

THE S I S F O R D E G R E E M . D .

OF

E D I N B U R G H U N I V E R S I T Y .

BY

DAVID YOUNG,  
M.B., Ch.B.

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### Infantilism due to Atrophy of Pancreas.

Infantilism, though a comparatively new term, is applied to a condition which has been observed since the earliest times. I have referred to several Medical Dictionaries for a definition without success. I would apply the term to a condition in which, - due to insufficient nutrition, - development is incomplete especially in regard to height and the changes which occur at puberty. The causes of Infantilism are numerous, but may be divided into Congenital and Acquired. As examples of Congenital cases, we have Cretins and those due to Congenital Syphilis, Heart Disease, etc. As Acquired cases, we have those due to Rickets and the early abuse of such drugs as Alcohol and Morphia. I think for a Clinical classification, cases of Infantilism might conveniently be divided into those due to deficiency of Thyroid secretion and those due to other causes. It appears that a sharp line cannot be drawn between these, but that they merge into one another, and many writers have described cases in which the Thyroid was not primarily at fault which had benefitted from Thyroid treatment. I have no intention of discussing the general question of

Infantilism, but would like to draw attention to the relation which the Pancreatic Secretion bears to some cases of arrested development. Although I have read widely on the subject both in home and continental books and papers, I have not found any case in which this condition has been discussed except in the Scottish Medical & Surgical Journal of March 1902, where mention is made of a case shown at the Medico Chirurgical Society on February 8th 1902 by Dr Byrom Bramwell. This case I had the opportunity of working at and I will describe it afterwards. Hertoghe however makes mention of cases of Infantilism associated with Diarrhoea, and other abdominal symptoms which did not do well on Thyroid extract (L'Hypothyroidie bélique Chronique, on Myxoedème fruste.) I have carefully studied two cases of arrested growth in which I believe the Pancreas was primarily at fault, but, thanks to the benefit derived in those cases from the administration of Pancreatic extract, I am not likely to be in a position to verify my diagnosis for some time to come.

The first of these cases I met by chance two years ago in Dispensary work. The patient came under my notice on account of persistent Diarrhoea, which

had previously been treated with various drugs and dieting, but without success. After administering the various routine drugs I did what I ought to have started with. I examined the Faeces. The faeces were fluid and I was struck with the amount of fat they contained. I thought such a condition might be benefitted by pancreatin, and so I prescribed it. There was an improvement in the number of motions but not so much as I had expected. They were reduced from four to six per day, to three or four. The improvement on the general condition however appears to have been so marked that the patient continued the treatment regularly till I again came across him nearly a year later. There was a very marked difference in his general condition, but I did not remember him sufficiently to be able to give any satisfactory description of the change. He and his friends however insisted on the change and this led them to tell me about his history, which I will give later. While working at, and thinking over this case I busied myself searching for another, presenting similar features. This case I ultimately found in the Wards of Edinburgh Infirmary under Dr Bramwell's care. He was being treated with Thyroid extract at the time. This was the case shown by Dr Bramwell at the Medico

Chirurgical Society on February 8th of this year.

I have also through the kindness of Dr. John Thomson, obtained a few notes about a case of Infantilism under his charge a number of years ago. This case he believes might easily have been accounted for by absence of Pancreatic secretion from the Intestine.

I have no doubt that there are many such cases, but if not diagnosed, the treatment would be of little avail, and, where the results are not good, unfortunately few cases are published.

As I had the opportunity of studying for a period of six months the case in Dr Bramwell's ward I propose to describe it in detail and to deal more shortly with my original case as I could not study it so carefully out of Hospital and as his condition had improved very greatly before I commenced to take notes. I will also mention the facts I have gathered about Dr. John Thomson's case.

The case which I am about to describe was sent to Hospital on account of persistent Diarrhoea. To remedy this he was placed on Milk diet and, on his age being noted, interest was at once centred on his obviously arrested growth and his Diarrhoea placed in the background.

The patient was a boy  $18\frac{1}{2}$  years of age and his complaint on admission to Hospital was Diarrhoea which had lasted nearly nine years.

Personal History. As a child he was healthy and well grown and appears to have suffered little from the ailments of childhood. At the age of ten years he was of normal height, intelligent, in the fifth standard at School and well able to keep up with those of his own age. After this age he was unable to attend School regularly on account of his frequent Diarrhoea. Before the age of 10 he had no trouble connected with his alimentary system. At the age of 10 years he suffered from a severe attack of Measles, and convalescence was much prolonged. He was confined to bed about six weeks but did not feel well until a considerable time after. Nothing definite can be elicited about abdominal trouble at this time, but his Father said that the Dr. in attendance told him the

prolonged convalescence was due to "stone". The nature of the stone he was either not told, or else had forgotten. Patient's troubles date from this illness. He did not feel well till nearly six months after. His Diarrhoea set in about this time and Father stated he had grown very little if at all in height since this illness. Diarrhoea has continued uninterruptedly notwithstanding various lines of treatment. Though often unfit for School, or work, since the Diarrhoea started, the following is the only definite illness from which he has suffered:-

At the age of 12 patient was in the Royal Infirmary, Edinburgh, under the care of Dr Andrew Smart, to whom I am indebted for the use of his Ward journal. Unfortunately the notes on the case are not very complete and his height and weight do not appear to have been charted.

