	Absent	*Hypo*sensitive	Delayed	Mechanical
Low	Cut-back	Urge	NO	A	A	-	Absent	Absent	Present	*Hyper*sensitive	-	Functional
Low	Anorectoplasty	Passive	YES	N	A	Bilateral	-	-	Present	*Hypo*sensitive	Delayed	Functional
Low	Anoplasty	Urge	NO	A	N	-	N	Fragmented	Present	*Hyper*sensitive	-	-
Low	Anal Transposition	Urge	NO	-	-	-	N	Scarred	-	-	-	-

Key to Table:
PSARP *(posterior sagittal anorectoplasty)*; **-** : test not performed; *Type of FI:* both = passive & urge; *Anal Pressures:* N = normal; A = abnormal; *PNTML (pudendal nerve terminal motor latencies):* N = normal; neuropathic = unilateral or bilateral; *Endosonography:* N = normal; *Rectal sensation:* N = normal; *Colonic transit:* N = normal; *Proctography*: Both = mechanical & functional; N = normal

Anorectal Anomaly Grade	Surgical Procedure	Type of FI	Constipation	Anal Pressures		PNTML	Endosonography		RAIR	Rectal Sensation	Colonic Transit	Proctography
				MRP	**MSP**		**IAS**	**EAS**				
Low	Abdominoperineal with PSARP	Passive	YES	A	A	-	Absent	Absent	Present	-	N	-
Intermediate	PSARP	Urge	NO	A	A	-	Absent	Absent	Present	*Hyper*sensitive	-	Functional
Intermediate	PSARP	Urge	YES	A	-	-	Fragmented	Fragmented	-	-	-	-
Intermediate	Unknown	Both	YES	A	A	Bilateral	Absent	Absent	Absent	*Hyper*sensitive	Delayed	N
Intermediate	Abdominal Perineal	Urge	YES	N	N	Bilateral	Fragmented	Scarred	Absent	N	N	Functional
Intermediate	Anal Transposition	Both	YES	A	A	N	Absent	Absent	-	*Hypo*sensitive	Delayed	Both
Intermediate	Anal Transposition	Urge	YES	A	A	Unilateral	Absent	Absent	Present	*Hypo*sensitive	Delayed	N

Anorectal Anomaly Grade	Surgical Procedure	Type of FI	Constipation	Anal Pressures		PNTML	Endosonography		RAIR	Rectal Sensation	Colonic Transit	Proctography
				MRP	MSP		IAS	EAS				
Intermediate	Anal Transposition	Both	YES	N	N	-	Fragmented	Fragmented	Present	-	N	-
Intermediate	Anal Transposition	Both	YES	A	N	-	Fragmented	Fragmented	Present	-	Delayed	-
High	PSARP	Urge	NO	A	A	-	Absent	Fragmented	-	N	-	N
High	PSARP	Passive	YES	A	A	-	Fragmented	Fragmented	Present	-	N	-
High	PSARP	Passive	YES	A	N	-	Fragmented	Fragmented	Present	-	-	-
High	PSARP	Urge	NO	A	-	-	Absent	Scarred	-	-	Normal	-
High	PSARP	Urge	NO	A	N	-	Fragmented	Fragmented	Present	-	Normal	-
High	PSARP	Urge	YES	A	A	-	Scarred	Scarred	Present	-	Normal	-

Anorectal Anomaly Grade	Surgical Procedure	Type of FI	Constipation	Anal Pressures		PNTML	Endosonography		RAIR	Rectal Sensation	Colonic Transit	Proctography
				MRP	MSP		IAS	EAS				
High	Anal Transposition	Both	YES	A	A	-	Absent	Absent	Present	*Hyper*sensitive	N	N
High	Anal Transposition	Both	NO	A	A	Bilateral	Absent	Absent	-	N	-	N
High	Anal Transposition + anorectoplasty	Urge	YES	A	-	-	Fragmented	Absent	Present	-	-	-
High	Stephens sacro-perineal	Passive	NO	A	A	Unilateral	Absent	Fragmented	Present	*Hyper*sensitive	-	Functional
High	Stephens sacro-perineal	Both	NO	A	A	Unilateral	Fragmented	Absent	-	*Hyper*sensitive	-	Functional

Anorectal Anomaly Grade	Surgical Procedure	Type of FI	Constipation	Anal Pressures		PNTML	Endosonography		RAIR	Rectal Sensation	Colonic Transit	Proctography
				MRP	MSP		IAS	EAS				
High	Stephens sacro-perineal	Both	NO	A	A	N	Fragmented	N	Present	N	-	-
High	Abdominoperineal + PSARP	Urge	YES	A	-	-	Fragmented	Fragmented	-	-	Delayed	-
High	Abdominal Perineal	Urge	NO	N	N	-	Fragmented	Fragmented	-	*Hyper*sensitive	-	-
High	Abdominal Perineal	Both	YES	N	A	-	-	-	Present	-	Delayed	-
High	Abdominal Perineal	Both	YES	A	A	Bilateral	Fragmented	Fragmented	-	-	N	Functional
Unknown	Abdominal Perineal	Urge	NO	A	A	Unilateral	-	-	Absent	*Hyper*sensitive	-	-

CHAPTER 6

DISCUSSION

6.0 DISCUSSION

6. 1 INTROUDCTION

This chapter is structured in a way that aims to guide the reader through some of the questions we addressed in Chapter 1, by attempting to provide a clearer understanding of the determinants behind the emotional strain and debilitating symptoms which patients with ARA experience.

6.1.1. Aims and Hypothesis

As discussed in Chapter 1, the two main aims of this thesis were to determine the:

i) impact of FI and constipation has on psychosocial functioning in the context of ARA compared to two control groups.
ii) pathophysiological mechanisms that might contribute to poor bowel function in patients with ARA.

We hypothesized the following:

i) Symptom scores assessing constipation and faecal continence will be major determinants for poor psychosocial functioning.
ii) Patients with ARA will have poorer symptom and quality of life scores in comparison to the controls groups.
iii) Patients with ARA will have poorer level of hopefulness, mental state (depression and anxiety) and different coping strategies in comparison to the control groups.
iv) Psychopathology in patients with ARA will have specific personality traits

compared to the control groups.

v) Patients with the more severe anatomical defect in ARA will have poorer symptom and quality of life scores.

vi) The pathophysiology in ARA will involve extra-sphincteric mechanisms.

vii) There will be a relationship between poor quality of life and poor pathophysiological outcomes in patients with ARA.

6. 2 DISCUSSION

6.2.1 Representation of study groups

The study population comprised 149 subjects with 91 males (61.1%) and 58 females (38.9%). There was a male predominance found overall ($p<0.01$) with higher frequency of males than females in the anorectal anomalies (ARA) and idiopathic constipation (IC) group. This has been confirmed by previous authors, who also found in Western communities, with 55-70 per cent of patients in larger series have being males (Pena, 2000, Rintala, 2005). This has also been confirmed in patients with IC with a 2-3 to 1 male to female ratio, yet with adults there is marked female predominance (Clayden, 1992). However, other authors have found the male-female ratio associated with ARA almost equal, with 56:44 male: female ratio (Smith, 1988, Endo et al., 1999).

Overall, the majority of our population were Caucasian in the total study population (73/149). It has been noted in the literature, that ARA appears to have worldwide incidence and have been reported from most countries, but there is great paucity of

information as to the relative incidence of ARA between ethnic groups. Smith (Smith, 1988) reviewed the reported incidence and suggested that factors such as definition and inclusion may account for many of the variations observed.

There was significantly a higher number of the second age group (>18 years) in the healthy controls ($p<0.0001$) in comparison to ARA and IC groups. This can be explained by the fact that the diagnosis of appendicitis is more commonly found in adolescents/adults compared to the paediatric population (Lee, 1962).

In the ARA sample, there were 7 patients with a low defect, 13 with intermediate and 23 with a high defect and 9 patients unknown. There was a male predominance found in each classification which was significant ($p<0.03$). Generally it has been noted in the literature, that low defects are more common in females than males, whereas > 50% of affected males have high lesions (Rintala, 2005, Cook, 1990, Endo et al., 1999, Cuschieri, 2001, Cuschieri, 2002). As mentioned in Chapter 1, ARA occur commonly in multi-anomaly sequences, such as the VACTERL association (vertebral, anorectal, cardiac, trachea-oesophageal, renal and limb (radius) (Davies et al., 2004, Czeizel and Ludanyi, 1985). In our population sample, 24/52 (46%) of patients with ARA had associated VACTERL conditions. This can be confirmed by other authors who have found similar associations with VACTERL conditions (Endo et al., 1999, Cuschieri, 2002). In patients with IC, 13/46 (28%) were diagnosed soley with a megarectum, 13/46 (28%) with a slow transit and 11/46 (24%) with both a megarectum and slow transit. It is important to note here, that slow transit studies were not performed in all patients or were missing from their medical records. This can be confirmed by other authors who have reported prevalence for megarectum in

constipated patients (van der Plas et al., 2000, Meunier et al., 1984, Loening-Baucke, 1984a).

6.2.2 What is the impact of faecal incontinence and constipation has on psychosocial functioning in the context of ARA compared to two control groups?

6.2.2.1. Patients with ARA will have poorer symptom scores in comparison to the controls groups.

In our research study, IC had the poorest KESS and Vaizey scores in comparison to ARA and healthy controls. However, both ARA and IC had a KESS total mean score >7 which is considered above the normal range of healthy controls (Knowles et al., 2000). Additionally, there was evidence of a significantly higher Vaizey scores found in patients with ARA (<0.0001) and IC (0.0002) compared to healthy controls. The Vaizey mean score found in our ARA and IC patients can be confirmed similar to other patient population groups with symptoms of FI (Vaizey et al., 1999a, Deutekom et al., 2005). Despite surgical advances, it is clear from our findings above, that voluntary bowel control is frequently poor following surgical care for ARA (Heikenen et al., 1999) with high rates of faecal incontinence (FI), and also constipation after all grades of reconstructive surgery (Rintala and Lindahl, 1995, Ong and Beasley, 1991, Rintala et al., 1993b).

Our hypothesis was partly met, in that ARA did have poorer symptom scores compared to healthy volunteers, but were similar to the IC group. In can be said, that both ARA and IC appear to have similar bowel characteristics despite the fact that IC

patients do not have a known anatomical defect and have intact sphincters compared to ARA.

6.2.2.2. Symptom scores assessing constipation and faecal continence will be major determinants for poor psychosocial functioning.

Overall, in our population study, IC had significantly poorer total GIQOL scores compared to healthy controls ($p<0.001$) and ARA compared to healthy controls ($p<0.01$). There was no significant difference found between ARA and IC ($p>0.05$), indicating similar gastrointestinal health related quality of life characteristics exists between these two groups. Varying degrees of constipation and FI in patients with ARA have profound effects on quality of life (Rintala et al., 1992) (Ludman et al., 1994, Diseth et al., 1998a, Diseth et al., 1998b, Ditesheim and Templeton, 1987), which has been confirmed in our study.

Studying the subgroups in the GIQOL, this study can clearly state that symptoms in patients with ARA and IC have a potential impact on the patient's lifestyle. Physical well being includes factors as general physical health and fitness and the ability to enjoy eating and leisure activities. Both ARA and IC significantly had poorer physical well being compared to healthy controls, however IC was found to be worse than ARA. IC had significantly poorer GIQOL scores for gastrointestinal digestion symptoms (such as abdominal pain, bloating, flatus, regurgitation, constipation, heartburn) compared to healthy controls ($p<0.01$) illustrating a more global dysfunction in comparison to ARA patients. Both ARA and IC had significantly poorer GIQOL life scores for gastrointestinal defaecation symptoms (such as bowel

frequency/urgency, uncontrolled stools, impaired sexual life, diarrhoea, blood in stools) and mental state (such as coping with stress, sad/nervous about illness, happy with life and frustrated by illness) compared to healthy controls. Items not included in a subscale ('other') included questions on restricted eating, wake up at night, bothered by treatment, worsened relations and dysphasia. Both ARA and IC had poorer GIQOL 'other' scores, compared to healthy controls.

Our hypothesis was partly met, in that ARA did have poorer quality of life compared to healthy volunteers, but were similar to the IC group. Thus, both ARA and IC appear to have similar psychosocial functioning. Our findings have also confirmed that FI and constipation are both major determinants for psychosocial functioning in patients with ARA and IC. Since patients with ARA are born with an anatomical defect, we expected poorer symptom scores which will have an impact on their quality of life. However, we did not expect the IC group to share such strong similarities to ARA, since they have normal anatomy of the anorectum with intact sphincters. This finding raises the question: Is childhood constipation a physical or behavioural problem in childhood? There are two ways of conceptualising these findings based on these results so far.

A possible suggestion to this question could be that the patient has a familial predisposition to delayed defecation by having a rectum of a larger capacity than the average individual. In our study population, the majority of our patients with IC had been diagnosed in their medical history to have a megarectum (with/without slow transit) . This suggest that these patients have a rectal evactory disorder which entails an increase rectal capacity and reduced sensation. In such cases, the patient has the

tendency to hold their stool rather than being forced to pass it (Clayden and Keshtgar, 2003). Therefore, if the patient has a larger capacity, it will need higher volume of stool to cause complete inhibition of their IAS. Eventually, the rectal volumes reaches the stage where the IAS is fully relaxed and the stool descends, which usually causes anal pain due to the difficulty in passing the stool. The patient then responds, by straining to withhold the stool in order to avoid the pain by contracting their EAS and pelvic floor muscles. However, the situation worsens by the fact that withholding eventually leads to episodes of overflow FI which in turn prevents intestinal obstruction (Clayden and Keshtgar, 2003). It has been found that withholding is a common behavioural factor of constipation in young children which can be due to psychological stressors (Mason et al., 2004, de Lorijn et al., 2004) or fear of using the toilet or potty (Clayden, 2004, Cladyen, 2005) or episodes of painful defaecation, often due to constipation. Thus, psychosocial stressors could be causing withholding which further leads on to ignoring the urge to defecate, and eventually the stool retained in the rectum becomes impacted leading to constipation (Rogers, 2003) (Clayden and Keshtgar, 2003). There remains continuous debate over the association between constipation and psychosocial problems, and whether constipation causes psychosocial problems or vice versa (Benninga et al., 2004). Studies have found that psychosocial and behavioural problems are the main cause of chronic idiopathic constipation (Coughlin, 2003, Southwell et al., 2005, Gabel et al., 1986, Friman et al., 1988). Whichever theory chosen, both could be responsible for our patient's poor symptoms and quality of life and no doubt, needs to be further investigated in order to solve the underlying problem.

Secondly, in our IC population group, all patients developed their symptoms in childhood with continuation of inadequately treated faecal retention. It has been suggested by authors that there is a tendency for increasing denial and dissociation from their problematic condition that limits the effectiveness of psychological input and any medical or surgical intervention (Keshtgar et al., 2004a, Ludman et al., 1994). For the treatment to be successful, a joint physical and psychological approach is important to encourage the patient to deal with their condition. Thus, it is vital to promote early effective treatment of constipation and the withholding habit in early childhood, which might reduce the incidence of chronic IC with faecal soiling and overflow later in adulthood.

6.2.2.3. Patients with ARA will have poorer level of hopefulness, mental state (depression and anxiety) and different coping strategies in comparison to the control groups.

Our findings indicated that ARA were, not significantly more depressed or anxious individuals compared to the control groups. However, in the literature, psychiatric morbidity has been found to coexist in patients with ARA, resulting in significant emotional and social difficulty for both the patients and their families (Hamid et al., 2007, Ludman and Spitz, 1996, Ditesheim and Templeton, 1987, Diseth and Emblem, 1996, Hassink et al., 1994, Ginn-Pease et al., 1991, Ludman and Spitz, 1995). It has been suggested that bowel dysfunction is one of the most important factors that influences the level of depression of children and adolescents with ARA (Amae et al., 2008, Hamid et al., 2007, Funakosi et al., 2005). In our research study, it was shown that patients who were clinically depressed and/or anxious, significantly had poorer

quality of life related to their symptoms, in comparison to those who were not. Additionally, patients with partial and full incontinence significantly had higher incidence of state anxiety compared to those who were fully clean. Similarly, Funakosi et al (2005) found in children with ARA, that the depression tended to be more severe as the degree of FI worsened and as the child reached adolescence, yet the association failed to reach statistical significance. Our findings imply that symptoms of gastrointestinal nature such as FI and constipation could influence the patient's psychiatric well being, despite not reaching statistical significance. Similar findings have been found in children and adolescents with Hirschsprung's disease (Athanasakos et al., 2006). Based on our findings so far, it appears that patients with ARA and IC have minimal psychiatric morbidity, but experience condition-specific psychosocial problems as demonstrated in our first two hypotheses above.

There was no significant difference between the three groups in terms of level of hopefulness in our population groups. If the subject had a good quality of life (according to the GIQOL measure), they were significantly more hopeful about their future in comparison to those with poor quality of life scores. Symptoms scores had no impact with level of hopefulness in this research study. Cappelli et al (1989) (Cappelli et al., 1989) found similar findings in adolescents with chronic illness which are in fact not at greater risk of developing psychopathology, yet they appeared to become more concerned about their health and future. There is currently limited literature investigating personal hopefulness in children with ARA to date, with one author having investigated this area (Hamid et al., 2007). Despite the reported high level of psychosocial morbidity found in patients with ARA, Hamid et al (Hamid et al., 2007) also found their level of hopefulness of the future to be positive. Similar

results have been found in patients with similar symptoms to ARA and IC, in patients with Hirschsprung's disease (Athanasakos et al., 2006). This raises the question as to how our patients with ARA and IC remain hopeful individuals, despite their disabling symptoms and distress.

The above question can be possibly explained by investigating the individual's coping strategies. Boekaerts and Roder (Boekaerts and Roder, 1999) found children with chronic conditions to use coping strategies in relation to common stressors that appeared to be similar to those of healthy children. As expected, we found a significance difference in overall coping mechanisms between ARA and healthy controls ($p<0.05$). ARA significantly used more 'positive reappraisal' which involves thinking of attaching a positive meaning in the event in terms of personal growth and also 'putting into perspective' by referring to thoughts of playing down the seriousness of the event or emphasizing the relativity when comparing it to other events (Garnefski, 2006).

