THE ROLE OF OBSTETRIC ULTRASOUND

IN THE ASSESSMENT OF FETAL

GROWTH AND DEVELOPMENT

by

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MB ChB MSc

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SUMMARY

Diagnostic ultrasound was introduced into obstetrics by
Donald in the late 1950's and since that time has played
an increasingly important role in the characterisation of
normal fetal growth and the detection of intrauterine
growth retardation. As a group intrauterine growth
retarded fetuses have a high incidence of perinatal
mortality and morbidity, and, in the long term, a higher
incidence of neurological and intellectual impairment.
Therefore, the antenatal detection of this group is
desirable to permit careful monitoring and delivery at the
optimal time, under the optimal circumstances.

The objectives of this thesis were therefore to study the
role of obstetric ultrasound in: (1) the determination of
birthweight for gestational age growth standards which
were displayed for all women with singleton live births,
attending The Queen Mother's Hospital (QMH) antenatal
clinic from 1985 to 1987; (2) the detection of
intrauterine growth retardation (IUGR) by evaluating the
effectiveness of seven single ultrasound measurements and
two of their combinations . The association of fetal
growth retardation with perinatal mortality and congenital
malformation was also studied.

In pursuit of the first objective a sample of 10259 births occurring in The QMH from 1985 to 1987 were analysed. Tables and curves were provided showing the means, standard deviations and 5th, 10th, 25th, 50th, 75th, 90th and 95th centiles of birthweight by gestational age for each week of gestation from 28 to 42 weeks. Tables and curves were classified according to the sex of the infant and parity of the mother. The sample was composed of singleton live infants born to women who had ultrasound dating of gestation prior to 20 weeks. This sample comprised 26% of all live birth in Greater Glasgow Health Board area and 5.2% of all live births in Scotland during the study period. Similar analysis was repeated on a subset of 3919 births selected from the above sample. Women included in this group had to meet a number of criteria in order to minimize the effect they might have on the distribution of birthweight for gestational age. These criteria were: (1) their babies were without congenital malformation; (2) spontaneous onset of labour; (3) not on the contraceptive pill for the three months before pregnancy; (4) certain date of last menstrual period; (5) gestational age confirmed by ultrasound prior to 20 weeks. The QMH based standards were then compared with a number of growth standards reported for other populations, including the widely adopted standards of Thomson and associates (1968) for Aberdeen 1948-64 and

Forbes and Smalls (1982) for Scotland 1975-79. The QMH based standards were comparable to the previous Scottish standards and slightly higher later in pregnancy. Similarly the 10th centile values were comparable with Scotland 1975-79 (Forbes & Smalls, 1982), but beyond 38 weeks of gestation they were significantly higher.

In contrast to previous growth standards, the QMH based standards were obtained from a group of women with accurate ultrasound dating early in pregnancy. These results would justify a further study based on a large population to establish a proper growth standard. Nevertheless, tables and curves will be a useful guide for the birthweigh monitoring of infants born in the QMH.

Other variables such as sex of the infant and parity of the mother were also examined in relation to birthweight. Male infants were heavier than females and infants of multiparae were heavier than infants of primiparae.

In pursuing the second objective, a total of 14791 consecutive ultrasound measurements of 2810 women with singleton pregnancies, were analysed. All pregnancies were dated before the 20th week by ultrasonic measurements and had a second ultrasonic examination between 28 and 36

weeks of gestation to permit measurements of 7 single measurements and 2 of their combinations to detect those fetuses whose birthweights were below the 10th centile line on the Scottish standards 1975-79 (Forbes & Smalls, 1982). The measurements of biparietal diameter (BPD), head area (HA), head circumference (HC), abdominal area (AA), abdominal circumference (AC) femur length (FL), amniotic fluid volume (LV), abdominal area x femur length (AAFL) and abdominal circumference x femur length (ACFL) were studied. The measurements below the 10th centile for gestational age were considered abnormal. Fetal head measurements had inferior predictive ability than abdominal measurements. The LV and FL measurements proved to be the least sensitive indicators of IUGR. The combination of FL measurement with that of abdomen had markedly improved the diagnostic accuracy over that of single measurement of FL, AA or AC. Also, the accuracy of the predictions of all measurements improved greatly when scans were performed within one week of delivery. The AAFL measurement was the most predictive of IUGR as it had the highest sensitivity, specificity and predictive value of positive and negative test rate, and lowest 'false-negative' rate. Despite a 'false-positive' rate of 24%, AAFL is more useful than the AA measurement, as it had a minimal average cost on the basis of the assumption that, in clinical term, the cost of 'false-negative' result is