The diagnosis was "Subacute pneumonia and Meningitis" (?)

I take the following extracts from the notes:-

"Patient has been subject to sick turns, but in the last few years they have been more frequent, and more severe, they consist of violent purging which comes on quite suddenly while running about".

"Considerable debility, he is a small child for his years."

"He has an oldish looking face."

"He is an intelligent looking boy."

He remained in Hospital from May 13th to June 3rd, and his motions as charted are interesting: the following figures refer to the number of motions per day - 4, 2, 2, 6, 7, 2, 4, 6, 4, 5, 7, 4, 3, 8, 2, 2, 8, 5, 7, 4, 6, 3.

On leaving Dr Smart's Ward he was sent to the Convalescent, and though his name is on the books, again no record is to be found of his height and weight.

Very soon after leaving the convalescent home he had his photo taken, i.e., 6 years ago, when he was 12 years of age. I managed to obtain a copy of this photo and have had it reproduced and show it in the Appendix, numbered I.

Family History. Father died last month, age 56, of Consumption. Mother died at age of 44, Dropsy said to have been the cause of death. Patient has had eight brothers and sisters:-

1. Brother - age 26.
2. Brother - died of Fever at age of 22.
3. Sister - age 22. 5 ft.  $\frac{3}{4}$  in. Weight 6 st.  $10\frac{3}{4}$  lbs.
4. Sister - age 21. 5 ft.  $1\frac{1}{4}$  in. Weight 6 st.  $12\frac{1}{4}$  lbs.
5. Patient himself 18 $\frac{1}{2}$ . 4 ft.  $4\frac{1}{8}$  in. Weight 4 st.  $12\frac{1}{4}$  lbs.
6. Brother - age 16. 5 ft.  $\frac{1}{2}$  in. Weight 6 st. 8 lbs.
7. Brother - age 14. 4 ft.  $7\frac{1}{2}$  in. Weight 5 st. 8 lbs.
8. Sister. - age 12. 4 ft. 8 in. Weight 5 st. 5 lbs.
9. Brother - age 10. 4 ft.  $2\frac{1}{8}$  in. Weight 4 st.  $2\frac{1}{2}$  lbs.



Photo numbered 2 in the Appendix shows the members of the family from the third to the eighth. The two girls in the back are older than Patient and are aged 22 and 21. All the others shown in the photo are younger than Patient, who is the smallest in the group and is in Hospital dress. The two brothers are 16 and 14 and the youngest is the sister aged 12. Of the other two surviving members the oldest of the family, who is 26 years of age, is 5 ft. 10 in. and well developed, while the youngest, who is ten years of age, is 4 ft. 2 in. in height and quite healthy, and is the only member of the family who is smaller than Patient. The brother who died at the age of 22 was 6 feet in height. There is no history of any of the other members of the family being ill developed; no history of Syphilis, Rheumatism or Rickets.

State on admission. At first sight Patient might pass for an ordinary individual somewhat undersized. He looked small on account of the relation of his breadth to his height, but, while many guessed his age none did so correctly; - the usual answer to the question being - "12 years of age". Knowing his age and his history of Diarrhoea it looked to me as if nature,

despairing of making a well grown individual, had chosen rather than have an ill developed man of normal height, to make a man in miniature; - what one might see on looking through the wrong end of a Field Glass. A Medical friend of mine remarked that he appeared to be looking at one older than he saw. Patient's face is full and fleshy; cheeks well coloured; eyes large and blue, and though his expression is rather heavy he does not look unpleasant. He is active in his movements, but when in repose gives the expression of lassitude. Head well covered with hair which is light in colour. There is no hair on his lips or cheeks; his face looks older than his body. Mouth small and feminine; Neck short, being about one quarter length of his head, but otherwise he is very well proportioned and I may give the following measurements taken soon after admission:-

Height - 4 ft.  $4\frac{1}{2}$  inches. Weight 4 st.  $12\frac{1}{4}$  lbs.

Tip of middle finger of right hand to tip of middle finger of left + arms outstretched = 4 ft. 5 inches.

Chest: - At level of nipple. Full expiration  $26\frac{1}{2}$  in:

Full inspiration 29 inches.

- Antero-posterior diameter  $7\frac{3}{4}$  inches  
- Transverse "  $9\frac{1}{4}$  inches.

Head:- Greatest circumference  $20\frac{1}{4}$  inches. Length 7 in:

Transverse diameter above ears  $5\frac{5}{8}$  inches.

Abdomen at level of umbilicus  $25\frac{1}{4}$  inches.

Upper border of sternum to upper border of symphysis pubis 18 inches.

From seventh servical vertebra to tip of coccyx  $19\frac{1}{2}$  in:

Intertrochanteric diameter  $9\frac{5}{8}$  inches.