In our study, patients with ARA and IC could be holding unrealistic positive beliefs about their condition and future as demonstrated in their level of hopefulness scores, however, this could assist the patients to cope with the stress of their condition (Scheier et al., 1989). Thus, being unrealistically positive may be a coping mechanism that helps people feel better and is related with positive social relationships and motivation to work. Thus, despite the unrealistic positive illusions the individual may have, it could assists them to approaching the situation realistically, once they have coped with the intense emotions associated with the condition first. Some authors describe the above coping mechanisms as a form of denial in such patients (Ludman and Spitz, 1996, Ludman et al., 1994). Freud (1961)

first used the concept of denial within the language of defence mechanism in psychoanalytical theory (Freud, 1961). Such defence mechanisms can be used by the ego to avoid the anxiety of a threatening or stressful situation. Freud described denial as the refusal to acknowledge the existence of an unbearable situation or the feelings associated with it, and saw it as one of the defence mechanisms use to protect the ego from anxiety. Through its use, painful or distressing thoughts and emotions were prevented from entering the consciousness, and this provided time for the ego to become strong enough to deal with a changed situation, but only up to point. If denial were prolonged, it would lead to pathology.

In summary, it is clear from our findings that patients with ARA and IC have poor quality of life specifically due to their disabling symptoms however this has not necessarily increased their psychiatric morbidity. These findings clearly show that symptoms (such as FI and constipation), drives an emotional response to the individual which can be further understood by how the individual copes with the stressor. For example, anything that induces fear or anger causes the heart to beat faster, increases the tension in our back and neck muscles, enhances the sensitivity of the bladder, the colon contracts vigorously and so on (Rang, 2003, Read, 2006). These natural physiological responses, indicates that changes in bodily function are brought about largely through both sympathetic (flight or fight response) and parasympathetic (conservation, restoration and recovery) responses to change. In the sympathetic state, there is an increase of blood pressure, respiration, heart rate and shuts down areas such as the gut, liver and kidneys. In the parasympathetic state, this induces a state of rest and calm, promotes sleep, stimulates the digestion and supports tissue growth and repair (Rang, 2003, Read, 2006). Unlike the sympathetic system, it

slows the heart, steadies the respiration and promotes the function of the gut, liver and kidneys. Furthermore, sympathetic and parasympathetic responses to change are often supported by the release of the stress hormone cortisol. If such emotions to the situation can't be resolved either sympathetic or parasympathetic withdrawal, then prolonged activation of these strategies will inevitable result in exhaustion, demoralisation and illness (Read, 2006). This could suggest that patients who are suffering ongoing symptoms of bowel function which leads to poor quality of life causing distress (as found in our patients) chronically as shown from our results, then their symptoms are even more amplified by their mental state. It is beyond the scope of this thesis to explore such brain-gut axis relationship, but it is important to note that illness is not all in the body nor all in the mind, but rather a dual relationship which is needed to resolve the patient's illness. This may explain why ARA and IC share similar psychological characteristics, no matter if one has a pathogenic cause and the other doesn't, because their ongoing distressing symptoms is causing them to behave the way they do.

6.2.2.4. Psychopathology in patients with ARA will have specific personality traits compared to the control groups.

Some authors believe that adolescents with a chronic illness could be at risk of developing psychopathology (Eiser, 1990, Gortmaker, 1990, Lavigne, 1992, Varni et al., 1992, Wolman et al., 1994). We aimed to investigate the association between psychopathology and specific personality traits that could be associated with patients with ARA. Based on the current situation in the literature, this is the first research study to include personality measures in patients with ARA. Overall, in our

population sample, there was no significant difference between the three subject groups, thus no specific personality trait was associated with patients with ARA. A study which looked at epilepsy in children and adolescents also found no specific personality traits that could be linked to their patients (Otero, 2009). Emotional states and personality traits may affect the physiology of the gut (Wood et al., 1999), and play a role in how symptoms are experienced and interpreted, and can thus influence treatment. Neuroticism and aggression are reported to be higher in patients with functional gastrointestinal disease without psychiatric comorbidity, and personality traits are believed to influence pain reporting (Tanum and Malt, 2001). In our study extroversion significantly was found to be associated with lower level of personal hopefulness and higher PILL score (i.e. more emphasis on physical health) and neuroticism significantly correlated with lower level of personal hopefulness, high state and trait anxiety. These findings do not indicate specific personality traits within the population group, but it does imply that traits such as extroversion and neuroticism do influence the patient's level of hopefulness about their future. This area needs to be further explored in future research.

6.2.2.5. Patients with the more severe anatomical defect in ARA will have poorer symptom and quality of life scores.

It may be expected that the more severe the condition is, the greater the probability of psychosocial difficulties. In our study, there was no relationship between severity of the anorectal defect with psychosocial adjustment and symptom scores, found in patients with ARA. This finding implies that it isn't the type or severity of the anatomical defect in patients ARA that influences the severity of the symptom or

psychopathology. There remains confusion within the literature about this area. It has been found in adolescence with ARA that had psychological morbidity tended to be more severe as the degree of FI worsened (Funakosi et al., 2005) (Diseth et al., 1998a). While others found no association with severity of the condition or symptom to psychological functioning (Ludman and Spitz, 1996). In fact more emphasis is apparently placed on the presence of the condition rather than its level of severity. In our study, we investigated the amount of emphasis an individual puts on their general health, by using the Pennebaker Inventory of Limbic Languidnes (PILL). In our study, IC significantly placed less emphasis on their general health, compared to ARA and healthy controls. Reasoning for this finding, could be that IC place their emphasis on the symptom that is most troublesome for them based on their poor symptom and quality of life scores and place less focus on other bodily sensations.

6.2.2.6. The ACE stoma is an effective treatment with good symptom and quality of life scores for both ARA and IC.

The ACE stoma is a treatment offered to patients when other forms of medication have failed for the patient suffering from FI and constipation. In our research study, patients with IC had significantly poorer KESS score compared to ARA and poorer continence scores when compared to ARA in the ACE population, which did not reach statistical significance. There was no significant difference between ARA and IC in terms of GIQOL in the ACE population. However, patients with an ACE had below the normal mean for GIQOL score compared to healthy volunteers and 80% of the ACE population had poor GIQOL which is the majority of the sample. Thus, we did not find that the ACE stoma significantly improves the quality of life for the

patient with symptoms of FI and constipation. There has been mixed perceptions about the success of the ACE. Some studies have found that the ACE stoma is an effective treatment for constipation and soiling (Yerkes et al., 2003, Searles et al., 2000, Herndon et al., 2004, Hutson et al., 2001, Clayden, 2004), while other studies, has not rated the ACE as highly (Rubin and Dale, 2006) due to the instances of repeated treatment failures, and they also identify that complications are common (stomal stenosis and pain with the enemas) (Dey et al., 2003). Studies (King et al., 2005) have found that the ACE stoma significantly improves the quality of life of children with chronic idiopathic constipation.

The above findings could imply that patients, who generally dislike having the ACE due its appearance or time consuming treatment, lead to non compliance and therefore unsuccessful outcomes. Non compliance is a characteristic that is often associated with being in denial (Anderson, 1991). People living with an ongoing condition often learn that their response to illness do not follow the patterns described by healthcare professionals as in the case in patients with an ACE. Thus, they begin to find their own self-care practices that fit within the context of their lives, even if it means not complying with the treatment they have been advised to pursue. Instead, patients may assert themselves by refusing to take medication, opposing treatments or giving healthcare professionals as little information as possible. Thus, patients are often labelled as problematic or in denial, but in fact, these actions could be explained as a way of asserting self-agency through realising personal needs and wishes in the life context. Thus individuals prioritise their own needs and wishes over the demands of medication instruction, even at the risk of poorer health outcomes. It is important to

note that the health professional needs to take into account the wider social context of the individual's setting (e.g. home, school, work, relationships etc).

6.2.3 What are the pathophysiological mechanisms that might contribute to poor bowel function in patients with ARA?

6.2.3.1. The pathophysiology in ARA will involve extra-sphincteric mechanisms

This study has demonstrated that in a cohort of symptomatic adult patients whose problems with FI have persisted since surgery for their ARA, pathophysiology was multifactorial in all. This supports contemporary thinking that anal sphincteric dysfunction is not solely responsible for FI, and that extra-sphincteric mechanisms may be equally important (Davies et al., 2004). The pathophysiologies encountered, namely attenuated anal sphincter function (structural neuropathic or both), altered rectal sensation, disordered rectal evacuation, and delayed colonic transit, occurred with all grades of anomaly following different procedures. Although there was a tendency for both clinical and pathophysiological differences to occur between subgroups (e.g. more high anomalies appeared to be hypersensate, and a greater proportion of intermediate anomalies had co-existent constipation) it is impossible, to draw firm conclusions. Appropriate statistical analyses could not be performed on the relationship between the types of anorectal anomalies, their surgical correction and the pathophysiology found, due to limited numbers. Furthermore, analysis was complicated by a lack of comprehensive information concerning the initial surgery and, the variety of procedures used.

With regard to surgical correction of ARA, some procedures involve division of the sphincter complex (Pena and Devries, 1982, deVries and Cox, 1985, Smith, 1987, Engel et al., 1995, Lunniss et al., 2004), as opposed to pull through techniques which also aim to conserve the IAS (Smith, 1987). It is notable and disappointing that most patients in this study who underwent posterior sagittal anorectoplasty, a popular technique, currently, demonstrated poor sphincter quality. Previously, in patients with acquired FI (usually due to obstetric or iatrogenic trauma), symptoms of passive incontinence have been shown to correlate with low anal resting tone and symptoms of urge FI often correlate with low squeeze pressures (Lunniss, 2007, Engel et al., 1995, Lunniss et al., 2004). The IAS plays a major role in continence, particularly in patients in whom EAS function is also deficient. The necessity to preserve the IAS at operations for anorectal and cloacal anomalies, which has been recommended by some authors, has either not been achieved in the majority of these patients or the sphincter was deficient from the start (deSouza et al., 1999).

Integrity of anal sphincter morphology and function are of fundamental importance to normal continence, but the contribution of extra-sphincteric components (both colonic and rectal) is increasingly recognised (Chan et al., 2005a, Lunniss, 2007, Williams et al., 2001, Bharucha et al., 2005, Bharucha, 2004, Salvioli et al., 2001, Chan et al., 2005c, Gladman et al., 2005). Pudendal neuropathy may underlie EAS weakness in patients with symptoms of FI. In addition, the frequent association of neuropathy with ARA, which may be either congenital or acquired as a result of surgery, may result in altered anorectal sensation, contributing to both constipation and incontinence (Hettiarachchi et al., 2002).

With regard to demonstration of rectal sensory dysfunction, it was found that patients with rectal hypersensitivity presented with symptoms of urge FI, and patients who were hyposensitive, presented with concomitant constipation and were found to have delayed colonic transit. The relationship between hypersensitivity and faecal urgency or urge incontinence has been reported previously (Lunniss, 2007, Williams et al., 2001, Bharucha et al., 2005, Chan et al., 2005c, Sun et al., 1990, Felt-Bersma et al., 2000). In those with significant blunting of the ability to sense distension (rectal hyposensitivity), all were in the low or intermediate category and had coexistent constipation comparable with previous findings (Gladman et al., 2006). Three of the four had incomplete evacuation on proctography. Whether the delay in transit was primary or secondary to disordered defecation is unknown. However FI occurring secondary to blunted rectal sensation and disordered defaecation is well established (Lunniss, 2007, Farthing and Lennard-jones, 1978, Rao et al., 2004, Lubowski and Nicholls, 1988, Di Lorenzo and Benninga, 2004).

6. 3 STRENGTHS AND LIMITATIONS

There are some limitations present in this research study. When recruiting patients with a rare condition such as ARA, sample size is always a potential problem. A large sample size is needed to ensure the generalisability and the accuracy of the results, but small enough so that the study question can be answered within the research resources that are available and time frame. As seen in Table 1.5 (Chapter 1), sample size for similar research studies, ranged from 17-286 patients with ARA. Despite the fact that our research patient population group (n = 52) was not as high as some authors (Poley

et al., 2004, Hamid et al., 2007, Amae et al., 2008, Bai et al., 2000, Hassink et al., 1994, Ludman and Spitz, 1996), control groups were absent (especially healthy subjects) and psychosocial measures were limited in their studies. Despite the presence of healthy control group (appendectomy subjects), there was significantly a higher number of the second age group (>18 years) in the healthy controls ($p<0.0001$) in comparison to ARA and IC groups which makes age matching not accurate when comparing between all groups. However, as discussed above, this can be explained by the fact that the diagnosis of appendicitis is more commonly found in adolescents/adults compared to the paediatric population (Lee, 1962).

Despite various perspectives in the literature, morbidity has been found to coexist in patients with ARA even after surgical repair, resulting in significant emotional and social difficulty for both the patients and their families. In our research study, we failed to include perspectives from the family members involved in the care of the child and adolescent with ARA. This information could be beneficial when talking about coping mechanisms, treatment compliance issues and generally trait characteristics which the parent and child have in common. Most studies have included a joint perspective of both the parent and patient involved when answering questions about their bowel and psychosocial functioning making it difficult to derive the patient's sole perspective of they are thinking rather than the parent/carer involved (Amae et al., 2008, Hamid et al., 2007, Iwai et al., 2007, Goyal et al., 2006, Poley et al., 2004, Funakosi et al., 2005, Hassink et al., 1994).

Limitations are also evident in the pathophysiology study of this thesis. All patients with ARA in this study were self selected with poor bowel function and were thus not

representative of the population as a whole. Therefore, the expected pattern of better outcomes in low and intermediate anomalies as opposed to high is not clearly apparent. It may be that patients with isolated deficiencies in function of either sphincteric or suprasphincteric components achieve better levels of continence. Additionally, patients included were symptomatic patients which attended our GI Physiology Unit with FI. This research failed to explore a more homogenous cohort of patients with equivalent anorectal anomaly and surgery, irrespective of whether the patient is symptomatic or not. Despite the considerable variability in this population sample and the investigations performed, it is important to appreciate the difficulties regarding recruitment and reproducibility. Nevertheless this study is unique despite these aforementioned limitations, as it considers other mechanistic processes involved in continence in addition to sphincteric factors in isolation.

However, this study does not have the limitations of similar studies which have shown to lack control groups, specific psychosocial measures (e.g. assessing level of hopefulness, personality, coping mechanisms) and symptoms scores which will be discussed. This research study was well designed in that groups were divided on the basis of major age groups such as high school (adolescence) and adulthood (work force/university/college etc). Few studies have looked at such a wide age range as our research project (age range: 11-45 years) (Hamid et al., 2007, Goyal et al., 2006, Poley et al., 2004, Hassink et al., 1994). Having a wide age group allows a better representation of the patient group and an insight to how patients are doing at different age groups (and development stage). It may also highlight certain bowel or psychosocial characteristics evident at certain age periods. There are several symptom scores available in the literature however authors fail to investigate the

relationship between bowel function using validated and well recognised symptoms scores with health-related quality of life measure and psychiatric measures in patients with ARA. The major strength to our study is the inclusion of control groups which has been discussed in Chapter 2. This thesis has age and sex matched control groups including patients with similar symptoms yet no anatomical defect compared to our patients with ARA and healthy volunteers without a chronic gastrointestinal condition. Finally, this is the first study to include personality and coping validated questionnaires in patients with ARA.

6. 4 IMPLICATIONS

There are several implications that can be derived from our research study. This study has clearly shown that symptoms of constipation and FI are ongoing and distressing for patients with ARA and IC. Despite, the fact that IC has an unknown underlying aetiology, they share similar bowel function to ARA and are equally challenging group of patients to treat.

Both FI and constipation are determinants of poor psychosocial functioning in patients with ARA and IC and thus, provision for adequate psychosocial support for these patients, should be an integral part of outpatient services. Regular follow-ups are crucial in order to become aware of any changes in stooling and behavioural patterns over time for the child with ARA and IC. From the very beginning the child is diagnosed with ARA and IC, patients and the family, should be informed of the potential risks, long term outcomes, general understanding of bowel functioning and treatment available. From the time child starts toilet training, the health professional

involved must begin to explain the importance of going to the toilet and along with explaining why soiling or constipation is happening and ways to deal with the situation. This needs to be further reinforced by the parent/carer involved to the child in order to create better communication and the best possible bowel outcome for the patient. Regular follow-ups may minimise and improve issues of withholding, behavioural problems and issues or fear of using the toilet or potty or episodes of painful defaecation.

Every institution varies in which operative technique is used, age at which the child is followed up, regularity of follow-ups, definitions of symptoms (such as FI) and many other factors. Thus it is important as healthcare professionals to become aware of such variability and to use caution when making generalisation and conclusions about patients with ARA and IC. A national standardised questionnaire or assessment tool would be of value for healthcare professionals to use when evaluating patients on a regular and long-term basis. Particular focus should be placed on definitions for constipation and FI to avoid discrepancies and severity confusion. Having the same questionnaire used by all institutions will provide:

- Clarity of the child's bowel functioning over time and at different ages.
- The opportunity to draw comparisons between groups
- Clearer understanding of potential risk target groups
- Improvement in clinical management
- Increase data quality and research.

General knowledge about the condition (e.g. CD, handbook) or additional facilities or aids within educational institutions (e.g. shower facilities if the child has had

explosive amounts of faecal soiling in underpants) are examples of ways to improve everyday functioning for the patient and family involved. Since ARA and IC are hidden conditions (i.e. it is not obvious like Haemophilia or Downs Syndrome), it is easy for education professionals to ignore or fail to appreciate the importance when a child needs to go to the toilet urgently or having 'smelly' underpants. Thus, regular contact with the school should be maintained since alterations in performance or behaviour may be sensitive predictors of future difficulties.