result is much higher than the 'false-positive' result. AAFL measurement is an advantage as part of a standard obstetrical ultrasound examination for the assessment of fetal growth in the second and third trimester. Furthermore, calculation of the AAFL measurement by a single examination around 34 weeks of gestation is practically simple. Combined with accurate ultrasound dating of gestational age early in pregnancy, the high sensitivity and predictive value of a negative test is an advantage as a screening procedure for the detection of IUGR.

There was an association of IUGR with perinatal mortality and fetal malformation. Infants of birthweight less than 5th centile for gestational age were at a greater risk of perinatal death than those whose birthweight lay between the 5th and 9th centiles.

1. INTRODUCTION

1.1 General Introduction to Ultrasound

1.1.1 Development of clinical applications

The first practical application of an ultrasonic imaging technique was in depth determination and submarine detection during World War 1. Improvement and miniaturisation of transducers led Firestone in 1945 to apply pulsed ultrasound to the detection of flaws in metal. From this use arose the idea of applying the imaging technique to clinical medicine, specifically to the study of soft tissue. The pioneer work in ultrasound as a medical tool was carried out by two workers in different centres, namely Donald and associates (1958) in Glasgow and Holmes and Howry (1963) in Denver, who both saw the medical potential of ultrasonic imaging and applied it to obstetrics and gynaecology. They introduced techniques and equipment which, with further development over a period of thirty years, have revolutionised the practice of obstetrics. Despite poor image quality in the early 1960s the growth of the fetal biparietal diameter was measured and growth charts constructed for the last two trimesters of pregnancy. Ultrasound also contributed since it can be used to detect the numbers of fetuses,

fetal position, placental location and the estimation of fetal age and growth. Due to continuous improvement in image quality, coupled with expanding experience, ultrasound has become an important diagnostic aid not only in the field of obstetrics and gynaecology but in almost every other branch of medicine.

1.1.2 The nature of ultrasound

Ultrasound is the name given to sound waves with frequencies beyond the range of human hearing, i.e. greater than 20 KHz. Audible sound spreads out from its source in a fashion similar to waves on a pond. Ultrasound can be made to be more directional and easily directed in a beam and can therefore be used diagnostically. The range available for diagnostically usable ultrasound is 1-10 MHz. Ultrasound is generated by a device, an ultrasonic transducer, using a piezo-electric element, this converts electrical energy into mechanical energy, which is propagated by vibration of the small elements of the media through which it travels. Some energy is reflected by interfaces in the tissue and the transducer acts a receiver able to convert the reflected ultrasound into electrical signals.

1.1.3 Instrumentation

The diagnostic ultrasound systems in general use can be divided into two groups, the A, and B scan machines which employ pulsed ultrasound, and the simpler doppler or motion-sensing machines which use continuous wave ultrasound (Burel & Kjaer, 1978; Chudleigh & Pearce, 1986).

Physical principle

In any ultrasonic equipment for medical diagnostics, the most vital part is the transducer which acts both as transmitter and receiver of ultrasound. Electrical impulses from the transmitter in the equipment are fed to the system's transducer and converted into rapid pressure oscillations of short duration. The resulting wave front is directed by the transducer into the tissue in a narrow beam. Whenever it hits a boundary between two tissues of different acoustic characteristics some of the energy will be reflected, the rest being transmitted and continuing into the tissue giving further reflection. If the boundary is perpendicular to the ultrasound beam, the reflected energy will go straight back to the transducer. The tranducer will convert some of the acoustic energy into electrical signals, which are fed to an amplifier

with an electronic depth attenuation compensation circuit, and eventually displayed on a screen or registration paper in one or more of several possible formats. Diagnosis by ultrasound is made by interpretation of echoes. These are produced from the reflection or scattering of ultrasound at tissue interfaces or from scattering from the heterogeneous structures within tissue. An echo is produced at a tissue interface if the acoustic impedance of the tissues on either side are different. The acoustic impedance of a tissue is a measure of the resistance of the tissue to the flow of ultrasound energy and is dependent upon the density of that medium. Information from returning echoes can be displayed in one of three ways, amplitude (A) mode, amplitude (B) mode and time motion (T-M) mode.