Tip of acromion to tip of olecranon 10 inches.

Tip of olecranon to tip of ulnar styloid  $8\frac{1}{2}$  inches.

Wrist joint to tip of middle finger  $6\frac{1}{2}$  inches.

Middle finger (longest)  $3\frac{1}{2}$  inches..

Upper arm at thickest part  $6\frac{1}{2}$  inches.

Forearm " " "  $7\frac{3}{4}$  "

Circumference at level of wrist  $5\frac{3}{8}$  inches.

Anterior superior iliac spine to knee joint 15 inches.

Knee joint to tip of external malleolus  $17\frac{7}{8}$  inches.

Length of foot  $8\frac{1}{2}$  inches.

Thigh at thickest part 15 inches. Calf at thickest part  $9\frac{3}{8}$  inches.

The following points show the body in good proportion:-

Height is just over seven times the length of his head.

When patient stands with his arm projecting from his side at right angles to his body, with the elbow bent, the tip of his middle finger just touches the middle line of his body. Length of his foot equals the

length of his Ulna. Transverse measurement of the head, just above the level of the ear, is equal to the distance between the external auditory meatus and the top of his head.

Hands and feet are well formed; fingers slender and tapering.

Skin fair and rather delicate, notably there is an entire absence of hair on lips, cheeks, axilla, and pubis, and of the soft hair on the arms and legs.

Genital organs small as before puberty.

Not stupid in manner and general behaviour but childish.

Voice has not broken. In singing he ranges between A. and G.

Once when pained he cried as a child would have done.

No signs of Rickets or Syphilis.

Temperature normal.

Alimentary system - Subjective:- Appetite good, but for a number of years patient has had decided repugnance for fatty foods. He always feels bad after them and says they increase his Diarrhoea. During the last four years he has never taken butter on his bread. For several years milk diet has disagreed with him, though it often was ordered to check his Diarrhoea. Before

present illness he was very fond of milk. He drinks rather more than an average amount of fluid. Deglutition easy for ordinary purposes. He had great difficulty in swallowing capsules which were given to him. On three occasions these stuck in Oesophagus and brought on severe attack of coughing and retching and patient was unable to retain fluids which he tried to swallow until bougie was passed down Oesophagus. He said capsule stuck at a point behind the junction of manubrium and body of sternum. There never appeared to be any stricture on passing bougie and, as many patients have trouble in swallowing capsules I do not attach any importance to this, and would not have mentioned it, had it not been for a case of Infantilism shown at the Medico Chirurgical Society by Dr Langwill of Leith Hospital. In this case one of the most notable features was the extraordinary regurgitation of food.

Patient has no discomfort as a rule after food but, if meal is large or contains fats he has a feeling of weight in abdomen, coming on three or four hours after eating, not relieved by vomiting but by Diarrhoea.

No tormina or tenesmus.

Diarrhoea persistent during last  $8\frac{1}{2}$  years, usually six to nine motions per day. This has been unaltered

though various diet<sup>a</sup>tries have been tried and many drugs given a fair chance. Drugs might diminish number of motions to three or four in the day but none had any permanent effect.

Objective:- Lips well formed, colour good.

Teeth:-

Upper jaw. I.= 2-2. C.= 1-1. B.I.=2-2. M.= 1-1.  
No signs of second or third Molars.

Lower jaw. I.= 2-2. C.=1-1. B.I.=2-2. M.=2-2.

This gives 26 teeth in all, while one expects 28 at the age of 13 years. Teeth are in good order except bicuspid of lower jaw, the first on each side being carious.

Gums in good condition.

Tongue larger than normal and slightly indented by teeth; moist no fur. The flabbiness is more marked than the enlargement.

Free secretion of Saliva.

Palate is well formed.

Pharynx appears healthy.

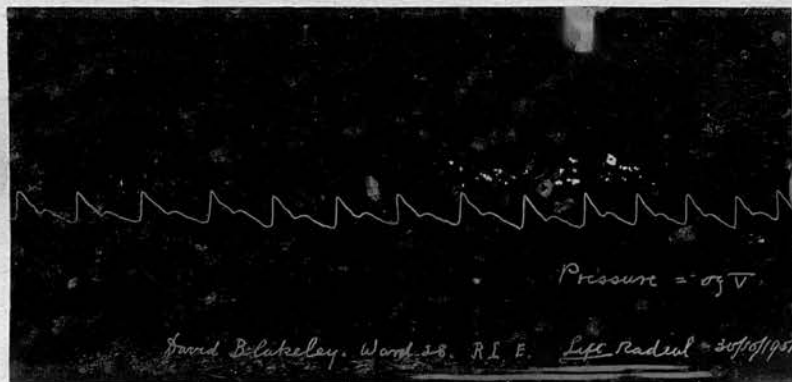
Stomach not enlarged and examination of its contents showed the presence of the active digestive principles.