Special efforts will be required to break through defences to insure that anxieties, conflicts and concerns about the future are identified early. Ideally psychosocial screening procedures should be developed and used routinely in the outpatient care of all adolescents with chronic disorders such as ARA and IC so that potential problems may be identified promptly and action taken to prevent their development. It is of equal importance to develop a program to insure that the child with ARA and IC is revaluated psychologically at regular intervals in the same way they are medically for bowel function. It is by identifying psychological and social adaptation problems early, that possible intervention to help the child successfully adjust to their illness becomes inevitable. The fact that children with ARA and IC have persisting bowel functioning problems after surgical correction, it is vital to counsel parents from the very beginning (i.e. at diagnosis) regarding realistic expectations of the child's long-term outcomes. Counselling should be offered for both the child with ARA and family. This will allow parents (and for older children) to become comfortable talking about 'that' region of the body (such as the buttocks) and grasp an understanding of why it is so difficult to do certain things (such as going to the toilet, stop soiling). Failure to address psychosocial problems from an early age could

increase the development of psychosocial morbidity in these patients. This can be accomplished by close cooperation of all professionals working locally (i.e. surgeons and psychiatrist working closer together), annual seminars or workshops within the medical field and for families, to keep updated with advanced treatments, concerns and other medical science advancements.

There is no doubt, that ARA forms a significant load on the surgical services worldwide, not only in the emergency situations but also in terms of long term corrective procedures and management of symptoms such as FI and constipation. As discussed in Chapter 1, there have been major advances in the surgical management of these children, but these patients still represent a continuing challenge as a result of the significant reconstructive problems involved, as well as the fact that a significant number suffer from ongoing symptoms in later life. This needs to be implemented when discussing the financial burden it has on the patient, family and medical system involved.

As seen by the complexity and multifactorial nature found in patients with ARA in respect to pathophysiology, it is clear that implementation of any treatment targeted on one area of dysfunction may fail and two or more treatment modalities may be necessary to achieve continence, i.e. rectoplasty and antegrade continence enema stoma, or sphincteroplasty or anal plug (Keshtgar et al., 2007b, Keshtgar et al., 2007a). Other more advanced surgical techniques may also be considered (Malouf et al., 2000, Saunders et al., 2004). Alternatively, colostomy may offer a solution.

6. 5 FUTURE DIRECTIONS

This research study opens doors for further research for patients with ARA. These include:

1) This study focused on how the patient is functioning at this moment of time. It may be that this time period was insufficient to capture all aspects of ARA and its impact on the individual. Ideally, a large multi-centred and longitudinal study in patients with ARA would be conducted and young people would be followed up into their 30s and 40s to evaluate the impact of ARA later in adult life.
2) This thesis purely gained the patient's perspective about their bowel and psychosocial functioning. In order to grasp how the family influences the patient's perspective and coping mechanism living with this condition, parental and sibling perspectives could be included.
3) To gain a better understanding of the brain-gut relationship in patients with ARA and IC, brain imaging and cortical evoked potential research could enhance our knowledge further.
4) Future pathophysiological research needs to explore a homogenous cohort of patients with equivalent anorectal anomaly and surgery, irrespective of whether the patient is symptomatic or not. It is only then that we will be able to confidently comment on the pathophysiologies observed in this study and if these are associated with symptom development or not. The importance of the psychological impact and coping mechanisms in such a group of patients needs also to be studied concurrently.

6. 6 CONCLUSION

Patients with anorectal anomalies (ARA) have a complex, structural developmental abnormality. Whilst surgical treatment aims to correct the anatomical defect, functional issues remain for years. The findings to this research study have shown that ongoing symptoms of FI and constipation are major determinants for poor quality of life in patients with ARA. However, contrary to our expectations, they share similar bowel and psychosocial functioning to patients with idiopathic constipation (IC) who unlike our ARA patients, have an intact sphincter mechanism. Despite the significant impairment of faecal continence and constipation in both ARA and IC groups, we found that adolescents have minimal psychiatric morbidity yet experience condition-specific psychosocial problems affecting their day to day life. It is shown from our findings that the chronic nature of the patient's problem appeared to have stimulated psychologically protective factors such as positive coping strategies to deal with their disease related stressors. Additionally, while the structural integrity of the anal sphincters (which may relate to surgical technique) is the major factor contributing to continence, this study confirms that extra-sphincteric mechanisms, particularly rectal sensory function, may be equally important. Prospective studies of operative techniques employed in patients with comparable anomalies are required.

As our findings have indicated, to achieve the best outcome for our patients, a joint physical and psychological approach is needed to encourage the patient to deal with their condition. At present the emphasis in clinical management of ARA is to ensure survival and normal bowel function for the child. Further focus should be placed in achieving good quality of life for the child and family dealing with ARA. This thesis

suggests that surgery is not the final point of treatment for children with ARA. It is vital to call attention to the introduction of long-term regular follow of patients after surgery for ARA. Good bowel functioning facilitates improvement for the quality of life for the adolescents with ARA, yet there is difficulty achieving this as emphasised by our results in the ACE population which is an advanced treatment modality. Living with ARA involves not only dealing with the underlying aetiology of the condition, but also the complications, stressors, confusion, hardship and emotional burden it places on the patient. When treating an adolescent with ARA, medical professionals are not only obtaining outcomes for treating the bowel disorder but also capable of achieving the best quality of life for their patients and family.

In conclusion, in the care of adolescents with chronic physical problems, one aim is to try to minimise the relationship between physical and emotional difficulties. This study has clearly shown that both FI and constipation produces effects on the adolescents/adult's psychological adjustment. A longitudinal study would confirm this. This research provides some insights into the factors associated with maladjustment among patients with ARA and may eventually prove to be of use in guiding intervention programs. Thus, outcome and compliance with treatment may be enhanced if, from an early age, psychological evaluation of the child and experienced advice and guidance for the families, regardless of the severity of the symptoms, becomes an integral part of their continuing care.

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APPENDICIES

Appendix – A Peer Review

Barts and The London NHS
NHS Trust

Neonatal Medicine
Directorate of Women & Children
The Royal London Hospital
Garden House – 2nd Floor
Whitechapel
London E1 1BB

Tel: 020 7377 7712/7188
Main switchboard: 020 7377 7000
Fax: 020 7377 7712
www.bartsandthelondon.nhs.uk

Consultants:

Dr M Hird 020 7377 7188
Dr S Kempley 020 7377 7712
Dr A Opute 020 7377 7188
Dr A Sinha 020 7377 7712
Dr R Ebel 020 7377 7712

Facsimile: 020 7377 7712

19 September 2006

Dr Eleni Athanasakos
The Wingate Institute
26 Ashfield Street
London E1 2AJ

Dear Dr Athanasakos

Re: Paediatric Peer Review – PRP 003

Thank you for clarifying these issues.

Please take this letter as confirmation that your project has been peer reviewed and approved by the R&D Committee for Paediatrics for Barts and the London NHS Trust subject to the cost of the physiological testing being met within the project costs.

Yours sincerely

Steve Kempley
R & D Lead for Women & Children's Directorate

c.c. Dr Nick Croft

Appendix – B Ethics Approval

Queen Mary
University of London

Barts and The London NHS
NHS Trust

FINAL R&D APPROVAL

Miss Eleni Athanasakos
Royal London Hospital
Barts & the London NHS Trust
The Wingate Institute
26 Ashfield Street
Whitechapel, London
E1 2AJ

Joint Research and Development Office
24-26 Walden Street
Whitechapel
London
E1 2AN

Tel: 0207 882 7272
Fax: 0207 882 7277
Email: david.jackson@bartsandthelondon.nhs.uk

07 June 2007

Dear Miss Athanasakos,

Re: Colonic and Anorectal Function with Psychosocial Assessment in Adolescents & Adults with Anorectal Anomalies

ReDA Reference: 004913

Thank you for sending confirmation of your approval from the ethics committee. I am now happy to inform you that the Joint R&D Office of Barts and The London NHS Trust and Queen Mary, University of London has arranged full indemnity cover for your study against any negligence that might occur during the course of your project.

Please note that all research with an NHS element is subject to the Research Governance Framework for Health and Social Care 2005. If you are unfamiliar with the standards contained in this document, or the BLT and QMUL policies that reinforce them, you can obtain details from the Joint R&D Office, tel 0207 882 7250 or go to http://www.dh.gov.uk/PolicyAndGuidance/ResearchAndDevelopment/ResearchAndDevelopmentAZ/ResearchGovernance/fs/en.

You must stay in touch with the Joint R&D Office during the course of the research project, particularly if/ when:

- There is a change of Principal Investigator;
- The project finishes;
- Amendments are made, whether minor or substantial;
- Serious Adverse Events have occurred (must be reported within 24 hours of becoming aware of the event).

This is necessary to ensure that your indemnity cover is valid. Should any untoward events occur it is **essential** that you contact the Joint R&D Office immediately. If patients or staff are involved in an incident, you should also contact the Clinical Risk Manager on 0207 480 4132.

I hope the project goes well, and if you need any help or assistance during its course, please do not hesitate to contact the Office.

Yours sincerely,

Gerry Leonard
Head of Research Resources

Appendix – C Letter of Invitation

Parent Version for ARA

Barts and The London NHS
NHS Trust

Eleni Athanasakos
Barts & The London Queen Mary
Department of Paediatric Surgery
The Royal London Hospital
Fielden House
Whitechapel
London
E1 1BB

Tel: 078 13682226
Main switchboard: 020 7377 7000 Ext 7799
Fax: 0207 377 7743
Email: e.athanasakos@qmul.ac.uk

Date:

To: FAMILY NAME/ADDRESS

Title: Anorectal Function and Quality of Life with Patients with Anorectal Anomalies (ARA).

Dear FAMILY NAME,

We would like to invite your child to take part in a research study at Barts and the London, Queen Mary University of London.

The purpose of this research study is to identify the reasons why some patients with anorectal anomalies, (like your child) can suffer from bowel difficulties after having surgery. It will give us the opportunity to further understand our knowledge of what causes these bowel difficulties by investigating the anatomy and physiology of the anorectum. Most of all once we have identified this, we can offer better treatment for the future.

Your child has been invited to this research study as they have been surgically corrected for ARA and followed up in clinics. We will be able to identify what is causing some children to have these difficulties and offer future treatment suggestions. At least 60 participants at the Royal London Hospital will be involved in this study that has been corrected with ARA.

Participation in this project is voluntary if your child decides not to take part or decide to withdraw at any time this will not otherwise affect their relationship with the hospital or have any impact on the care your child may be receiving.

I have attached a 'Participants Information Sheet' for your convenience. Please feel free to contact the research doctor in charge Eleni Athanasakos who will be able to answer any questions and further explain the research project if needed.

If your child is interested in participating please call Eleni Athanasakos on 0207 882 2626 or 078 1368 2226.

Thank you kindly

Eleni Athanasakos
Clinical Researcher

Appendix – C Letter of Invitation

Patient Version for ARA

Barts and The London NHS
NHS Trust

Eleni Athanasakos
Barts & The London Queen Mary
Department of Paediatric Surgery
The Royal London Hospital
Fielden House
Whitechapel
London
E1 1BB

Tel: 078 13682226
Main switchboard: 020 7377 7000 Ext 7799
Fax: 0207 377 7743
Email: e.athanasakos@qmul.ac.uk

Date:

To: PARTICIPANT'S NAME/ADDRESS

Title: Anorectal Function and Quality of Life with Patients with Anorectal Anomalies (ARA).

Dear PARTICIPANT'S NAME,

We would like to invite you to take part in a research study at Barts and The London, Queen Mary University of London.

The purpose of this research study is to identify the reasons why some patients with anorectal anomalies, (like yourself) are suffering from bowel difficulties after having surgery. It will give us the opportunity to further understand our knowledge of what causes these bowel difficulties by investigating the anatomy and physiology of the anorectum. Most of all once we have identified this, we can offer better treatment for the future.

You have been invited to this research study as you have been surgically corrected for ARA and followed up in clinics. We will be able to identify what is causing some patients to have these difficulties and offer future treatment suggestions. At least 60 participants at the Royal London Hospital will be involved in this study that has been corrected with ARA.

Participation in this project is voluntary if you decide not to take part or decide to withdraw at any time this will not otherwise affect your relationship with the hospital or have any impact on the care you may be receiving.

I have attached a 'Participants Information Sheet' for your convenience. Please feel free to contact the research doctor in charge Eleni Athanasakos who will be able to answer any questions and further explain the research project if needed.

If you are interested in participating please call Eleni Athanasakos on 0207 882 2626 or 078 1368 2226.

Thank you kindly

Eleni Athanasakos
Clinical Researcher

Appendix – C Letter of Invitation

Parent Version for IC

Barts and The London NHS
NHS Trust

Eleni Athanasakos
Barts & The London
Queen Mary University of London
Department of Paediatric Surgery

The Wingate Institute of Neurogastroenterology
26 Ashfield Street
Whitechapel
London
E1 2AJ

Tel:0207 882 2626
Fax:0207 375 2103
Email: e.athanasakos@qmul.ac.uk

Date

To: FAMILY NAME/ADDRESS

Title: Quality of life with patients with Idiopathic Constipation

Dear FAMILY NAME,

As discussed on the telephone, we would like to invite your child to take part in a research study at Barts and The London, Queen Mary University of London.

The purpose of this research study is to access the quality of life of your child who has been diagnosed with idiopathic constipation. It will give us the opportunity to further understand our knowledge of what life has been like for your child living with this condition and to compare results to other bowel diseases.

Your child has been invited to this research study as they have been seen and followed up in clinics here at the Royal London Hospital. At least 60 participants at the Royal London Hospital will be involved in this study that have the same condition.

Participation in this project is voluntary if your child decides not to take part or decide to withdraw at any time this will not otherwise affect their relationship with the hospital or have any impact on the care your child may be receiving.

Please feel free to contact the research doctor in charge Eleni Athanasakos who will be able to answer any questions and further explain the research project if needed.

Your appointment is on 21/08/08 at 10.30AM. If you have any questions, please contact Eleni Athanasakos on 0207 882 2626 or on 07813 682226.

Thank you kindly

Eleni Athanasakos
Clinical Researcher

Appendix – C Letter of Invitation

Patient Version for IC

Barts and The London NHS
NHS Trust

Eleni Athanasakos
Barts & The London
Queen Mary University of London
Department of Paediatric Surgery

The Wingate Institute of Neurogastroenterology
26 Ashfield Street
Whitechapel
London
E1 2AJ

Tel:0207 882 2626
Fax:0207 375 2103
Email: e.athanasakos@qmul.ac.uk

Date

To: PARTICIPANT'S NAME/ADDRESS

Title: Quality of life with patients with Idiopathic Constipation

Dear PARTICIPANT'S NAME

As discussed on the telephone, we would like to invite you to take part in a research study at Barts and The London, Queen Mary University of London.

The purpose of this research study is to access the quality of life with living with idiopathic constipation. It will give us the opportunity to further understand our knowledge of what life has been like for you living with this condition and to compare results to other bowel diseases.

You have been invited to this research study you have been seen and followed up in clinics here at the Royal London Hospital. At least 60

participants at the Royal London Hospital will be involved in this study that have the same condition.

Participation in this project is voluntary if you decide not to take part or decide to withdraw at any time this will not otherwise your relationship with the hospital or have any impact on the care you may be receiving.

Please feel free to contact the research doctor in charge Eleni Athanasakos who will be able to answer any questions and further explain the research project if needed.

Your appointment is on 18/08/08 at 11AM at the above address (see attached map). Please call Eleni Athanasakos on 0207 882 2626 or 07813 682226 if needed.

Thank you kindly

Eleni Athanasakos
Clinical Researcher

Appendix – C Letter of Invitation

Parent Version for healthy controls

Barts and The London NHS
NHS Trust

Eleni Athanasakos
Barts & The London
Queen Mary University of London
Department of Paediatric Surgery

The Wingate Institute of Neurogastroenterology
26 Ashfield Street
Whitechapel
London
E1 2AJ

Tel:0207 882 2626
Fax:0207 375 2103
Email: e.athanasakos@qmul.ac.uk

Date:

To: FAMILY NAME/ADDRESS

Title: Quality of life of patients who have had an appendectomy

Dear FAMILY NAME

We would like to invite your child to take part in a research study at Barts and The London, Queen Mary University of London.

The purpose of this research study is to access the quality of life after suffering from appendicitis. It will give us the opportunity to further understand our knowledge of what life has been like for your child since having their operation for appendicitis and to compare results to other bowel diseases.

Your child has been invited to this research study as they have been surgically corrected for appendicitis and followed up in clinics here at the Royal London Hospital. At least 60 participants at the Royal London Hospital will be involved in this study that have been operated on for their appendicitis.

Participation in this project is voluntary if your child decides not to take part or decide to withdraw at any time this will not otherwise affect their relationship with the hospital or have any impact on the care your child may be receiving.

I have attached a 'Participants Information Sheet' for your convenience. Please feel free to contact the research doctor in charge Eleni Athanasakos who will be able to answer any questions and further explain the research project if needed.

If your child is interested in participating please call Eleni Athanasakos on 0207 882 2626.

Thank you kindly

Eleni Athanasakos
Clinical Researcher

Appendix – C Letter of Invitation

Participant Version for healthy controls

Barts and The London NHS
NHS Trust

Eleni Athanasakos
Barts & The London
Queen Mary University of London
Department of Paediatric Surgery

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26 Ashfield Street
Whitechapel
London
E1 2AJ

Tel:0207 882 2626
Fax:0207 375 2103
Email: e.athanasakos@qmul.ac.uk

Date:

To: PARTICIPANT'S NAME/ADDRESS

Title: Quality of life of patients who have had an appendectomy

Dear PARTICIPANT'S NAME

We would like to invite you to take part in a research study at Barts and the London, Queen Mary University of London.

The purpose of this research study is to access the quality of life after suffering from appendicitis. It will give us the opportunity to further understand our knowledge of what life has been like for you since having your operation for appendicitis and to compare results to other bowel diseases.

You have been invited to this research study as you have been surgically corrected for appendicitis and followed up in clinics here at the Royal London Hospital. At least 60 participants at the Royal London Hospital

will be involved in this study that have been operated on for their appendicitis.