(A) mode display

In the simple A-mode equipment, the detection and display of the echoes are performed by horizontally sweeping a trace across an oscilloscope screen started at the emission of the ultrasound pulse. The screen is calibrated with distance markers so that the horizontal position will correspond to the depth in tissue and the detected echoes will deflect the trace vertically in proportion to the reflection amplitude (Fig. 1).
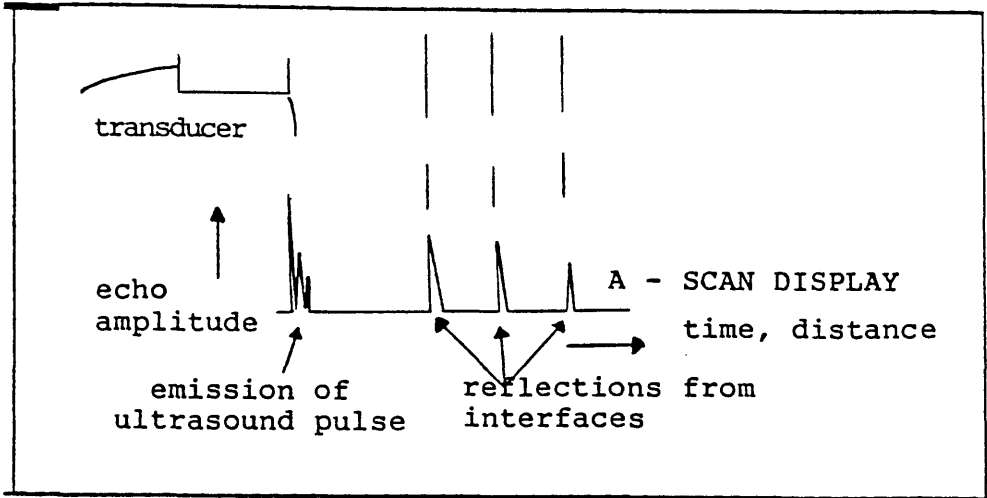
Figure 1: A - mode display
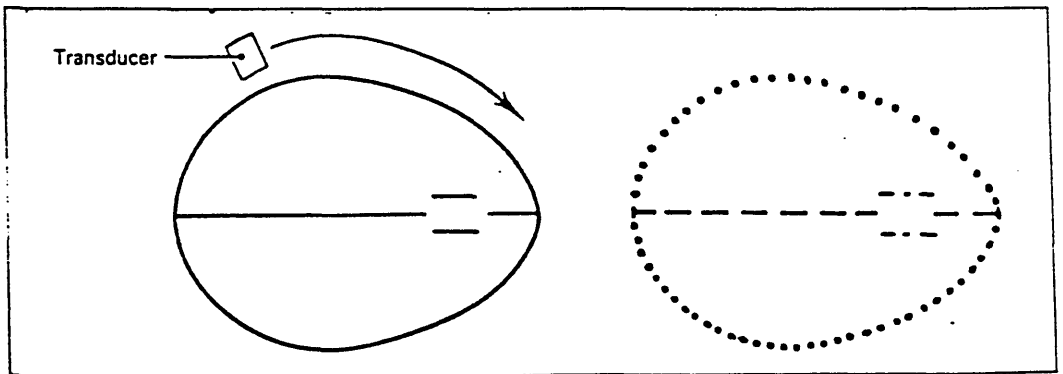
Figure 2: A diagram to illustrate how coalescing echoes
form a two-dimentional image of the fetal
head in B-mode scanning.

This type of display has its main uses in cardiology and ophthalmology. It is also important as an aid to determining the amplitude differences between the echoes displayed in some of the more complex formats. The main advantage of an A-mode equipment is its simplicity and the aid it gives to determine the optimum tranducer position and equipment setting. However, it cannot display echoes other than those which fall in a single line in the tissue along the transducer axis. As it gives no two-dimensional information and since amplitude of the echoes depends on the angle of incidence, the transducer is difficult to orientate, except when used for cardiological purposes where the characteristic movements of certain parts of the heart can be used to orientate the transducer. Thus this type of equipment has been used for the examination of certain characteristic parts of the heart, the localization of such easily recognised structures as the midline of the brain, for measuring the BPD of the fetus and for looking at fetal heart movement. A-mode display is now rarely used in obstetric application.