Abdomen full but no distention, covering good. Examination of abdomen was entirely negative. Liver of

normal size. Examination of Rectum negative.  
Motions quite unformed, never solid, pale - clayey or light cinnamon in colour - about the consistence of thick gruel and obviously containing undigested fats; have a peculiar putrid odour. Reaction alkaline.  
While on light diet the fat was present in globules which floated on water, and in masses about the size of a grain of barley, but, when patient was made to swallow pieces of cooked fats these were passed unchanged by the bowel.  
When on Milk diet no curds were observed in the motions. Never any trace of worms.

Circulatory and Respiratory systems. No subjective phenomena.

Chest well formed. Careful examination of the Vascular system revealed no abnormality. Pulse 66 per minute, volume good. No narrowing of vessels.



No symptoms of congenital or acquired heart disease. Result of examination of the respiratory system also was negative.

Urinary system. Urine:- Amount 38 ounces; straw coloured. Specific gravity 1024 acid. Urea 360 grains per day, with an ordinary diet and moderate amount of exercise. No trace of sugar found though Urine was repeatedly examined. Never lipuria while under observation. No abnormal constituent detected.

Though stools were offensive and decomposed readily there was no increase of the indogens in the Urine, in fact, they appeared decreased. The Diarrhoea must have prevented the absorption of decomposition products.

Reproductive. No pubic hairs. Organs of generation small. Testes are small as before puberty. Appears to have no sexual instincts.

Haemopoietic System. No Glandular enlargement. No change observed in Thyroid. Spleen not enlarged.



Examination of blood revealed nothing abnormal. The various forms of leuco-cytes are in good proportion and the total number not increased.

Locomotory System. Limbs well formed. All the epiphyseal lines are perfect.

The Skiagraphs in appendixs show the wrist, elbow and knee joints. Muscles are of good size, & tone is good.

Nervous System. Patient is intelligent but Cerebration is inclined to be slow. Education has been hindered as he was unable to attend School regularly on account of his Diarrhoea. At the age of 17 he had charge of a Telephone Exchange and appears to have done his work satisfactorily. His mental state is very much what one would have expected in a boy of 14 or 15 years .

Memory is good. Patient is not emotional. Speech is quite natural and articulation clear. Sleeps well. All active movements are carried out neatly.

Dynamometer. R. 45, - 45. L. 40, - 35.

Reflexes. Knee and Achillis jerks active and equal. Plantar response is flexion.

Gluteal abdominal and Cremasteric reflexes all obtained. Scapular reflex absent.

The four great organic reflexes are normal.

Muscles react actively to faradic current.

No trophic changes observed in skin, bones, joints or muscles.

Sensibility to touch, pain and temperature perfect all over the body.

Special senses are all in good order.

My first case resembled the one just described in so many details that I think it unnecessary to discuss it at length, more especially as I did not recognise its nature until it had been under treatment for nearly a year, and it was during this period that most of the improvement in the patient's condition took place. This patient was 22 years of age. He looked like a boy of 15 or 16, but the lines of his face seemed to indicate that his troubles had lasted over a considerably longer period. He was 5 ft. 2 in. in height, and his weight was 6 st.  $1\frac{1}{2}$  lbs. He was pale and was not well built. He is said to have had the Diarrhoea since shortly after birth. There was no apparent cause. His motions were liquid and distinctly fatty. Mental condition was good. Sugar never detected in the Urine.

Dr John Thomson's case I have been unable to trace. He measured 4 ft. 4 in. at the age of 17. When Dr Thomson saw the first case which I have described, he was so struck by the resemblance to the case which was under his charge  $2\frac{1}{2}$  years previously, that he thought he was dealing with the same boy. Diarrhoea of a fatty nature was also the leading feature in this case, along with arrested growth. His mental condition

was rather dull. No sugar in Urine.

Reasons for believing that Pancreatic secretion was absent from the Intestine.

My observations were conducted along three lines -

- I. Testing for the presence of Pancreatic ferments in the bowel.
- II. Experimental observations on animals.
- III. Results of Treatment.

I.

Testing for the presence of Pancreatic ferments in the Bowel.

Of the four Pancreatic ferments, Steapsin, Trypsin, Amylo-pepsin, and the milk curdling ferment, I found it only possible to examine two, Steapsin and Trypsin.

(a) Steapsin. Presence of free fat in the stools was very noticeable. Masses of fat given by the mouth were practically passed unchanged.

The amount of fat excreted does not depend entirely on the amount injected as hemi-peptone is decomposed by bacteria in fatty and amide acids, such as leucin, and aromatic bodies as indol and skatol.