Participation in this project is voluntary if you decide not to take part or decide to withdraw at any time this will not otherwise affect your relationship with the hospital or have any impact on the care you may be receiving.

I have attached a 'Participants Information Sheet' for your convenience. Please feel free to contact the research doctor in charge Eleni Athanasakos who will be able to answer any questions and further explain the research project if needed.

If you are interested in participating please call Eleni Athanasakos on 0207 882 2626.

Thank you kindly

Eleni Athanasakos
Clinical Researcher

Appendix – D Patient Information Sheet

Parents Version (ARA)

Barts and The London NHS
NHS Trust

Participant Information Sheet

Project Title: Anorectal Function and Quality of Life of Patients with Anorectal Anomalies (ARA).

Your child is being invited to take part in a research study. Before you and your child decide it is important for you to understand why the research is being done and what it will involve for your child. Please take time to read the following information carefully. Talk to others about the study if you wish. This information sheet tells you the purpose of the study and what will happen to your child if they take part. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish your child to take part.

Q: What is the purpose of the study?
Anorectal anomalies (or ARA) is a condition which affects how your child goes to the toilet. People with ARA can suffer from bowel difficulties such as faecal incontinence (soiling). Often ARA is treated surgically. The purpose of this research study is to identify the reasons why patients with ARA suffer from these bowel difficulties after having surgery. It will give us the opportunity to widen our understanding of what causes these bowel difficulties.

Additionally, this research project will be towards a university research thesis (PhD) which is supervised by Mr Harry Ward and Professor Norman Williams.

Q: Why has my child been chosen?
Your child has been invited to this research study as your child has been surgically corrected for ARA and has been followed up in clinics. We hope to identify what is causing some children to have these difficulties. At least 60 patients who have had similar surgery will be invited to participate in this study.

Q: Does my child have to take part?
No. It is up to you and your child to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form with your child. Your child is still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to

take part, will not affect the standard of your child's care. Your child will be expected to do all the tests since we need a good understanding of their current bowel function.

Q: Does my child need to do anything before the appointment?
Your child will be required to stop all laxative medication and the use of suppositories (if they are taking any) three days prior to their second appointment. Otherwise, your child does not need to do anything different before their arrival at the Unit. They can eat and drink as normal and continue to take any medication (not related to their bowels) that they would normally take.

We will send you a small capsule in the post, which we will ask your child to swallow three days before their second appointment.

Q: Does my child need to bring anyone with them?
Yes. It is important for you to come with your child in order for you to give consent.

Q: What will happen when my child arrives for their appointment?
Your child will be asked some questions relating to how their bowel works and the problems they may be having. The clinical researcher (Eleni Athanasakos) will explain the procedures to you and your child then you and your child will be asked to sign a consent form, giving us permission to do the tests.

Q: What will my child need do for the tests?
In order for us to carry out the tests, your child will be asked to lie on a couch on their left side and we will explain what we are doing at each stage of every test.

Q: Are these tests painful at all?
No. It can be embarrassing and a little uncomfortable to have these tests done to your back passage, but your child should not feel any pain. These tests are carried out by Eleni Athanasakos whom you and your child will have already spoken to on a number of occasions. She is committed to ensuring that any discomfort is minimised and that your child's privacy is maintained at all times.

Q: Why are these tests needed?
These tests are an important part of the investigation and results will be available to your child's doctor. If you have any concerns or want further

information about these tests please do not hesitate to contact Eleni Athanasakos on 0207 882 2626.

Q: So tell me about these tests:
First of all you will get a call from the clinical researcher: Eleni Athanasakos. She will answer any questions you may have and organise a time for you and your child to come in. The research study will be done over two days (but not consecutive days) at you and your child's convenience.

DAY 1
We will require your child to come in for 1 hour. Eleni Athanasakos will ask your child some questions about their quality of life living with ARA. These questions will ask your child about their everyday life, their views about the future and level of sadness and anxiety.
DAY 2
We will require your child to come for 1 hour to undergo some tests on their lower bowel/ back passage. Each of the tests can tell the doctor something different about how your child's bowel is working, and enable them to decide on the best treatment for their problem (if needed). You and your child will have the chance to have a chat about any bowel difficulties they may be experiencing with Eleni Athanasakos who will be performing the tests and who will go through them step by step with you and your child.

The tests will include:

- Anal pressure measurements: this test measures the strength of the muscles in the back passage. To do this, we insert a small tube (only 2mm thick) and ask your child either to relax or squeeze the muscles of their back passage. This enables us to tell whether the muscles are functioning correctly.
- Rectal Sensation & Barostat: this test enables us to measure how much volume the rectum can hold. To do this a small tube with a small balloon attached to it is passed into the back passage. We then inflate the balloon with air to determine what your child can feel and the size of their rectum. During the test we also look to see if your child has a nerve reflex in their back passage.
- Ultrasound: this test can tell if the muscles around the back passage are intact or if they are damaged. To do this, a finger sized probe is inserted into the back passage and gently moved in and out so that we can take scans (pictures) at different positions in the back passage. This procedure can be a little uncomfortable, but is not painful.
- Colonic Transit: for this test your child will be asked to swallow a small capsule that we will send to your home. This capsule contains 50 markers which can be seen on a standard x-ray. On the day of the appointment

your child will have an x-ray of their stomach area, which will show up any markers left in their bowel. Although your child will be exposed to radiation, this is a routine x-ray that we would do if they needed an x-ray in hospital, with minimal risk involved.

Q: How long will these visits be?
A maximum of 2 hrs.

Q: Expenses and payments:
As mentioned above, your child will be making two visits to the Gastrointestinal Unit at the Royal London Hospital. Travelling expenses will be paid for you and your child and child-care expenses if needed. If you or your child requires a letter of absence from work/school or any other commitments, this can also be arranged.

Q: What are the side effects?
There are no side effects of these tests for your child. However, if any support is needed during or after these tests please contact Eleni Athanasakos on 0207 882 2626.

Q: What are the other possible disadvantages and risks of taking part?
As mentioned above, your child may be embarrassed and a little uncomfortable doing these tests but there are no risks involved and your child should not feel any pain. The presence of professional staff will ensure your child's privacy at all times.

Q: Will my child have an x-ray?
Yes, as mentioned above they will have what is called a 'colonic transit test'. This is not harmful but simply a chance to see how their bowel works. However, if your child is pregnant they should not have this test because of exposure to radiation to their unborn baby. If you are unsure whether your child is pregnant, we can perform a pregnancy test to clarify this prior to the x-ray. Although your child will be exposed to radiation, this is a routine x-ray that that they would have if they needed an x-ray in hospital, with minimal risk involved.

Q: What are the possible benefits of taking part?
The research project will provide an idea of what is causing your child to suffer from bowel difficulties (if any). This research project will attempt to provide an answer as to why those with ARA suffer from bowel problems and how we can improve future management and other forms of treatment. We cannot promise that the study will help your child but the information we get might help improve the treatment of people with ARA.

Q: What happens when the research study stops?

We will inform you of the results of your tests when completed and analysed. You will, at all times get feedback about your child's participation. After the research study you will have an idea of how your child is doing and why children with ARA after surgery can have bowel difficulties.

The results of this research study will be written for a medical audience in the form of publications or presentations but your child's name will not be revealed at any time. You and your child will not be identified in any report or publication.

Q: What if there is a problem?
If your child is harmed by taking part in this research project, there are no special compensation arrangements. If your child is harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you or your child have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

If you have a concern about any aspect of this study, you can speak to Eleni Athanasakos 0207 882 2626. You and your child can also contact the Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you and your child have received, or as an initial point of contact if you have a complaint. Please telephone 020 7377 6335, minicom 020 7943 1350, or email pals@bartsandthelondon.nhs.uk, You can also visit PALS by asking at any hospital reception.

Q: Will my child taking part in the study be kept confidential?
Yes. All the information about your child's participation in this study will be kept confidential. All test results, questionnaire answers and records from your child's hospital notes will be kept on a computer file. This file can only be accessed by the researchers involved in this project.

Q: What will happen if my child doesn't want to carry on with the study?
Please remember that your child doesn't have to join the study and you and your child are free to decline our invitation. If your child decides against joining the study, this will in no way affect their medical care. If they decide to take part but at some stage wish to discontinue with the study, this will not affect their continuing medical care and all results will be discarded and not used for the research study.

Q: Involvement of the General Practitioner/Family doctor (GP)
Your child's GP will be notified of your child's participation in this research study, if you and your child consent. If your GP requests the information or results from this research study this will only be with you and your child's consent.

Q: Will any genetic tests be done?
No.

Q: Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the East London and the City Research Ethics Committee 3.

Q: Contact Details:
For further information about the study please call Eleni Athanasakos who is in charge of this research study on 0207 882 2626.

***Thank you* for taking time to read this information sheet.**

Appendix – D Patient Information Sheet

Patient Version (ARA)

Barts and The London NHS
NHS Trust

Participant Information Sheet

Project Title: Anorectal Function and Quality of Life of Patients with Anorectal Anomalies (ARA).

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. This information sheet tells you the purpose of the study and what will happen to you if you take part. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Q: What is the purpose of the study?
Anorectal anomalies (or ARA) is a condition which affects how you go to the toilet. People with ARA can suffer from bowel difficulties such as faecal incontinence (soiling). Often ARA is treated surgically. The purpose of this research study is to identify the reasons why patients with ARA, like yourself are suffering from these bowel difficulties after having surgery. It will give us the opportunity to further understand what causes these bowel difficulties by investigating the anatomy and physiology of the anorectum.

Additionally, this research project will be towards a university research thesis (PhD) which is supervised by Mr Harry Ward and Professor Norman Williams.

Q: Why have I been chosen?
You have been invited to this research study as you have been surgically corrected for ARA. We hope to identify what is causing some patients to have difficulties with their condition. At least 60 patients who have had similar surgery will be invited to participate in this study.

Q: Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to *take part, will not affect the standard*

of care you receive. You will be expected to do all the tests since we need a good understanding of your current bowel function.

Q: Do I need to do anything before the appointment?

You will be required to stop all laxative medication and the use of suppositories (if taking any) three days prior to your second appointment. Otherwise, you do not need to do anything before your arrival at the Unit. You can eat and drink as normal and continue to take any medication (not related to your bowels) that you would normally take. You do not need to use any bowel preparation (laxative, enemas). We will send you a small capsule in the post, which we will ask you to swallow three days before your second appointment.

Q: Do I need to bring anyone with me?

No. There is no reason why the tests should have any adverse effects. However, you are welcome to bring along somebody for support if you so require.

Q: What will happen when I arrive for my appointment?

You will be asked some questions relating to how your bowel works and any problems you may be having. The clinical researcher (Eleni Athanasakos) will explain the procedures to you and you will be asked to sign a consent form, giving us permission to do the tests.

Q: What will I need do for the tests?

In order for us to carry out the tests, you will be asked to lie on a couch on your left side and we will explain to you what we are doing at each stage of every test.

Q: Are these tests painful at all?

No. It can be embarrassing and a little uncomfortable to have these tests done on your back passage, but you should not feel any pain. These tests are carried out by Eleni Athanasakos whom you will have already spoken to on a number of occasions prior to doing these tests. She is committed to ensuring that any discomfort is minimised and that your privacy is maintained at all times.

Q: Why are these tests needed?

These tests are an important part of the investigation and your results will be available to your doctor taking care of you.. If you have any concerns or want further information about these tests please do not hesitate to contact Eleni Athanasakos on 0207 882 2626.

Q: So tell me about these tests:
First of all you will get a call from the clinical researcher: Eleni Athanasakos. She will answer any questions you may have and organise a time to come in. The research study will be done over two days (but not consecutive days) at your convenience.

DAY 1:
We will require you to come in for 1 hour. Eleni Athanasakos will ask you some questions about your quality of life living with ARA. These questions will ask you about your everyday life, your views about the future and level of sadness and anxiety.

DAY 2:
We will require you to come for 1 hour to undergo some tests on your lower bowel/ back passage. Each of the tests can tell the doctor something different about how your bowel is working, and enable them to decide on the best treatment for your problem (if needed). You will have the chance to have a chat about the bowel difficulties you may be experiencing with Eleni Athanasakos who will be performing the tests and who will thoroughly go through each test step by step with you.

The tests will include:

- Anal pressure measurements: this test measures the strength of the muscles in the back passage. To do this, we insert a small tube (only 2mm thick) and ask you either to relax or squeeze the muscles of the back passage. This enables us to tell whether the muscles are functioning correctly.
- Rectal Sensation & Barostat: this test enables us to measure how much volume your rectum can hold. To do this a small tube with a small balloon attached to it is passed into your back passage. We then inflate the balloon with air to determine what you can feel and the size of your rectum. During the test we also look to see if you have a nerve reflex in your back passage.
- Ultrasound: this test can tell if the muscles around your back passage are intact or if they are damaged. To do this, a finger sized probe is inserted into your back passage and gently moved in and out so that we can take scans (pictures) at different positions in your back passage. This procedure can be little uncomfortable, but is not painful.
- Colonic Transit: for this test you will be asked to swallow a small capsule that we will send to your home. This capsule contains 50 markers which can be seen on a standard x-ray. On the day of your appointment you will have an x-ray of your stomach area, which will show up any markers left in your bowel. Although you will be exposed to radiation, this is a routine x-ray that we would do if they needed an x-ray in hospital, with minimal risk involved.

Q: How long will these visits be?
A maximum of 2 hours.

Q: Expenses and payments:
As mentioned above, you will be making two visits to the Gastrointestinal Physiology Unit at the Royal London Hospital. Your travelling expenses will be paid for and if needed child-care expenses. If you require a letter of absence from work or any other commitment, this can be also arranged for you if required.

Q: What are the side effects?
There are no side effects after these tests for you. However, if any support is needed during or after these tests please contact Eleni Athanasakos on *0207 882 2626.*

Q: What are the other possible disadvantages and risks of taking part?
As mentioned above, you may be embarrassed and a little uncomfortable doing these tests but there are no risks involved. The presence of professional staff will ensure your privacy at all times.

Q: Do I have an x-ray?
Yes, as mentioned above you will have what is called a 'colonic transit test'. This is not harmful, but simply a chance to see how your bowel works. However, if you are pregnant, you should not have this test due to exposure to radiation to your unborn baby. If you are unsure if you are pregnant, we can perform a pregnancy test to clarify this prior to the x-ray. As indicated, you will be exposed to radiation on your stomach area, however this is a routine x-ray that you would have if they needed an x-ray in hospital, with minimal risk involved.

Q: What are the possible benefits of taking part?
The research project will provide an idea of what is causing you to suffer from bowel difficulties. It will attempt to provide an answer as to why those with ARA suffer from bowel problems and how we can improve future management and other forms of treatment. We cannot promise the study will help you but the information we get might help improve the treatment of people with ARA.

Q: What happens when the research study stops?
We will inform you of the results of your tests when completed and analysed. You will at all times get feedback about your participation. After the research study you will have an idea why you are having bowel difficulties.

The results of this research study will be written for a medical audience in the form of publications or presentations, but your name will not be revealed at any time. You will not be identified in any report or publication.

Q: What if there is a problem?
If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

If you have a concern about any aspect of this study, you can to Eleni Athanasakos on 0207 882 2626. You can also contact Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you have received, or as an initial point of contact if you have a complaint. Please telephone 020 7377 6335, minicom 020 7943 1350, or email pals@bartsandthelondon.nhs.uk, you can also visit PALS by asking at any hospital reception.

Q: Will my taking part in the study be kept confidential?
Yes. All the information about your participation in this study will be kept confidential. All test results, questionnaire answers and records from your hospital notes will be kept on a computer file. This file can only be accessed by the researchers involved in this project.

Q: What will happen if I don't want to carry on with the study?
Please remember that you do not have to join the study and are free to decline our invitation. If you decide against joining the study, this will in no way affect your medical care. If you decide to take part but at some stage wish to discontinue with the study, this will not affect your continuing medical care and all results will be discarded and not used for the research study.

Q: Involvement of the General Practitioner/Family doctor (GP)?
Your GP will be notified of your participation in this research study, with your consent. If your GP requests information or results from this research study this will be with your consent also.

Q: Will any genetic tests be done?
No.

Q: Who has reviewed the study?

This study was given a favourable ethical opinion for conduct in the NHS by the East London and the City Research Ethics Committee 3.

Q: Contact Details:
For further information about the study please call Eleni Athanasakos who is in charge of this research study on 0207 882 2626.

***Thank you* for taking time to read this information sheet.**

Appendix – D Patient Information Sheet

Parents Version (IC)

Barts and The London NHS
NHS Trust

Participant Information Sheet

Project Title: Quality of life with patients with Idiopathic Constipation

Your child is being invited to take part in a research study. Before you and your child decide it is important for you to understand why the research is being done and what it will involve for your child. Please take time to read the following information carefully. Talk to others about the study if you wish. This information sheet tells you the purpose of the study and what will happen to your child if they take part. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish your child to take part.

Q: What is the purpose of the study?

Constipation is passage of small amounts of hard, dry bowel movements, usually fewer than three times a week. People who are constipated may find it difficult and painful to have a bowel movement. Idiopathic constipation is a condition that refers to an inability to regularly pass stool. The term 'idiopathic' means that the origin of the problem is unknown. It is one of the most common bowel movement disorders among children and adolescents. The purpose of this research study is to access the quality of life of your child who has been diagnosed with idiopathic constipation. It will give us the opportunity to further understand our knowledge of what it has been like for your child living with this condition and to compare results to other bowel diseases.

Additionally, this research project will be towards a university research thesis (PhD) which is supervised by Mr Harry Ward and Professor Norman Williams.

Q: Why has my child been chosen?

Your child has been invited to this research study as they have been seen and followed up in clinics here at the Royal London Hospital. At least 60 participants at the Royal London Hospital will be involved in this study that have the same condition.

Q: Does my child have to take part?

No. It is up to you and your child to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form with your child. Your child is still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of your child's care.

Q: Does my child need to do anything before the appointment?

Your child does not need to do anything before their appointment with us.