B-mode display

In B-mode scanning the returning echo is converted into a voltage and then displayed at the appropriate point on the screen as a bright spot. When these spots coalesce they produce a two-dimensional image (Fig. 2).

1. Static B-mode display

By converting the vertical deflection on the A-representation to light dots on the time-baseline, a two-dimensional so called B-mode picture can be made if the baseline is tilted and positioned according to the position and direction of the transducer cross-section in the scanning plane chosen. This can be achieved if the transducer is mounted on a scanning arm or frame and the echo dots are stored on the display as the transducer is moved by hand over the skin surface. This method of scanning (Fig. 3), has been widely used in abdominal diagnostics, and in gynaecology and obstetrics.

2. Real-time B-mode

Instead of moving the transducer by hand in order to look in various direction inside the patient it is possible to move the beam of ultrasound electronically or by a small
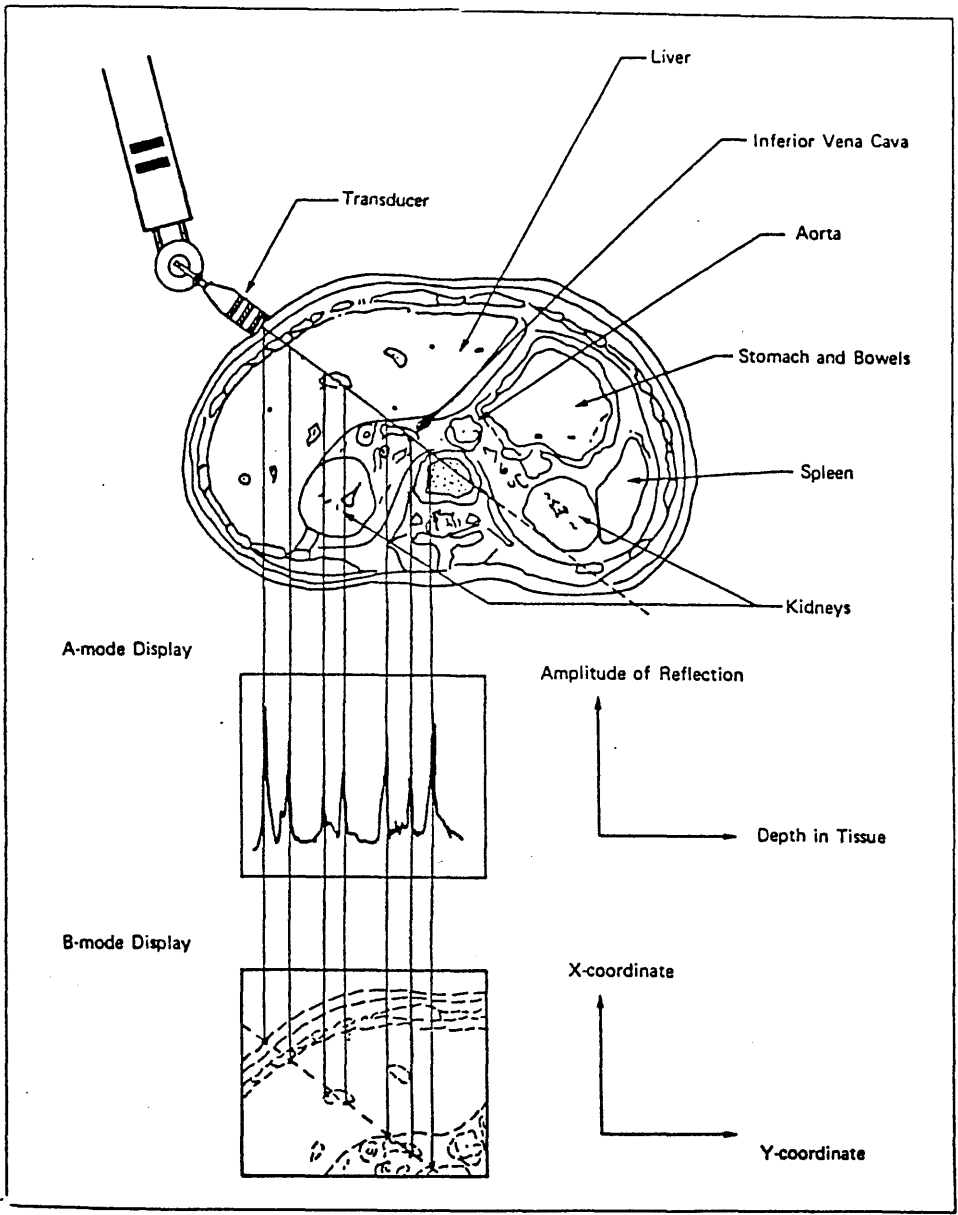
Figure 3: Static B-mode display.