The pancreatic secretion is largely responsible for the digestion of fats. Only 18% of the fats of milk

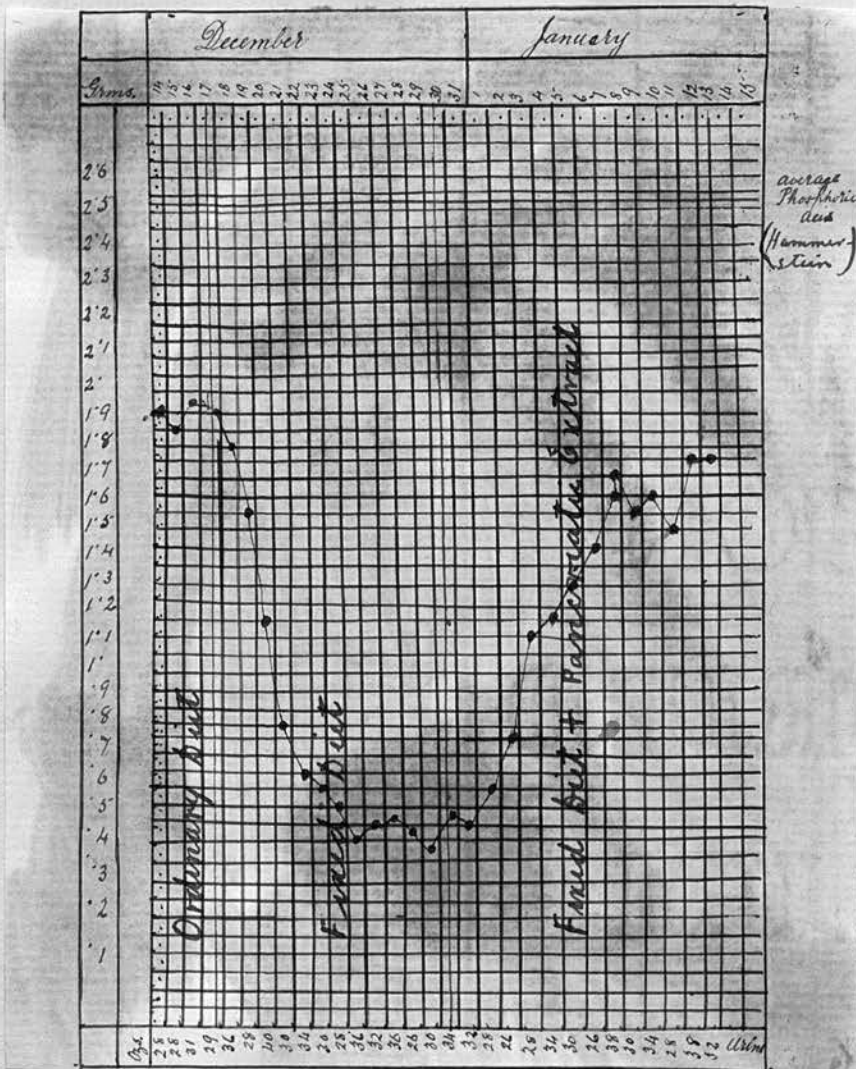
is split up in the stomach. It is now known that the bile has little action on the digestion of fats though it is probably in a great part responsible for their absorption by stimulating the intestinal villi. It is doubtful if the intestinal secretion proper has any action in splitting fats.

Putting patient on a fixed diet of an ordinary kind I extracted the fats from the Faeces with Ether. I found the average amount of fat excreted daily was 5% of the total amount of Faeces. Keeping the patient on the same diet but administering a suitable form of Pancreatic extract at a suitable time, the average amount of fat excreted daily fell to 1.7%. In a healthy individual of the same weight on the same diet the amount of fat excreted was .8% of the whole.

Normally 84% of the fats of the faeces is in the form of fatty acids and soaps. In this case only 46% of the fats were present in this form. This disproportion, according to Leo, indicates with certainty the absence of pancreatic secretion from the intestine.

(b) Trypsin. The principal constituent of Milk is Caseinogen. It forms 66% of the whole. This is split up in the stomach by the Pepsin-acid Proteolysis into Paranuclein and a Proteid. Paranuclein is insoluble in the intestine and so is not absorbed. The Paranuclein which contains 4% of Phosphorus is normally

broken up in the Intestine into Paranucleic acid and Albumose. This Paranucleic acid is the source of body Phosphorus for a person but on a milk diet; other things being equal, the amount of Phosphoric acid excreted in the Urine depends on the amount absorbed from the Intestine. I kept the patient on a constant diet, three pints of milk and two slices of bread daily, and then carefully estimated for a period of three weeks the amount of Phosphoric acid excreted daily. The accompanying chart shows the result.



The transverse red line shows the average amount of Phosphoric acid excreted daily by a healthy individual. The first three days shows the amount of Phosphoric acid excreted daily by the patient on an ordinary diet where the source of Phosphorus is different from that while on a Milk diet, and the amount absorbed from the Intestine does not to such an extent depend on the action of the Pancreatic juice. The amount of Phosphoric acid excreted daily fell, as the supply in the body gave out, till it reached .7 grms, when it remained fairly constant. The amount would probably have fallen lower were it not for the fact that Paranuclcin is very slowly broken up, in the absence of Pancreatic juice, by prolonged Peptic digestion, into its constituent parts. Otherwise the Phosphoric acid might almost have disappeared altogether from the Urine. Still keeping the diet constant I administered Pancreatic extract. The amount of Phosphoric acid excreted soon rose far above the level of that excreted with the same diet, but without the administration of the extract. The deposit of Phosphates in the Urine is no guide to the amount of Phosphorus being excreted. In making my calculation I observed that when the amount of Phosphorus being excreted was at its lowest, the deposit of Phosphates came down more quickly than at any

other time. This, I take it, was due to the diminution of Acid Sodic Phosphate in the Urine which normally keeps the earthy Phosphates in solution.