Q: Does my child need to bring anyone with them?

Yes. It is important for you to come with your child in order for you to give consent.

Q: What will happen when my child arrives for their appointment?

Your child will be asked some questions about their general quality of life. The clinical researcher (Eleni Athanasakos) will explain the questionnaires to you and your child then you and your child will be asked to sign a consent form, giving us permission to continue with the questionnaires.

Q: So tell me about the appointment:

First of all you will get a call from the clinical researcher: Eleni Athanasakos. She will answer any questions you may have and organise a time for you and your child to come in. The research study will be done in one day at you and your child's convenience. We will require your child to come in for 1 hour. Eleni Athanasakos will ask your child some questions about their quality of life living with idiopathic constipation. These questions will ask your child about their everyday life, their views about the future and level of sadness and anxiety.

Q: How long will these visits be?

A maximum of 1 hr.

Q: Expenses and payments:

Travelling expenses will be paid for you and your child and child-care expenses if needed. If you or your child requires a letter of absence from work/school or any other commitments, this can also be arranged.

Q: What are the possible disadvantages and risks of taking part?

There are no risks involved and the presence of professional staff (Eleni Athanasakos) will ensure your child's privacy at all times.

Q: What are the possible benefits of taking part?

The research project will provide an idea how your child is coping with everyday life living with idiopathic constipation.

Q: What happens when the research study stops?
We will inform you of the results of your tests when completed and analysed. You will, at all times get feedback about your child's participation.

The results of this research study will be written for a medical audience in the form of publications or presentations but your child's name will not be revealed at any time. You and your child will not be identified in any report or publication.

Q: What if there is a problem?
If your child is harmed by taking part in this research project, there are no special compensation arrangements. If your child is harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you or your child have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

If you have a concern about any aspect of this study, you can speak to Eleni Athanasakos 0207 882 2626. You and your child can also contact the Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you and your child have received, or as an initial point of contact if you have a complaint. Please telephone 020 7377 6335, minicom 020 7943 1350, or email pals@bartsandthelondon.nhs.uk, You can also visit PALS by asking at any hospital reception.

Q: Will my child taking part in the study be kept confidential?
Yes. All the information about your child's participation in this study will be kept confidential. All questionnaire answers and records from your child's hospital notes will be kept on a computer file. This file can only be accessed by the researchers involved in this project.

Q: What will happen if my child doesn't want to carry on with the study?
Please remember that your child doesn't have to join the study and you and your child are free to decline our invitation. If your child decides against joining the study, this will in no way affect their medical care. If they decide to take part but at some stage wish to discontinue with the study, this will not affect their continuing medical care and all results will be discarded and not used for the research study.

Q: Involvement of the General Practitioner/Family doctor (GP)

Your child's GP will not be notified of your child's participation in this research study.

Q: Will any genetic tests be done?
No.

Q: Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the East London and the City Research Ethics Committee 3.

Q: Contact Details:
For further information about the study please call Eleni Athanasakos who is in charge of this research study on 0207 882 2626.

***Thank you* for taking time to read this information sheet.**

Appendix – D Patient Information Sheet

Patient Version (IC)

Barts and The London NHS
NHS Trust

Participant Information Sheet

Project Title: Quality of life with patients with Idiopathic Constipation

You are being invited to take part in a research project. Before you decide it is important for you to understand why the research is being done in the first place and what it will involve. Please take time to read this information sheet carefully. Have a chat to others about the study if you wish. This information sheet tells you about the research project and what will happen to you if you take part. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. You should have a chat with your parent/s or carer/s before deciding to become involved.

Q: What is the purpose of the study?

Constipation is passage of small amounts of hard, dry bowel movements, usually fewer than three times a week. People who are constipated may find it difficult and painful to have a bowel movement. Idiopathic constipation is a condition that refers to an inability to regularly pass stool. The term 'idiopathic' means that the origin of the problem is unknown. It is one of the most common bowel movement disorders among children and adolescents. The purpose of this research study is to access your quality of life with idiopathic constipation. It will give us the opportunity to further understand our knowledge of what it has been like for you living with this condition and to compare results to other bowel diseases.

Additionally, this research project will be towards a university research thesis (PhD) which is supervised by Mr Harry Ward and Professor Norman Williams.

Q: Why have I been chosen?
You have been invited to this research study as you have been seen and followed up in clinics here at the Royal London Hospital. At least 60 participants at the Royal London Hospital will be involved in this study that have the same condition.

Q: Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of your care.

Q: Do I need to do anything before the appointment?
You do not need to do anything before the appointment with us.

Q: Do I need to bring anyone with them?
No, unless you would like to.

Q: What will happen when I arrive for their appointment?
You will be asked some questions about your general quality of life. The clinical researcher (Eleni Athanasakos) will explain the questionnaires to you and then you will be asked to sign a consent form, giving us permission to continue with the questionnaires.

Q: So tell me about the appointment:
First of all you will get a call from the clinical researcher: Eleni Athanasakos. She will answer any questions you may have and organise a time for you to come in. The research study will be done in one day at your convenience. We will require you to come in for 1 hour. Eleni Athanasakos will ask you some questions about your quality of life living with idiopathic constipation. These questions will ask you about your everyday life, your views about the future and level of sadness and anxiety.

Q: How long will these visits be?
A maximum of 1 hr.

Q: Expenses and payments:
Travelling expenses will be paid for you and child-care expenses if needed. If you require a letter of absence from work/school or any other commitments, this can also be arranged.

Q: What are the possible disadvantages and risks of taking part?
There are no risks involved and the presence of professional staff (Eleni Athanasakos) will ensure your privacy at all times.

Q: What are the possible benefits of taking part?
The research project will provide an idea how you are coping with everyday life living with idiopathic constipation.

Q: What happens when the research study stops?
We will inform you of the results of your tests when completed and analysed. You will, at all times get feedback about your participation.

The results of this research study will be written for a medical audience in the form of publications or presentations but your child's name will not be revealed at any time. You will not be identified in any report or publication.

Q: What if there is a problem or something goes wrong?
If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

If you have a concern about any aspect of this study, you can to Eleni Athanasakos on 0207 882 2626. You can also contact Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you have received, or as an initial point of contact if you have a complaint. Please telephone 020 7377 6335, minicom 020 7943 1350, or email pals@bartsandthelondon.nhs.uk, you can also visit PALS by asking at any hospital reception.

Q: Will my taking part in the study be kept confidential?
Yes. All the information about you in this study will be kept confidential. All questionnaire answers and records from your hospital notes will be kept on a computer file. This file can only be accessed by the researchers involved in this project.

Q: What will happen if I don't want to carry on with the study?
Please remember that you do not have to join the study and are free to say no. If you decide against joining the study, this will not affect your medical care. If you decide to take part but at some stage wish to drop out of the study, this

will not affect your continuing medical care and all results will be discarded and not used for the research study.

Q: Involvement of the General Practitioner/Family doctor (GP)
Your GP will not be notified of your child's participation in this research study.

Q: Will any genetic tests be done?
No.

Q: Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the East London and the City Research Ethics Committee 3.

Q: Contact Details:
For further information about the study please call Eleni Athanasakos who is in charge of this research study on 0207 882 2626.

***Thank you* for taking time to read this information sheet.**

Appendix – D Patient Information Sheet

Parents Version (healthy controls)

Barts and The London NHS
NHS Trust

Participant Information Sheet

Project Title: Quality of life of patients who have had an appendectomy

Your child is being invited to take part in a research study. Before you and your child decide it is important for you to understand why the research is being done and what it will involve for your child. Please take time to read the following information carefully. Talk to others about the study if you wish. This information sheet tells you the purpose of the study and what will happen to your child if they take part. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish your child to take part.

Q: What is the purpose of the study?
Appendicitis is an inflammation of the appendix, a small worm-like pouch attached to the large bowel. Surgical removal of the appendix (appendicectomy) is the most common procedure. The purpose of this research study is to access the quality of life after suffering from appendicitis. It will give us the opportunity to further understand our knowledge of what life has been like for your child since having their operation for appendicitis and to compare results to other bowel diseases.

Additionally, this research project will be towards a university research thesis (PhD) which is supervised by Mr Harry Ward and Professor Norman Williams.

Q: Why has my child been chosen?
Your child has been invited to this research study as they have been surgically corrected for appendicitis and followed up in clinics here at the Royal London Hospital. At least 60 participants at the Royal London Hospital will be involved in this study that have been operated on for their appendicitis.

Q: Does my child have to take part?
No. It is up to you and your child to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form with your child. Your child is still free to withdraw at any time

and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of your child's care.

Q: Does my child need to do anything before the appointment?
Your child does not need to do anything before their appointment with us.

Q: Does my child need to bring anyone with them?
Yes. It is important for you to come with your child in order for you to give consent.

Q: What will happen when my child arrives for their appointment?
Your child will be asked some questions about their general quality of life. The clinical researcher (Eleni Athanasakos) will explain the questionnaires to you and your child then you and your child will be asked to sign a consent form, giving us permission to continue with the questionnaires.

Q: So tell me about the appointment:
First of all you will get a call from the clinical researcher: Eleni Athanasakos. She will answer any questions you may have and organise a time for you and your child to come in. The research study will be done in one day at you and your child's convenience. We will require your child to come in for 1 hour. Eleni Athanasakos will ask your child some questions about their general quality of life. These questions will ask your child about their everyday life, their views about the future and level of sadness and anxiety.

Q: How long will these visits be?
A maximum of 1 hour.

Q: Expenses and payments:
Travelling expenses will be paid for you and your child and child-care expenses if needed. If you or your child requires a letter of absence from work/school or any other commitments, this can also be arranged.

Q: What are the possible disadvantages and risks of taking part?
There are no risks involved and the presence of professional staff (Eleni Athanasakos) will ensure your child's privacy at all times.

Q: What are the possible benefits of taking part?
The research project will provide an idea how your child is coping with everyday life..
Q: What happens when the research study stops?

We will inform you of the results of your tests when completed and analysed. You will, at all times get feedback about your child's participation.

The results of this research study will be written for a medical audience in the form of publications or presentations but your child's name will not be revealed at any time. You and your child will not be identified in any report or publication.

Q: What if there is a problem?
If your child is harmed by taking part in this research project, there are no special compensation arrangements. If your child is harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you or your child have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

If you have a concern about any aspect of this study, you can speak to Eleni Athanasakos 0207 882 2626. You and your child can also contact the Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you and your child have received, or as an initial point of contact if you have a complaint. Please telephone 020 7377 6335, minicom 020 7943 1350, or email pals@bartsandthelondon.nhs.uk, You can also visit PALS by asking at any hospital reception.

Q: Will my child taking part in the study be kept confidential?
Yes. All the information about your child's participation in this study will be kept confidential. All questionnaire answers and records from your child's hospital notes will be kept on a computer file. This file can only be accessed by the researchers involved in this project.

Q: What will happen if my child doesn't want to carry on with the study?
Please remember that your child doesn't have to join the study and you and your child are free to decline our invitation. If your child decides against joining the study, this will in no way affect their medical care. If they decide to take part but at some stage wish to discontinue with the study, this will not affect their continuing medical care and all results will be discarded and not used for the research study.

Q: Involvement of the General Practitioner/Family doctor (GP)
Your child's GP will not be notified of your child's participation in this research study.

Q: Will any genetic tests be done?
No.

Q: Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the East London and the City Research Ethics Committee 3.

Q: Contact Details:
For further information about the study please call Eleni Athanasakos who is in charge of this research study on 0207 882 2626.

Thank you **for taking time to read this information sheet.**

Appendix – D Patient Information Sheet

Participant Version (healthy controls)

Barts and The London NHS
NHS Trust

Participant Information Sheet

Project Title: Quality of life of patients who have had an appendectomy

You are being invited to take part in a research project. Before you decide it is important for you to understand why the research is being done in the first place and what it will involve. Please take time to read this information sheet carefully. Have a chat to others about the study if you wish. This information sheet tells you about the research project and what will happen to you if you take part. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. You should have a chat with your parent/s or carer/s before deciding to become involved.

Q: What is the purpose of the study?
Appendicitis is an inflammation of the appendix, a small worm-like pouch attached to the large bowel. Surgical removal of the appendix (appendicectomy) is the most common procedure. The purpose of this research study is to access the quality of life after suffering from appendicitis. It will give us the opportunity to further understand our knowledge of what life has been like for you since having their operation for appendicitis and to compare results to other bowel diseases.

Additionally, this research project will be towards a university research thesis (PhD) which is supervised by Mr Harry Ward and Professor Norman Williams.

Q: Why have I been chosen?
You have been invited to this research study as you have been surgically corrected for appendicitis and followed up in clinics here at the Royal London Hospital. At least 60 participants at the Royal London Hospital will be involved in this study that have been operated on for their appendicitis.

Q: Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of your care.

Q: *Do I need to do anything before the appointment?*

You do not need to do anything before the appointment with us.

Q: *Do I need to bring anyone with them?*

No, unless you would like to.

Q: *What will happen when I arrive for their appointment?*

You will be asked some questions about your general quality of life. The clinical researcher (Eleni Athanasakos) will explain the questionnaires to you and then you will be asked to sign a consent form, giving us permission to continue with the questionnaires.

Q: So tell me about the appointment:
First of all you will get a call from the clinical researcher: Eleni Athanasakos. She will answer any questions you may have and organise a time for you to come in. The research study will be done in one day at your convenience. We will require you to come in for 1 hour. Eleni Athanasakos will ask you some questions about your general quality of life. These questions will ask you about your everyday life, your views about the future and level of sadness and anxiety.

How long will these visits be?
A maximum of 1 hour.

Q: Expenses and payments:
Travelling expenses will be paid for you and child-care expenses if needed. If you require a letter of absence from work/school or any other commitments, this can also be arranged.

Q: What are the possible disadvantages and risks of taking part?
There are no risks involved and the presence of professional staff (Eleni Athanasakos) will ensure your privacy at all times.

Q: What are the possible benefits of taking part?
The research project will provide an idea how you are coping with everyday life living with idiopathic constipation.

Q: What happens when the research study stops?
We will inform you of the results of your tests when completed and analysed. You will, at all times get feedback about your participation.

The results of this research study will be written for a medical audience in the form of publications or presentations but your child's name will not be revealed at any time. You will not be identified in any report or publication.

Q: What if there is a problem or something goes wrong?
If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

If you have a concern about any aspect of this study, you can to Eleni Athanasakos on 0207 882 2626. You can also contact Patient Advisory Liaison Service (PALS) if you have any concerns regarding the care you have received, or as an initial point of contact if you have a complaint. Please telephone 020 7377 6335, minicom 020 7943 1350, or email pals@bartsandthelondon.nhs.uk, you can also visit PALS by asking at any hospital reception.

Q: Will my taking part in the study be kept confidential?
Yes. All the information about you in this study will be kept confidential. All questionnaire answers and records from your hospital notes will be kept on a computer file. This file can only be accessed by the researchers involved in this project.

Q: What will happen if I don't want to carry on with the study?
Please remember that you do not have to join the study and are free to say no. If you decide against joining the study, this will not affect your medical care. If you decide to take part but at some stage wish to drop out of the study, this will not affect your continuing medical care and all results will be discarded and not used for the research study.

Q: Involvement of the General Practitioner/Family doctor (GP)
Your GP will not be notified of your child's participation in this research study.

Q: Will any genetic tests be done?

No.

Q: Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the East London and the City Research Ethics Committee 3.

Q: Contact Details:
For further information about the study please call Eleni Athanasakos who is in charge of this research study on 0207 882 2626.

Thank you for taking time to read this information sheet.

Appendix – E Consent Form

For ARA, IC and healthy controls

Barts and The London NHS
NHS Trust

CONSENT FORM (Version 1 01/08/2006)

Title of project:
Investigator: Eleni Athanasakos

Centre Number: Study Number: Patient Identification Number for this trial:

Please initial box to indicate agreement

1.	I confirm that I have read and understand the information sheet dated ..... (version .....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3.	I understand that relevant sections of any of my medical notes and data collected during the study, may be looked at by responsible individuals from Barts and the London from regulatory authorities or from the Barts and the London/ Queen Mary University of London , where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4.	I agree to my GP being informed of my participation in the study.	
5.	I agree to take part in the above study.	