The importance of Pancreatic juice will be noted when the fall in the excretion of Phosphoric acid due to its absence is observed, for the amount of Phosphorus absorbed depends on the proper digestion of Caseinogen, which forms 58% of milk.

(c). It has long been known that the absorption of Salol depends on its being broken up by the Pancreatic secretion. I gave the patient 45 grains daily for a week. No constitutional symptoms developed and no reaction was obtained on testing Urine with Perchloride of Iron, or Fehling's solution.

(d). A short time ago Professor Sahli of Berne described Capsules which he used to test the activity of the Pancreatic secretion. These he principally used in cases of persistent Jaundice in adults where, he believed, there might be malignant disease of the head of the Pancreas. The capsules were made of a glutoid substance which is only dissolved by the Pancreatic secretion. They contained Iodoform. After the capsules are dissolved in the Intestine the Iodoform is absorbed, and quickly excreted in the saliva in the form of Iodides, and Iodates. After administration



the person under observation is instructed to spit into vessels at periods of half an hour. The Saliva is then tested; one inch is placed in a test tube and one quarter inch of Chloroform added. Nitric acid is then added drop by drop to break up the Iodides and Iodates, setting free the Iodine which is dissolved and kept in solution by the Chloroform which sinks to the bottom of the tube. If Iodine is present a beautiful pale rose red colour is developed at the foot of the tube. The reaction is usually obtained in the Saliva about three hours after taking of the Capsules, which should be given with a meal in order to stimulate the flow from the Pancreas. A box of these capsules were kindly sent to me by Professor Sahli. I tested them twice on myself and obtained the Iodine reaction on both occasions. I tried them several times on the first and second cases which I have described. I never obtained any reaction in the Saliva, and the Capsules were afterwards found in the stools swollen but not dissolved. Again I gave these Capsules to each of the patients at meal time, and followed them up by 2 drachms of the B.P. liquor Pancreaticus. On all occasions the Iodine reaction was obtained and no trace of the Capsules could be found in the stools.

II.

Experimental observations on Animals.

My experiments with kittens and young rabbits were attended by a high mortality. Yet, I think I managed to obtain a number of definite results.

I tried in several cases to entirely destroy the Pancreas but the subjects never lived long enough to give any reliable information. In one case I found sugar in the Urine.

I tied the Pancreatic duct in a number of kittens. Four of these lived to give definite results. I observed that the rabbits died much more quickly than the kittens, possibly because of the greater activity of the gland in rabbits. In one case sugar appeared in the Urine, but here an inflammatory change in the gland was afterwards found. One kitten lived for 63 days, but its motions became very fluid and contained an increased quantity of fat. It did not grow more than  $\frac{3}{4}$  of an inch in length during this time but gradually lost weight and died of Asthenia. After death the remains of a Pancreatic cyst was found. The gland was anaemic and the gland cells showed very marked fatty degeneration. The cells of Langerhans were only affected to a slight degree.

To another kitten I tried to administer the extract by subcutaneous injection, but the injections appeared to do more harm than good, though none of them became septic. Diarrhoea set in and the kitten rapidly fell off in weight and died.

One kitten did well however when fed on Peptonised milk. It seemed to make no difference whether the milk was peptonised with Pepsin, or Liquor Pancreaticus. There was a growth of  $\frac{1}{2}$  an inch in four weeks. There was no marked Diarrhoea. The kitten was examined after being killed and showed that no secretion from the Pancreatic duct was entering the Intestine.

### III.

Results of Treatment.

Seen later.

Aetiology and Pathology.

As I only saw these cases a number of years after the condition had started, and, as the history of the onset is indefinite in both, and as I have no Post Mortem evidence, it is impossible to be definite concerning the Aetiology and Pathology.

Two forms of Sclerosis of the Pancreas are described - the Intra-Lobular and Intra-Acinar. Literature on the subject is very indefinite, but I should imagine that the Intra-Lobular form will be more likely to follow an infection through the blood; while the Intra-Acinar form might quite well result from the blocking of the Pancreatic duct by a Calculus, peripancreatic adhesions, or other cause. The stone which the Dr. mentioned after the attack of Measles in the first case which I have described might have been an attack of Pancreatic Colic and the Atrophy have resulted from backward pressure. There was no Jaundice or Haematuria at time of Colic. On the other hand the Atrophy might have been due to some infection following the Measles (though very many troubles are dated from an attack of Measles, which is a much used time post in the lives of many children). Trousseau described six cases of Atrophy of the Pancreas due to Alcohol,

similar to Atrophy of the Liver from a like cause. Hertoghe has described a case of Infantilism following Scarlet Fever. I am told that Sclerosis is not at all uncommon in the Post Mortem though it is seldom diagnosed before death. The involvement of the islands of Langerhans is the great point of distinction between the two forms of Atrophy. The absence of sugar from the Urine would point to these being active, and so to the Intra-Acinar rather than the Intra-Lobular form of Atrophy being present.

I do not think that the Pancreas influences growth by means of any internal secretion. I think the arrest of growth is due to the inefficient digestion of the foods, and to the Diarrhoea. I administered small doses of Pulv: Jalap: Co: to a kitten two months old. It produced frequent liquid motions. The kitten lost weight and only grew  $\frac{1}{4}$  of an inch in five weeks.

Infantilism due to Diarrhoea is analogous to a case due to excessive excretion of Urea, described in 1896 by Hertoghe in his paper "Ou diagnostic de la possibilité d'une reprise de croissance". Other similar cases have since been described.

A parallel can also be drawn between this case and the case of Infantilism shown by Dr Langwill at the

Medico-Chirurgical Society on November 7th 1900. In this case the arrest of development appeared to be due to persistent regurgitation of food through the Oesophagus. The boy at the age of 19 years looked like a boy of 12 years. In both cases malnutrition appears to have been the cause of non-growth.

The fact that growth continued after administration of Pancreatic extract does not indicate that it has any direct effect. Any property which it might contain acting through the blood after administration as extract by the mouth would probably be entirely changed in the Intestine and so have no action when absorbed. This of course would differ from administration of Thyroid extract where the Iodothyryn is absorbed unchanged.

The fact that a kitten with Pancreatic duct ligatured was not benefitted by subcutaneous injections of soluble Pancreatic extracts favours this view.

#### Symptoms and Physical signs.

The importance of the Pancreatic secretion is very great. Its ferments affect the albuminoids, carbohydrates, and fats.

Max Leinhorn says it is the most energetic and general

in its action of all the digestive juices. It unites in itself the action of the saliva, and the gastric juice, besides having properties of its own.

The symptoms usually associated with Chronic disease of the Pancreas are Diabetis, and Fatty Diarrhoea. It is noticeable how little work has been done in connection with the Pancreas in this country. Diabetis, as I have pointed out, would appear to depend on the form of Sclerosis. It is rarely associated with Pancreatic cysts where the change is intra-~~acinar~~.

Removal of the Pancreas in a grown animal has been <sup>believed</sup> always to cause marked loss in weight; while in the case I have described the boy's weight was quite up to the standard required for his height. Though nature is unable to nourish fully a grown animal without the aid of the Pancreas, there seems to be no reason why an under-grown animal should not be well nourished. H. Leo of Bonn on the other hand describes cases in which no pancreatic secretion entered the Intestine in which, "the general state of nutrition left nothing to be desired". Arrested development would of course vary according to the age of the patient. A feature of my case was the amount of development with-out ~~growth~~.

As Dr John Thomson remarked that his case resembled so greatly the first one I have described, I thought it

well to attempt to sketch my case, and show it in Appendix No. 6.

The distaste for fatty foods no doubt is an acquired taste, depending on the discomfort induced by their being included in the patient's diet. I would lay special stress on the constant, painless, fatty Diarrhoea. Diarrhoea contrasts markedly with the other class of cases of Infantilism, - the Myxoedamatus class, - where constipation is an almost constant symptom, and probably has much to do with the size of the Abdomen and the frequency of Umbilical hernia in these cases.

The motions in my two cases were pale, but this is no indication of the absence of Bile from the Intestine. The colouring agent in the faeces is Hydrobilirubin, and this is only formed by the inter-action of Bile, and the Pancreatic secretion. This was pointed out a number of years ago by a Dr. Walker of Peterborough. Only Bile thus altered is excreted, the rest in the form of Bilirubin and Bilifuscin is absorbed and so does not colour the stools.

#### Diagnosis.

1. History. I have never heard of Congenital absence



of the Pancreatic secretion.

Fatty Diarrhoea starting and persisting in a previously healthy individual should rouse suspicion, and lead one to examine for the presence of Pancreatic secretion in the Intestine.

2. Signs and symptoms as above.

3. Examination of the patient in regard to:-

(a) Absence of other causes of arrested development such as Cretinism, Congenital Syphilis, Rickets, excessive secretion of the Urea, presence of grave disorders of the Vascular system.

(b) Tests for the presence of Pancreatic juice in the Intestine:- i.e. Estimation of the fat in the faeces, or observations on the digestion of the Pancreatins as I have described. I would specially recommend the use of the Capsules described by Professor Sahli, on account of their simplicity.

#### 4. Result of treatment.

Thyroid extract which frequently gives such striking results in Cretins has also been strongly recommended in non-myxoedematous cases; Hertoghe and Bourneville have both claimed good results ("L'Hyperthyroidie bénigne chronique ou myxoedemic fruste" Hertoghe). Thyroid was tried in the case in Dr Byrom

Bramwell's ward for six weeks. The most careful observations failed to show any advantage derived from its use. Of course while the Diarrhoea continued it could not be expected that Thyroid would improve the patient's condition. After Pancreatic extract had been administered and the Diarrhoea held in check, I again tried Thyroid, still continuing the Pancreatic extract, but I did not observe any advantage gained by using it.