Name of Patient	Date	Signature
Name of Person taking consent (if different from Investigator)	Date	Signature
Investigator	Date	Signature

1 copy for Patient, 1 for Investigator and original to be kept in medical notes

Appendix – E Ascent Form

For ARA, IC and healthy controls

Barts and The London NHS
NHS Trust

ASSENT FORM (Version 1 01/08/2006)

Title of project:
Investigator: Eleni Athanasakos

Child (or if unable, parent on their behalf)/young person to circle all they agree with please:

Centre Number: Study Number: Patient Identification Number for this trial:

Please circle Yes or No

1. Have you read (or had read to you) about this project?	Yes/No
2. Has somebody else explained this project to you?	Yes/No
3. Do you understand what this project is about?	Yes/No
4. Have you asked all the questions you want?	Yes/No
5. Have you had your questions answered in a way you understand?	Yes/No
6. Do you understand it's OK to stop taking part at any time?	Yes/No
7. Are you happy to take part?	Yes/No

If any answers are 'no' or you **don't** want to take part, **don't** sign your name!
If you do want to take part, please write your name and today's date

Your name _____

Date _____

Your parent or guardian must write their name here too if they are happy for you to do the project
Print Name _____

Sign _____

Date _____

The doctor who explained this project to you needs to sign too:
Print Name _____

Sign _____

Date _____

_____ _____ _____
Name of Patient Date Signature

1 copy for Patient, 1 for Investigator and original to be kept in medical notes

Appendix – F Knowles-Eccersley-Scott-Symptom (KESS) questionnaire

Duration of constipation	
0-18 months	0
18 months to 5 years	1
5-10 years	2
10-20 years	3
>20 years (or all life)	4

Time (minutes in lavatory / attempt)	
< 5 minutes	0
5-10 minutes	1
10-30 minutes	2
> 30 minutes	3

Assistance (laxatives)	
none	0
laxatives prn or short duration	1
laxatives regular, long duration	2
laxatives long duration, failed	3

Difficulty: painful evacuation effort (%)	
never	0
rarely	1
occasionally	2
usually	3
always	4

Freq bowel movement with assistance	
1-2 times / 1-2 days	0
2 or less times / week	1
less than once per week	2
less than once per 2 weeks	3

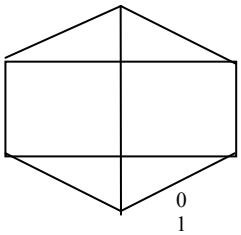
Rectal	☐
Vaginal	☐
Perineal	☐
Anal	☐
Other	☐

Unsuccessful evacuatory attempts (%)	
never	0
occasionally	1
usually	2
always = manual evacuation	3

Stool consistency without laxatives	
soft / loose/ normal	0
occasionally hard	1
always hard	2
always hard, usually pellets	3

Feeling incomplete evacuation (%)	
never	0
rarely	1
occasionally	2
usually	3
always	4

Abdominal pain (%)	
Never	0
Rarely	1
Occasionally	2
Usually	3
Always	4



Bloating	
never	0
perceived	1
visible	2
severe + effect on satiety or nausea	3
severe + vomiting	4

Family history	
not known	0
none	1
yes	2

Assistance	
none	0
enemata or suppositories prn	1
enemata or suppositories regular	2
manual evacuation as required	3
manual evacuation always	4

$KESS_{TOTAL}$	**/ 39**

$KESS_{MONITORING}$	**/ 35**

NOTES

Laxatives:

Supp/enema:

Bhabit in days:

FHx: brief detail:

Other:

Appendix – G Vaizey Incontinence Questionnaire

	Never	*Rarely*	*Sometimes*	*Weekly*	*Daily*
Incontinence for solid stool	0	1	2	3	4
Incontinence for liquid stool	0	1	2	3	4
Incontinence for gas	0	1	2	3	4
Alteration in lifestyle	0	1	2	3	4
				No	*Yes*
Need to wear a pad or plug				0	2
Taking constipating medicines				0	2
Lack of ability to defer defecation for 15 minutes				0	4

Never, no episodes in the past four weeks; rarely, 1 episode in the past four weeks; sometimes, >1 episode in the past four weeks but <1 a week; weekly, 1 or more episodes a week but <1 a day; daily, 1 or more episodes a day.
Add one score from each row: minimum score = 0 = perfect continence; maximum score = 24 = totally incontinent.

Today

(1) Did you leak, without being aware of it at first? Yes/No

If yes, was it : gas ☐ (1) small stain ☐ (0.5)
liquid ☐ (1.5) large stain ☐ (1)
solid ☐ (2) half an egg cup ☐ (1.5)
whole motion ☐ (2)

(2) Did you have great urgency when you felt you would not make it to the toilet in time to open your bowels? Yes/No (1)

If yes, did you actually lose some stool before getting to the toilet? Yes/No

If yes, was it: pea sized ☐ (1)
half an egg cup ☐ (1.5)
whole motion ☐ (2)

(3) Did you wear a pad or use a plug of tissue paper? Yes/No (0.5)

If yes, did it get soiled? Yes/No (0.5)

(4) Did you take imodium (loperamide), codeine or any other medicine today? Yes/No (1)

If yes, what _____

(5) Did your loss of stool or fear of loss of stool stop you from doing anything? Yes/No (1)

Appendix – H Gastrointestinal Quality of Life Index (GIQOL)

The Gastrointestinal Quality of Life Index

These questions ask about the effect of bowel symptoms on your quality of life. Please tick one box for each question.

1 How often during the past 2 weeks have you had pain in the abdomen?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

2 How often in the past 2 weeks have you had a feeling of fullness in the upper abdomen?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

3 How often in the last 2 weeks have you had bloating (sensation of too much gas in the abdomen)?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

4 How often during the past 2 weeks have you been troubled by excessive passage of gas through the back passage?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

5 How often during the past 2 weeks have you been troubled by strong burping or belching?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

6 How often during the past 2 weeks have you been troubled by gurgling noises from the abdomen?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

7 How often during the past 2 weeks have you been troubled by frequent bowel movements?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

8 How often during the past 2 weeks have you found eating to be a pleasure?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

9 Because of your disorder, to what extent have you restricted the kinds of foods that you eat?

- ☐ Not at all
- ☐ A little
- ☐ Somewhat
- ☐ Much
- ☐ Very much

10 During the past 2 weeks, how well have you been able to cope with everyday stresses?

- ☐ Extremely poorly
- ☐ Poorly
- ☐ Moderately well
- ☐ Well
- ☐ Extremely well

11 How often during the past 2 weeks have you been sad about being ill?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

12 How often during the past 2 weeks have you been nervous or anxious about your disorder?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

Appendix – H Gastrointestinal Quality of Life Index (GIQOL)

13 How often during the past 2 weeks have you been happy with life in general
- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

14 How often during the past 2 weeks have you been frustrated about your disorder?
- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

15 How often during the past 2 weeks have you been tired or fatigued?
- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

16 How often during the past 2 weeks have you felt unwell?
- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

17 Over the past week, have you woken up in the night?
- ☐ Every night
- ☐ 5-6 nights
- ☐ 3-4 nights
- ☐ 1-2 nights
- ☐ Never

18 Since your disorder started, have you been troubled by changes in your appearance?
- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ A moderate amount
- ☐ A great deal

19 Because of your disorder, how much physical strength have you lost?
- ☐ A great deal
- ☐ A moderate amount
- ☐ Somewhat
- ☐ A little bit
- ☐ Not at all

20 Because of your disorder, to what extent have you lost your endurance?
- ☐ Not at all
- ☐ A little bit
- ☐ Somewhat
- ☐ A moderate amount
- ☐ A great deal

21 Because of your disorder, to what extent do you feel unfit?
- ☐ Extremely unfit
- ☐ Moderately unfit
- ☐ Somewhat unfit
- ☐ A little unfit
- ☐ Fit

22 During the past 2 weeks how often have you been able to complete you normal daily activities? (school, work, household)
- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

23 During the past 2 weeks how often have you been able to take part in your usual patterns of leisure or recreational activities?
- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

24 During the past 2 weeks, how much have you been troubled by the treatment for your disorder?
- ☐ Not at all
- ☐ A little
- ☐ Somewhat
- ☐ Much
- ☐ Very much

Appendix – H Gastrointestinal Quality of Life Index (GIQOL)

25 To what extent have your personal relations with people close to you (family or friends) worsened because of your disorder?

- ☐ Very much
- ☐ Much
- ☐ Somewhat
- ☐ A little
- ☐ Not at all

26 To what extent has your sex life been impaired (harmed) because of your disorder?

- ☐ Not at all
- ☐ A little
- ☐ Somewhat
- ☐ Much
- ☐ Very much

27 How often during the past 2 weeks have you been troubled by fluid or food coming up into your mouth (regurgitation)?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

28 How often during the past 2 weeks have you felt uncomfortable because of your slow speed of eating?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

29 How often during the past 2 weeks have you had trouble swallowing your food?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

30 How often during the past 2 weeks have you been troubled by urgent bowel movements?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

31 How often during the past 2 weeks have you been troubled by diarrhoea?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

32 How often during the past 2 weeks have you been troubled by constipation?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

33 How often during the past 2 weeks have you been troubled by nausea?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

34 How often during the past 2 weeks have you been troubled by blood in the stools?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

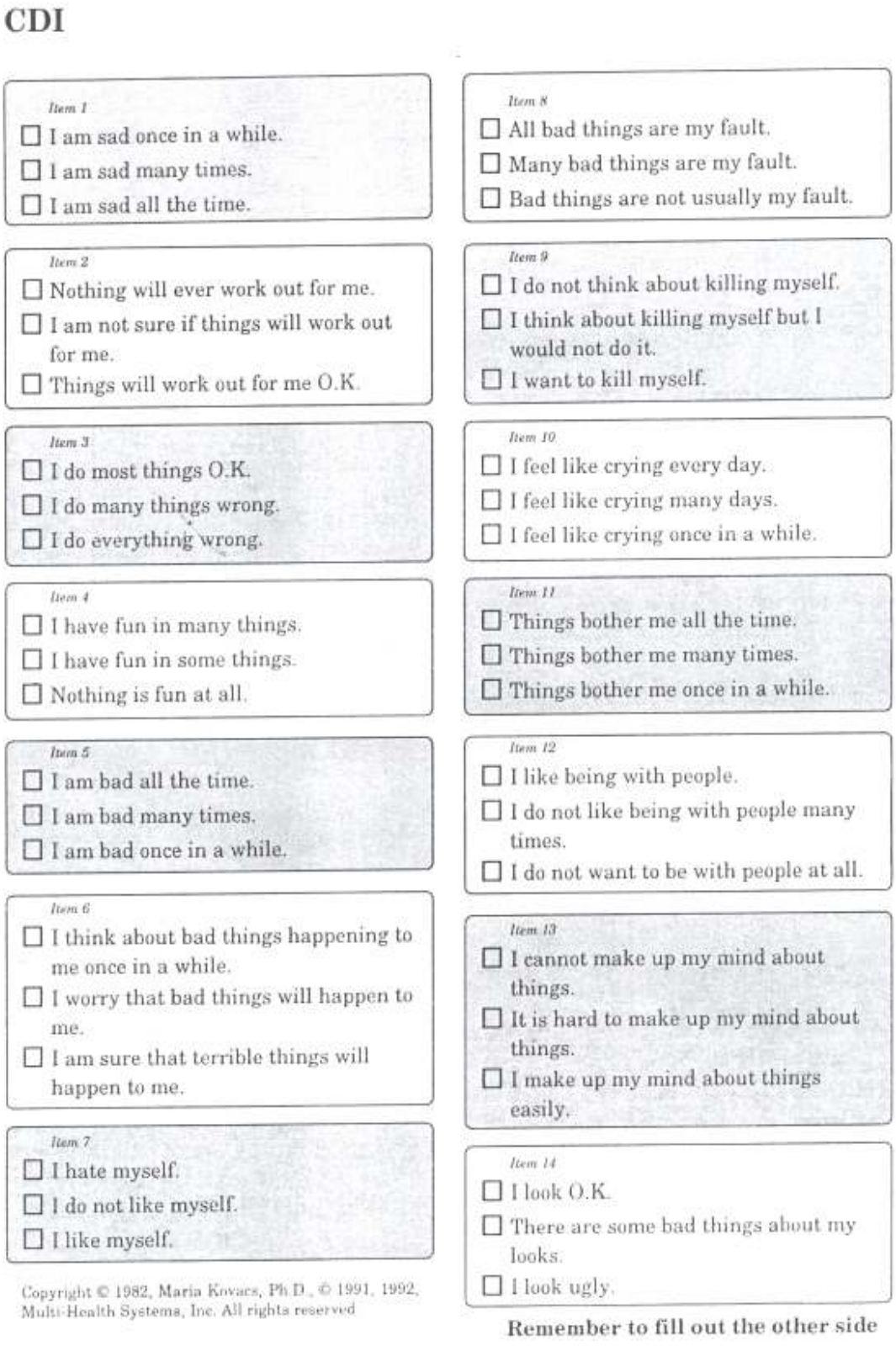
35 How often during the past 2 weeks have you been troubled by heartburn?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ Never

36 How often during the past 2 weeks have you been troubled by uncontrolled stools?

- ☐ Never
- ☐ A little of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

Appendix – I Children's Depression Inventory (CDI)



CDI

Item 1
- ☐ I am sad once in a while.
- ☐ I am sad many times.
- ☐ I am sad all the time.

Item 2
- ☐ Nothing will ever work out for me.
- ☐ I am not sure if things will work out for me.
- ☐ Things will work out for me O.K.

Item 3
- ☐ I do most things O.K.
- ☐ I do many things wrong.
- ☐ I do everything wrong.

Item 4
- ☐ I have fun in many things.
- ☐ I have fun in some things.
- ☐ Nothing is fun at all.

Item 5
- ☐ I am bad all the time.
- ☐ I am bad many times.
- ☐ I am bad once in a while.

Item 6
- ☐ I think about bad things happening to me once in a while.
- ☐ I worry that bad things will happen to me.
- ☐ I am sure that terrible things will happen to me.

Item 7
- ☐ I hate myself.
- ☐ I do not like myself.
- ☐ I like myself.

Item 8
- ☐ All bad things are my fault.
- ☐ Many bad things are my fault.
- ☐ Bad things are not usually my fault.

Item 9
- ☐ I do not think about killing myself.
- ☐ I think about killing myself but I would not do it.
- ☐ I want to kill myself.

Item 10
- ☐ I feel like crying every day.
- ☐ I feel like crying many days.
- ☐ I feel like crying once in a while.

Item 11
- ☐ Things bother me all the time.
- ☐ Things bother me many times.
- ☐ Things bother me once in a while.

Item 12
- ☐ I like being with people.
- ☐ I do not like being with people many times.
- ☐ I do not want to be with people at all.

Item 13
- ☐ I cannot make up my mind about things.
- ☐ It is hard to make up my mind about things.
- ☐ I make up my mind about things easily.

Item 14
- ☐ I look O.K.
- ☐ There are some bad things about my looks.
- ☐ I look ugly.

Remember to fill out the other side

Appendix – I Children's Depression Inventory (CDI)

CDI

Remember, describe how you have been in the past two weeks.....

Item 15
- ☐ I have to push myself all the time to do my schoolwork.
- ☐ I have to push myself many times to do my schoolwork.
- ☐ Doing schoolwork is not a big problem.

Item 16
- ☐ I have trouble sleeping every night.
- ☐ I have trouble sleeping many nights.
- ☐ I sleep pretty well.

Item 17
- ☐ I am tired once in a while.
- ☐ I am tired many days.
- ☐ I am tired all the time.

Item 18
- ☐ Most days I do not feel like eating.
- ☐ Many days I do not feel like eating.
- ☐ I eat pretty well.

Item 19
- ☐ I do not worry about aches and pains.
- ☐ I worry about aches and pains many times.
- ☐ I worry about aches and pains all the time.

Item 20
- ☐ I do not feel alone.
- ☐ I feel alone many times.
- ☐ I feel alone all the time.

Item 21
- ☐ I never have fun at school.
- ☐ I have fun at school only once in a while.
- ☐ I have fun at school many times.

Item 22
- ☐ I have plenty of friends.
- ☐ I have some friends but I wish I had more.
- ☐ I do not have any friends.

Item 23
- ☐ My schoolwork is alright.
- ☐ My schoolwork is not as good as before.
- ☐ I do very badly in subjects I used to be good in

Item 24
- ☐ I can never be as good as other kids.
- ☐ I can be as good as other kids if I want to.
- ☐ I am just as good as other kids.

Item 25
- ☐ Nobody really loves me.
- ☐ I am not sure if anybody loves me.
- ☐ I am sure that somebody loves me.

Item 26
- ☐ I usually do what I am told.
- ☐ I do not do what I am told most times.
- ☐ I never do what I am told.

Item 27
- ☐ I get along with people.
- ☐ I get into fights many times.
- ☐ I get into fights all the time.

MHS

Remember to fill out the other side

Appendix – J Beck Depression Inventory (BDI)

BDI-II

Date:

Name: _____ Marital Status: _____ Age: _____ Sex: _____

Occupation: _____ Education: _____

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness

0 I do not feel sad.
1 I feel sad much of the time.
2 I am sad all the time.
3 I am so sad or unhappy that I can't stand it.

2. Pessimism

0 I am not discouraged about my future.
1 I feel more discouraged about my future than I used to be.
2 I do not expect things to work out for me.
3 I feel my future is hopeless and will only get worse.

3. Past Failure

0 I do not feel like a failure.
1 I have failed more than I should have.
2 As I look back, I see a lot of failures.
3 I feel I am a total failure as a person.

4. Loss of Pleasure

0 I get as much pleasure as I ever did from the things I enjoy.
1 I don't enjoy things as much as I used to.
2 I get very little pleasure from the things I used to enjoy.
3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings

0 I don't feel particularly guilty.
1 I feel guilty over many things I have done or should have done.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6. Punishment Feelings

0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7. Self-Dislike

0 I feel the same about myself as ever.
1 I have lost confidence in myself.
2 I am disappointed in myself.
3 I dislike myself.

8. Self-Criticalness

0 I don't criticize or blame myself more than usual.
1 I am more critical of myself than I used to be.
2 I criticize myself for all of my faults.
3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes

0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10. Crying

0 I don't cry anymore than I used to.
1 I cry more than I used to.
2 I cry over every little thing.
3 I feel like crying, but I can't.

_____ Subtotal Page 1

Continued on Back

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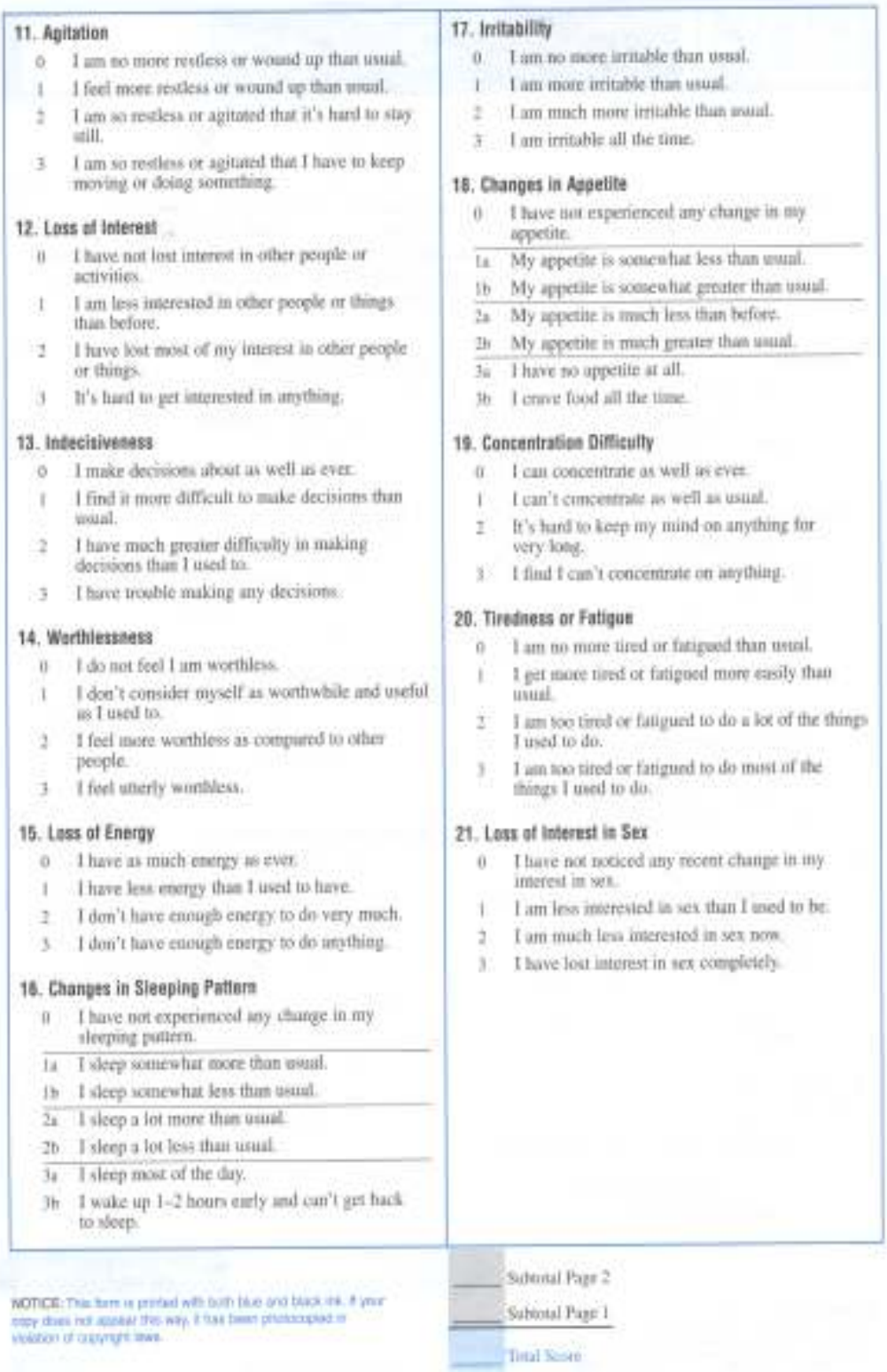
Appendix – J Beck Depression Inventory (BDI)



11. Agitation

0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it's hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0 I have not lost interest in other people or activities.
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things.
3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.
1 I find it more difficult to make decisions than usual.
2 I have much greater difficulty in making decisions than I used to.
3 I have trouble making any decisions.

14. Worthlessness

0 I do not feel I am worthless.
1 I don't consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.
1 I have less energy than I used to have.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern.
1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.
2a I sleep a lot more than usual.
2b I sleep a lot less than usual.
3a I sleep most of the day.
3b I wake up 1–2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite.
1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.
2a My appetite is much less than before.
2b My appetite is much greater than usual.
3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.
1 I can't concentrate as well as usual.
2 It's hard to keep my mind on anything for very long.
3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.
1 I get more tired or fatigued more easily than usual.
2 I am too tired or fatigued to do a lot of the things I used to do.
3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

SCORE ABOVE

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Subtotal Page 2
Subtotal Page 1
Total Score

Appendix – K General Health Questionnaire-28 (GHQ-28)

THE GENERAL HEALTH QUESTIONNAIRE

GHQ 28

David Goldberg

Please read this carefully.

We should like to know if you have had any medical complaints and how your health has been in general, *over the past few weeks*. Please answer ALL the questions on the following pages simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

Thank you very much for your co-operation.

Have you recently

A1 – been feeling perfectly well and in good health?	Better than usual	Same as usual	Worse than usual	Much worse than usual
A2 – been feeling in need of a good tonic?	Not at all	No more than usual	Rather more than usual	Much more than usual
A3 – been feeling run down and out of sorts?	Not at all	No more than usual	Rather more than usual	Much more than usual
A4 – felt that you are ill?	Not at all	No more than usual	Rather more than usual	Much more than usual
A5 – been getting any pains in your head?	Not at all	No more than usual	Rather more than usual	Much more than usual
A6 – been getting a feeling of tightness or pressure in your head?	Not at all	No more than usual	Rather more than usual	Much more than usual
A7 – been having hot or cold spells?	Not at all	No more than usual	Rather more than usual	Much more than usual
B1 – lost much sleep over worry?	Not at all	No more than usual	Rather more than usual	Much more than usual
B2 – had difficulty in staying asleep once you are off?	Not at all	No more than usual	Rather more than usual	Much more than usual
B3 – felt constantly under strain?	Not at all	No more than usual	Rather more than usual	Much more than usual
B4 – been getting edgy and bad-tempered?	Not at all	No more than usual	Rather more than usual	Much more than usual
B5 – been getting scared or panicky for no good reason?	Not at all	No more than usual	Rather more than usual	Much more than usual
B6 – found everything getting on top of you?	Not at all	No more than usual	Rather more than usual	Much more than usual
B7 – been feeling nervous and strung-up all the time?	Not at all	No more than usual	Rather more than usual	Much more than usual

Please turn over

Appendix – K General Health Questionnaire-28 (GHQ-28)

C1 – **been managing to keep yourself busy and occupied?**	More so than usual	Same as usual	Rather less than usual	Much less than usual
C2 – **been taking longer over the things you do?**	Quicker than usual	Same as usual	Longer than usual	Much longer than usual
C3 – **felt on the whole you were doing things well?**	Better than usual	About the same	Less well than usual	Much less well
C4 – **been satisfied with the way you've carried out your task?**	More satisfied	About same as usual	Less satisfied than usual	Much less satisfied
C5 – **felt that you are playing a useful part in things?**	More so than usual	Same as usual	Less useful than usual	Much less useful
C6 – **felt capable of making decisions about things?**	More so than usual	Same as usual	Less so than usual	Much less capable
C7 – **been able to enjoy your normal day-to-day activities?**	More so than usual	Same as usual	Less so than usual	Much less than usual

D1 – **been thinking of yourself as a worthless person?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D2 – **felt that life is entirely hopeless?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D3 – **felt that life isn't worth living?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D4 – **thought of the possibility that you might make away with yourself?**	Definitely not	I don't think so	Has crossed my mind	Definitely have
D5 – **found at times you couldn't do anything because your nerves were too bad?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D6 – **found yourself wishing you were dead and away from it all?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D7 – **found that the idea of taking your own life kept coming into your mind?**	Definitely not	I don't think so	Has crossed my mind	Definitely has

A ☐ B ☐ C ☐ D ☐ TOTAL ☐

Appendix – L State-Trait Anxiety Inventory for Children (STAIC)

mind garden

HOW-I-FEEL QUESTIONNAIRE

Developed by C.D. Spielberger, C.D. Edwards, J. Montuori, and R. Lushene

STAIC Form C-1

Name: _____ Age: _____ Date: _____

DIRECTIONS: A number of statements which boys and girls use to describe themselves are given below. Read each statement carefully and decide how you feel *right now*. Then put an X in the box in front of the word or phrase which best describes how you feel. There are no right or wrong answers. Don't spend too much time on any one statement. Remember, find the word or phrase which best describes how you feel right now, *at this very moment*.

1. I feel	❑ very calm	❑ calm	❑ not calm
2. I feel	❑ very upset	❑ upset	❑ not upset
3. I feel	❑ very pleasant	❑ pleasant	❑ not pleasant
4. I feel	❑ very nervous	❑ nervous	❑ not nervous
5. I feel	❑ very jittery	❑ jittery	❑ not jittery
6. I feel	❑ very rested	❑ rested	❑ not rested
7. I feel	❑ very scared	❑ scared	❑ not scared
8. I feel	❑ very relaxed	❑ relaxed	❑ not relaxed
9. I feel	❑ very worried	❑ worried	❑ not worried
10. I feel.....	❑ very satisfied	❑ satisfied	❑ not satisfied
11. I feel.....	❑ very frightened	❑ frightened	❑ not frightened
12. I feel.....	❑ very happy	❑ happy	❑ not happy
13. I feel.....	❑ very sure	❑ sure	❑ not sure
14. I feel.....	❑ very good	❑ good	❑ not good
15. I feel.....	❑ very troubled	❑ troubled	❑ not troubled
16. I feel.....	❑ very bothered	❑ bothered	❑ not bothered
17. I feel.....	❑ very nice	❑ nice	❑ not nice
18. I feel.....	❑ very terrified	❑ terrified	❑ not terrified
19. I feel.....	❑ very mixed-up	❑ mixed-up	❑ not mixed-up
20. I feel.....	❑ very cheerful	❑ cheerful	❑ not cheerful

STAIP-CH Test Booklet

Appendix – L State-Trait Anxiety Inventory for Children (STAIC)

HOW-I-FEEL QUESTIONNAIRE

STAIC Form C-2

Name: _____ Age: _____ Date: _____

DIRECTIONS: A number of statements which boys and girls use to describe themselves are given below. Read each statement carefully and decide if it is *hardly-ever*, or *sometimes*, or *often* true for you. Then for each statement, put an X in the box in front of the word that seems to describe you best. There are no right or wrong answers. Don't spend too much time on any one statement. Remember, choose the word which seems to describe how you usually feel.

1. I worry about making mistakes	❑ hardly-ever	❑ sometimes	❑ often
2. I feel like crying	❑ hardly-ever	❑ sometimes	❑ often
3. I feel unhappy	❑ hardly-ever	❑ sometimes	❑ often
4. I have trouble making up my mind	❑ hardly-ever	❑ sometimes	❑ often
5. It is difficult for me to face my problems	❑ hardly-ever	❑ sometimes	❑ often
6. I worry too much	❑ hardly-ever	❑ sometimes	❑ often
7. I get upset at home	❑ hardly-ever	❑ sometimes	❑ often
8. I am shy	❑ hardly-ever	❑ sometimes	❑ often
9. I feel troubled	❑ hardly-ever	❑ sometimes	❑ often
10. Unimportant thoughts run through my mind and bother me	❑ hardly-ever	❑ sometimes	❑ often
11. I worry about school	❑ hardly-ever	❑ sometimes	❑ often
12. I have trouble deciding what to do	❑ hardly-ever	❑ sometimes	❑ often
13. I notice my heart beats fast	❑ hardly-ever	❑ sometimes	❑ often
14. I am secretly afraid	❑ hardly-ever	❑ sometimes	❑ often
15. I worry about my parents	❑ hardly-ever	❑ sometimes	❑ often
16. My hands get sweaty	❑ hardly-ever	❑ sometimes	❑ often
17. I worry about things that may happen	❑ hardly-ever	❑ sometimes	❑ often
18. It is hard for me to fall asleep at night	❑ hardly-ever	❑ sometimes	❑ often
19. I get a funny feeling in my stomach	❑ hardly-ever	❑ sometimes	❑ often
20. I worry about what others think of me	❑ hardly-ever	❑ sometimes	❑ often

STAIP-CH Test Booklet

Appendix – M State-Trait Anxiety Inventory (STAI)

mind garden

SELF-EVALUATION QUESTIONNAIRE STAI Form Y-1

Please provide the following information:

Name_____ Date_____ S_____

Age_____ Gender (*Circle*) **M F** T_____

DIRECTIONS:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel *right* now, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. I feel calm	1	2	3	4
2. I feel secure	1	2	3	4
3. I am tense	1	2	3	4
4. I feel strained	1	2	3	4
5. I feel at ease	1	2	3	4
6. I feel upset	1	2	3	4
7. I am presently worrying over possible misfortunes	1	2	3	4
8. I feel satisfied	1	2	3	4
9. I feel frightened	1	2	3	4
10. I feel comfortable	1	2	3	4
11. I feel self-confident	1	2	3	4
12. I feel nervous	1	2	3	4
13. I am jittery	1	2	3	4
14. I feel indecisive	1	2	3	4
15. I am relaxed	1	2	3	4
16. I feel content	1	2	3	4
17. I am worried	1	2	3	4
18. I feel confused	1	2	3	4
19. I feel steady	1	2	3	4
20. I feel pleasant	1	2	3	4

Appendix – M State-Trait Anxiety Inventory (STAI)

SELF-EVALUATION QUESTIONNAIRE

STAI Form Y-2

Name_____ Date_____

DIRECTIONS

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you *generally* feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
21. I feel pleasant	1	2	3	4
22. I feel nervous and restless	1	2	3	4
23. I feel satisfied with myself	1	2	3	4
24. I wish I could be as happy as others seem to be	1	2	3	4
25. I feel like a failure	1	2	3	4
26. I feel rested	1	2	3	4
27. I am "calm, cool, and collected"	1	2	3	4
28. I feel that difficulties are piling up so that I cannot overcome them	1	2	3	4
29. I worry too much over something that really doesn't matter	1	2	3	4
30. I am happy	1	2	3	4
31. I have disturbing thoughts	1	2	3	4
32. I lack self-confidence	1	2	3	4
33. I feel secure	1	2	3	4
34. I make decisions easily	1	2	3	4
35. I feel inadequate	1	2	3	4
36. I am content	1	2	3	4
37. Some unimportant thought runs through my mind and bothers me	1	2	3	4
38. I take disappointments so keenly that I can't put them out of my mind	1	2	3	4
39. I am a steady person	1	2	3	4
40. I get in a state of tension or turmoil as I think over my recent concerns and interests	1	2	3	4

Appendix – N Pennebaker Inventory of Limbic Languidness

The PILL

Several common symptoms or bodily sensations are listed below. Most people have experienced most of them at one time or another. We are currently interested in finding out how prevalent each symptom is among various groups of people. On the page below, write how frequently you experience each symptom. For all items, use the following scale:

A	B	C	D	E
Have never or almost never experienced the symptom	Less than 3 or 4 times per year	Every month or so	Every week or so	More than once every week

For example, if your eyes tend to water once every week or two, you would answer "D" next to question #1.

___1. Eyes water
___2. Itchy eyes or skin
___3. Ringing in ears
___4. Temporary deafness or hard of hearing
___5. Lump in throat
___6. Choking sensations
___7. Sneezing spells
___8. Running nose
___9. Congested nose
___10. Bleeding nose
___11. Asthma or wheezing
___12. Coughing
___13. Out of breath
___14. Swollen ankles
___15. Chest pains
___16. Racing heart
___17. Cold hands or feet even in hot weather
___18. Leg cramps
___19. Insomnia or difficulty sleeping
___20. Toothaches
___21. Upset stomach
___22. Indigestion
___23. Heartburn or gas
___24. Abdominal pain
___25. Diarrhea
___26. Constipation
___27. Hemorrhoids
___28. Swollen joints
___29. Stiff or sore muscles
___30. Back pains
___31. Sensitive or tender skin
___32. Face flushes
___33. Tightness in chest
___34. Skin breaks out in rash
___35. Acne or pimples on face
___36. Acne/pimples other than face
___37. Boils
___38. Sweat even in cold weather
___39. Strong reactions to insect bites
___40. Headaches
___41. Feeling pressure in head
___42. Hot flashes
___43. Chills
___44. Dizziness
___45. Feel faint
___46. Numbness or tingling in any part of body
___47. Twitching of eyelid
___48. Twitching other than eyelid
___49. Hands tremble or shake
___50. Stiff joints
___51. Sore muscles
___52. Sore throat
___53. Sunburn
___54. Nausea

Since the beginning of the semester, how many:

_____ Visits have you made to the student health center or private physician for illness

_____ Days have you been sick

_____ Days your activity has been restricted due to illness

Appendix – O Big Five Inventory Transition to College (BFI-TTC)

Directions: Read each sentence. **Circle** the answer that describes you the best. Use the following scale to help you answer each statement:
1 = **Strongly Disagree** – you strongly disagree with the sentence; it really does not describe you at all.
2 = **Disagree** – you disagree with the sentence; it does not describe you.
3 = **In-between** – you are not sure whether you agree or disagree with this sentence; you are undecided.
4 = **Agree** – you agree with this sentence; it describes you**.**
5 = **Strongly Agree** - you strongly agree with the sentence; it really describes you.
Remember, answer all of the questions honestly. **All of your answers will be kept confidential**. **No parent or teacher will ever see your individual answers.**

	Strongly Disagree	Disagree	In-Between	Agree	Strongly Agree
1. I try to get along with other people, even if I don't agree with them.	1	2	3	4	5
2. I am always very careful when I am doing school work.	1	2	3	4	5
3. My mood goes up and down more than most people.	1	2	3	4	5
4. I like meeting new people.	1	2	3	4	5
5. I like to learn about new ways of doing things.	1	2	3	4	5
6. I sometimes make fun of other kids in school.	1	2	3	4	5
7. I always finish everything I start.	1	2	3	4	5
8. Sometimes I don't feel like I'm worth much.	1	2	3	4	5
9. It is hard for me to make new friends.	1	2	3	4	5
10. I would like to keep going to school for many years just to learn new things.	1	2	3	4	5
11. People who know me well think I am a very nice, kind person.	1	2	3	4	5
12. I like to plan things before I do them.	1	2	3	4	5
13. I often feel tense or stressed out.	1	2	3	4	5
14. I am very outgoing and talkative.	1	2	3	4	5
15. I like to read books on different subjects.	1	2	3	4	5
16. If anybody says something mean to me, I say something mean right back to them.	1	2	3	4	5
17. I am always on time for meetings with other people.	1	2	3	4	5
18. I sometimes feel like everything I do is wrong or turns out bad	1	2	3	4	5
19. I smile a lot when I am around other people.	1	2	3	4	5

20. I like to try new things.	1	2	3	4	5
21. I am very easy to get along with.	1	2	3	4	5
22. I try to be very neat and organized in my homework and class assignments.	1	2	3	4	5
23. I feel like I can't handle everything that is going on in my life.	1	2	3	4	5
24. I like to go to big parties where there are a lot of people.	1	2	3	4	5
25. I like to take classes where I learn something I never knew before.	1	2	3	4	5
26. I sometimes trick other people into doing what I want them to do.	1	2	3	4	5
27. My teachers can always count on me to do what they ask me to do in class.	1	2	3	4	5
28. I sometimes feel like I'm going crazy.	1	2	3	4	5
29. It is fun for me to talk to people I have just met.	1	2	3	4	5
30. I like to work on problems and puzzles.	1	2	3	4	5
31. I am always polite to other people.	1	2	3	4	5
32. I like to keep everything I own in its proper place.	1	2	3	4	5
33. I get mad easily.	1	2	3	4	5
34. I am a fairly quiet person in most group settings.	1	2	3	4	5
35. I like to visit new places.	1	2	3	4	5
36. I sometimes like to argue with other people just for fun.	1	2	3	4	5
37. I put away all of my things when I am done with them.	1	2	3	4	5
38. I sometimes feel sad or blue.	1	2	3	4	5
39. If I am in a group and no one says anything, I will say something first.	1	2	3	4	5
40. I like to find out how people live in other places in the world.	1	2	3	4	5
41. I like to help other people whenever they need it.	1	2	3	4	5
42. I always clean up after I have made a mess.	1	2	3	4	5
43. I feel good about myself most of the time.	1	2	3	4	5
44. I am usually a cheerful person.	1	2	3	4	5
45. I would like to learn how to read and speak a foreign language.	1	2	3	4	5
46. I like to learn new games and hobbies.	1	2	3	4	5
47. Sometimes I say things on purpose to hurt other people's feelings.	1	2	3	4	5
48. I enjoy coming up with new solutions for everyday problems.	1	2	3	4	5

Appendix – O Big Five Inventory (BFI)

Here are a number of characteristics that may or may not apply to you. For example, do you agree that you are someone who likes to spend time with others? Please write a number next to each statement to indicate the extent to which you agree or disagree with that statement.