The obvious indication was to check the Diarrhoea, and do so if possible by supplying the absent secretion or a suitable substitute for it. I started the patient with one drachm of the B.P. Liquor Pancreaticus, given two hours after each meal. The reasons for giving it at this time were:-

1. It is the natural time for the Pancreatic secretion to act on the Chyme.
2. Because the extract is inactive while the food is still acid.

Under this treatment Patient grew  $\frac{5}{8}$  of an inch in  $2\frac{1}{2}$  months and gained 4 lbs. 2 ounces in weight. During this time he was not kept in bed, but was up and had a considerable amount of exercise. - I might mention that for three years before coming to Hospital, Patient had been well fed and cared for in a Home.

The motions which previously had varied from

6 to 9 per day now varied from 3 to 5. With patient on an ordinary diet his motions became darker in colour, but still remained fluid, and still contained fat.

Suspecting that the B.P. Liquor Pancreaticus might not be the best, I tried Benger's and Armour's preparations but with no better results. I also tested the action of these outside the body, and found that in all of them the Trypsin was active in the presence of heat, but that they contained very little fat splitting ferment. This is no doubt due to all of them being watery extracts, whilst Steapsin (the fat splitting ferment) is only extracted by Glycerine. With this in view I had a special preparation made, extracting the Steapsin with Glycerine. This preparation is described in Appendix No.7. I administered this along with the B.P. preparation two hours after food with Sod: Bicarb: gr: X. to render the Chyme less acid. The result was very striking, over a period of three months the motions which were well formed only averaged slightly over two per day. All this time Patient was kept on an ordinary diet, which he had previously been unable to take, on account of the discomfort and excessive Diarrhoea induced. While still a Hospital Patient, he frequently had a meal outside, and so missed his dose of extract: diarrhoea invariably followed. Patient was out of Hospital one week

and while at home he continued the extract, and was not troubled with Diarrhoea.

Results of Treatment.

The most striking result was the diminutions in the daily number of motions, these falling from 5 to 9 per day before treatment, to just over 2 per day while on an ordinary diet and taking the extract. Had this been the only result obtained I would almost have been satisfied, but having had his limbs skiagraphed and, finding all the Epiphyses intact I hoped that patient might yet grow. I was not disappointed and here give my results up till the end of April on the case which I first described.

During first 2½ months patient was treated with Liq. Pancreaticus.

During second 2½ months with special Steapsin extract.

<u>On admission.</u>	<u>After 2½ months.</u>	<u>After 5 months.</u>
4 ft. 4⅛ inches.	4 ft. 4¾ inches.	4 ft. 5⅝ inches.
4 st. 12 lb. 4 oz.	5 st. 2 lb. 6 oz.	5 st. 8 lb. 9 oz.
<u>1st 2½ Months.</u>	<u>2nd. 2½ Months.</u>	
Gain (Height= ⅝ inch.	(Height= ⅞ inch	
Gain (Weight= 4 lb. 2 oz.	(Weight= 6 lb. 3 oz.	

This represents a total growth of 1½ inches in height and 10 lbs. 5 oz. in weight in five months. I have

no doubt that patient will still continue to grow.

The accompanying photos show the change for the five months -

Appendix 8 shows patient before treatment.

" 9 " " after five months treatment.

By the aid of a magnifying glass the numbers on the measuring rod can be made out, showing a growth of  $1\frac{1}{2}$  inches. Patient is stouter: - abdominal wall is more thickly covered. Expression is brighter. Genital organs are increased in size, and better developed.

Patient is brighter and more manly. He himself feels much stronger, and more fit for work.

Concerning my first case (the second I have described), there appears to have been marked growth in this case, and corresponding improvement in the Diarrhoea, but as my facilities for observing the changes were very poor and, as my notes are incomplete, and were not started till the case had been treated for nearly a year, I will not attempt to describe the change. The boy's friends however stated that, during the past year and a half while taking the pancreatic extract, he must have grown over 3 inches. The boy himself has felt the improvement so markedly in his condition, especially the Diarrhoea that it would be difficult to

persuade him to stop taking his extract for any length of time.

The non success of the Pancreatic extract in Dr Thomson's case was probably due to the absence of Steapsin from the preparation which he used. I think he agrees with me in this view.

I do not wish to dogmatise on this subject, as I have only seen two cases but, from the striking results in each, I think that if the condition were brought before the profession, results might be obtained in a number of cases quite as striking as those obtained by the administration of Thyroid, in the much talked of, and greatly benefitted cases of Infantile Myxoedema.

A P P E N D I X.

I







II







VI



Method of preparing Steapsin Extract.

One pig's pancreas is thoroughly broken up by being pounded in a mortar with purified sand. This is then treated with almost pure Glycerine made alkaline with Sod: Bicarb: Preparation is now kept three to four days in a dark room, and shaken up at times, the ferments are then probably in form of zymogens: - this is then kept during a period of twenty four hours at body heat. The zymogens are thus transformed into enzymes, and administered in this form after being strained through fine muslin.

VIII



*IX.*