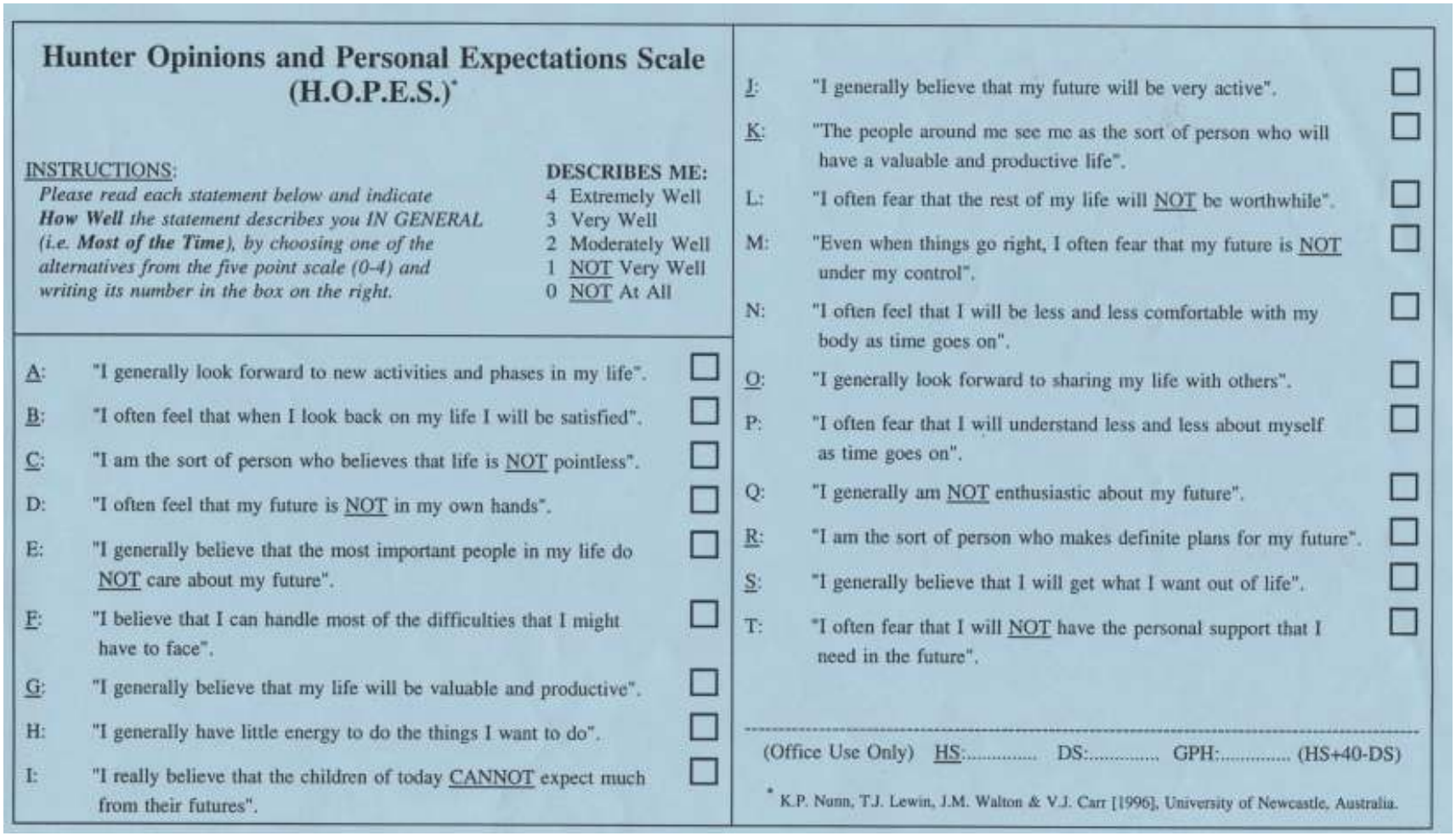
Disagree strongly	Disagree a little	Neither agree nor disagree	Agree a little	Agree Strongly
1	2	3	4	5

I see myself as someone who ...

___ 1. Is talkative
___ 2. Tends to find fault with others
___ 3. Does a thorough job
___ 4. Is depressed, blue
___ 5. Is original, comes up with new ideas
___ 6. Is reserved
___ 7. Is helpful and unselfish with others
___ 8. Can be somewhat careless
___ 9. Is relaxed, handles stress well
___ 10. Is curious about many different things
___ 11. Is full of energy
___ 12. Starts quarrels with others
___ 13. Is a reliable worker
___ 14. Can be tense
___ 15. Is ingenious, a deep thinker
___ 16. Generates a lot of enthusiasm
___ 17. Has a forgiving nature
___ 18. Tends to be disorganized
___ 19. Worries a lot
___ 20. Has an active imagination
___ 21. Tends to be quiet
___ 22. Is generally trusting
___ 23. Tends to be lazy
___ 24. Is emotionally stable, not easily upset
___ 25. Is inventive
___ 26. Has an assertive personality
___ 27. Can be cold and aloof
___ 28. Perseveres until the task is finished
___ 29. Can be moody
___ 30. Values artistic, aesthetic experiences
___ 31. Is sometimes shy, inhibited
___ 32. Is considerate and kind to almost everyone
___ 33. Does things efficiently
___ 34. Remains calm in tense situations
___ 35. Prefers work that is routine
___ 36. Is outgoing, sociable
___ 37. Is sometimes rude to others
___ 38. Makes plans and follows through with them
___ 39. Gets nervous easily
___ 40. Likes to reflect, play with ideas
___ 41. Has few artistic interests
___ 42. Likes to cooperate with others
___ 43. Is easily distracted
___ 44. Is sophisticated in art, music, or literature

Please check: Did you write a number in front of each statement?

Appendix – P Hunter Opinions and Personal Expectations Scale (H.O.P.E.S)



Hunter Opinions and Personal Expectations Scale (H.O.P.E.S.)*

INSTRUCTIONS:
Please read each statement below and indicate ***How Well*** *the statement describes you IN GENERAL (i.e.* ***Most of the Time****), by choosing one of the alternatives from the five point scale (0-4) and writing its number in the box on the right.*

DESCRIBES ME:
4 Extremely Well
3 Very Well
2 Moderately Well
1 NOT Very Well
0 NOT At All

A: "I generally look forward to new activities and phases in my life". ☐
B: "I often feel that when I look back on my life I will be satisfied". ☐
C: "I am the sort of person who believes that life is NOT pointless". ☐
D: "I often feel that my future is NOT in my own hands". ☐
E: "I generally believe that the most important people in my life do NOT care about my future". ☐
F: "I believe that I can handle most of the difficulties that I might have to face". ☐
G: "I generally believe that my life will be valuable and productive". ☐
H: "I generally have little energy to do the things I want to do". ☐
I: "I really believe that the children of today CANNOT expect much from their futures". ☐
J: "I generally believe that my future will be very active". ☐
K: "The people around me see me as the sort of person who will have a valuable and productive life". ☐
L: "I often fear that the rest of my life will NOT be worthwhile". ☐
M: "Even when things go right, I often fear that my future is NOT under my control". ☐
N: "I often feel that I will be less and less comfortable with my body as time goes on". ☐
O: "I generally look forward to sharing my life with others". ☐
P: "I often fear that I will understand less and less about myself as time goes on". ☐
Q: "I generally am NOT enthusiastic about my future". ☐
R: "I am the sort of person who makes definite plans for my future". ☐
S: "I generally believe that I will get what I want out of life". ☐
T: "I often fear that I will NOT have the personal support that I need in the future". ☐

(Office Use Only) HS:..... DS:..... GPH:..... (HS+40-DS)

* K.P. Nunn, T.J. Lewin, J.M. Walton & V.J. Carr [1996], University of Newcastle, Australia.

Appendix – Q Cognitive Emotion Regulation Questionnaire (CERQ)

CERQ

How do you cope with events?

Everyone gets confronted with negative or unpleasant events now and then and everyone responds to them in his or her own way. By the following questions you are asked to indicate what you generally think, when you experience negative or unpleasant events.

	(almost) never	**some-times**	**regu-larly**	**often**	**(almost) always**
1. 1 feel that I am the one to blame for it	1	2	3	4	5
2. I think that I have to accept that this has happened	1	2	3	4	5
3. I often think about how I feel about what I have experienced	1	2	3	4	5
4. I think of nicer things than what I have experienced	1	2	3	4	5
5. I think of what I can do best	1	2	3	4	5
6. I think I can learn something from the situation	1	2	3	4	5
7. I think that it all could have been much worse	1	2	3	4	5
8. I often think that what I have experienced is much worse than what others have experienced	1	2	3	4	5
9. I feel that others are to blame for it	1	2	3	4	5
10. I feel that I am the one who is responsible for what has happened	1	2	3	4	5
11. I think that I have to accept the situation	1	2	3	4	5
12. I am preoccupied with what I think and feel about what I have experienced	1	2	3	4	5

13. I think of pleasant things that have nothing to do with it	1	2	3	4	5
14. I think about how I can best cope with the situation	1	2	3	4	5
15. I think that I can become a stronger person as a result of what has happened	1	2	3	4	5
16. I think that other people go through much worse experiences	1	2	3	4	5
17. I keep thinking about how terrible it is what I have experienced	1	2	3	4	5
18. I feel that others are responsible for what has happened	1	2	3	4	5
19. I think about the mistakes I have made in this matter	1	2	3	4	5
20. I think that I cannot change anything about it	1	2	3	4	5
21. I want to understand why I feel the way I do about what I have experienced	1	2	3	4	5
22. I think of something nice instead of what has happened	1	2	3	4	5
23. I think about how to change the situation	1	2	3	4	5
24. I think that the situation also has its positive sides	1	2	3	4	5
25. I think that it hasn't been too bad compared to other things	1	2	3	4	5
26. I often think that what I have experienced is the worst that can happen to a person	1	2	3	4	5
27. I think about the mistakes others have made in this matter	1	2	3	4	5
28. I think that basically the cause must lie within myself	1	2	3	4	5
29. I think that I must learn to live with it	1	2	3	4	5
30. I dwell upon the feelings the situation has evoked in me	1	2	3	4	5
31. I think about pleasant experiences	1	2	3	4	5
32. I think about a plan of what I can do best	1	2	3	4	5
33. I look for the positive sides to the matter	1	2	3	4	5
34. I tell myself that there are worse things in life	1	2	3	4	5
35. I continually think how horrible the situation has been	1	2	3	4	5
36. I feel that basically the cause lies with others	1	2	3	4	5

Thank you for filling out the questionnaire!

Appendix – Q Cognitive Emotion Regulation Questionnaire - kids (CERQ-kids)

CERQ-kids

How do you cope with events?

Sometimes nice things happen in your life and sometimes unpleasant things might happen.

When something unpleasant happens, you can think about it for a long time.

When something unpleasant happens to you, what do you usually think?

	(almost) never	some-times	regu-larly	often	(almost) always
1. I think that I am to blame	1	2	3	4	5
2. I think that I have to accept it	1	2	3	4	5
3. Again and again, I think of how I feel about it	1	2	3	4	5
4. I think of nicer things	1	2	3	4	5
5. I think about what would be the best for me to do	1	2	3	4	5
6. I think that I can learn from it	1	2	3	4	5
7. I think that worse things can happen	1	2	3	4	5
8. I often think that it's much worse than what happens to others	1	2	3	4	5
9. I think that others are to blame	1	2	3	4	5
10. I think that I have been stupid	1	2	3	4	5
11. It just happened; there is nothing I can do about it	1	2	3	4	5
12. I often think of what I am thinking and feeling about it	1	2	3	4	5
13. I think of nicer things that have nothing to do with it	1	2	3	4	5

14. I think of how I can cope with it	1	2	3	4	5
15. I think that it makes me feel ‘older and wiser’	1	2	3	4	5
16. I think that worse things happen to others	1	2	3	4	5
17. Again and again, I think about how terrible it all is	1	2	3	4	5
18. I think that others have been stupid	1	2	3	4	5
19. I think that it’s my own fault	1	2	3	4	5
20. I think that I can’t change it	1	2	3	4	5
21. All the time, I think that I want to understand why I feel that way	1	2	3	4	5
22. I think of something nice and not about what happened	1	2	3	4	5
23. I think of how I can change it	1	2	3	4	5
24. I think that there are good sides to it as well	1	2	3	4	5
25. I think that it’s not as bad as other things that could happen	1	2	3	4	5
26. All the time, I think that this is the worst thing that can happen to you	1	2	3	4	5
27. I think that it’s the fault of others	1	2	3	4	5
28. I think that it’s all caused by me	1	2	3	4	5
29. I think that I can’t do anything about it	1	2	3	4	5
30. I often think of how I feel about what happened	1	2	3	4	5
31. I think of nice things that have happened to me	1	2	3	4	5
32. I think of what I can do best	1	2	3	4	5
33. I think that it’s not all bad	1	2	3	4	5
34. I think that there are worse things in the world	1	2	3	4	5
35. I often think about how horrible the situation was	1	2	3	4	5
36. I think that it’s all caused by others	1	2	3	4	5

Thank you for filling out the questionnaire!

Appendix – R Weinberger Adjustment Inventory

The purpose of these questions is to understand what you are **usually** like or what you have usually felt, not just during the past few weeks, but over the **past year** or more.

Please read each sentence carefully and circle the number that best describes you. For each sentence, decide whether it is false or mostly false for you, somewhat false (more false than true), somewhat true (more true than false), or true (or mostly true) for you. If you really can't say whether it is more true or more false for you, choose **not sure**.

Example: If a sentence read: "I spend a lot of time reading", and you read some but not that much, you would put a '2' for somewhat false in the space next to that sentence.

1= False; 2=Somewhat False; 3=Not Sure; 4= Somewhat True; 5=True

1. I usually think of myself as a happy person ____
2. There have been times when I said I would do one thing but then did something else ____
3. I really don't like myself very much ____
4. I can remember a time when I was so angry at someone that I felt like hurting him or her ____
5. Once in a while, I don't do something that someone asks me to do. ____
6. There have been times when I didn't let people know about something I did wrong ____
7. I'm not very sure of myself ____
8. I never act like I know more about something than I really do ____
9. I am answering these questions truthfully ____
10. Once in a while, I say bad things about people that I would not say in front of them ____
11. People who get me angry better watch out ____
12. I have done some things that weren't right and felt sorry about it later ____
13. I worry too much about things that aren't important ____
14. Once in a while, I break a promise that I've made ____
15. I'm the kind of person who has a lot of fun ____
16. There have been times when I did not finish something because I spent too much time "goofing off" ____
17. I am never unkind to people I don't like ____

Appendix – R Weinberger Adjustment Inventory

WEINBERGER ADJUSTMENT INVENTORY

18. Everyone makes mistakes at least once in a while _____

19. I often feel sad or unhappy _____

20. Once in a while, I say things that are not completely true _____

21. I usually feel I'm the kind of person I want to be. _____

Part II. The purpose of these next questions is to understand *how often* you think, feel or act in a certain way. Again we wish to know what is usual for you, even if it hasn't happened in the past couple of days or last few weeks. After you have read each sentence, decide whether it is **almost never** or never true, **not often** true, **sometimes** true, **often** true, or **almost always** true for you and then circle the number which corresponds to your answer.

1= Almost Never; True 2=Not Often; True 3=Sometimes; True 4= Often True; 5=Almost always True

22. I do things without giving them enough thought. _____

23. When I have the chance, I take things I want that don't really belong to me. _____

24. If someone tries to hurt me, I make sure I get even with them. _____

25. I feel nervous or afraid that things won't work out the way I would like them to. _____

26. I become "wild and crazy" and do things that other people might not like. _____

27. I feel lonely. _____

28. Before I do something, I think about how it will affect the people around me. _____

29. I will cheat on something if I know no one will find out. _____

30. When I'm doing something for fun (for example, partying, acting silly), I tend to get carried away and go too far. _____

31. I do things that I know really aren't right. _____

32. I get into such a bad mood that I just feel like sitting around doing nothing. _____

33. I lose my temper and "let people have it" when I'm angry _____

34. In recent years, I have felt more nervous or worried about things than I have needed to. _____

35. I feel very happy. _____

36. I think about other people's feelings before I do something they might not like. _____

37. I make sure that doing what I want will not cause problems for other people. _____