motor. It is possible to do this very rapidly, repeating the scan at up to 30 or 40 times per second. This produces a "cine" image as opposed to a static one and is usually called a real-time image. Real-time B-mode may be performed by three means: mechanical sector scanners, electronic linear array scanners and electronic phased array scanners. The ultrasound equipment principally used in obstetrics is the linear array real time scanner. Occasionally the mechanical sector scanner or phased array scanner is preferred in early pregnancy or for specialised indications such as fetal cardiac scanning because of the smaller tranducer head.

Time-motion display

If an object is moving, the A-mode representation will show the corresponding echoes moving in the horizontal direction. By converting these to light dots, and by slowly displacing them with fixed velocity, a number of curves can be stored indicating the movements of the structures under study as shown (Fig. 4). This type of display is called the time-motion display, and is used mainly in cardiology.
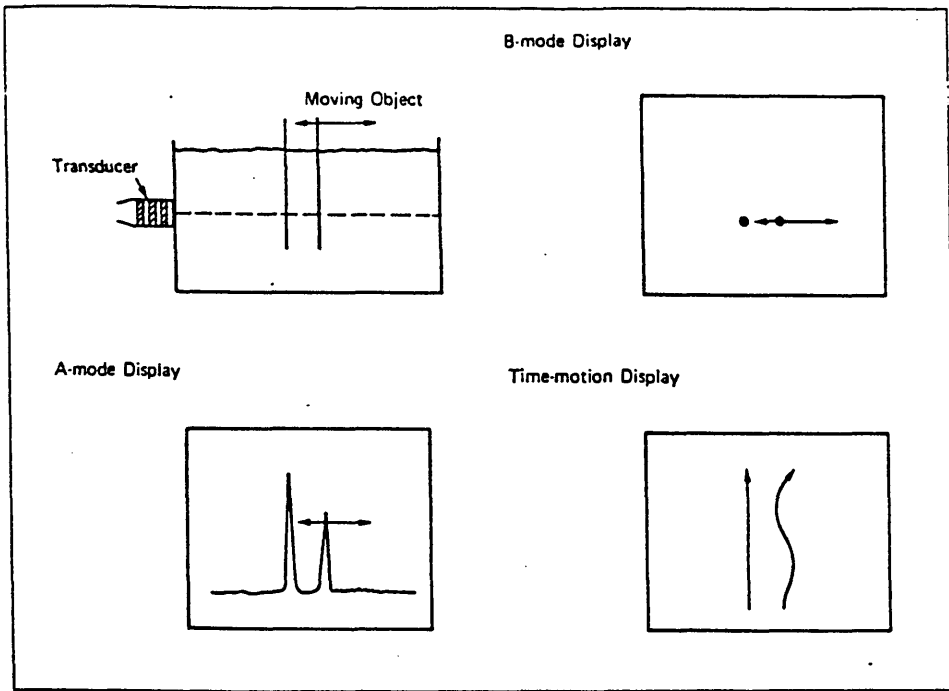
Figure 4: Build-up of a time-motion display.

1.1.4 <u>Safety of diagnostic ultrasound</u>

A great deal of animal and human research has been undertaken in the past decade on the biological effect of ultrasound, though no reliable evidence has been produced to suggest that diagnostic ultrasound is harmful at the power levels used in clinical work. The mechanisms whereby ultrasound exerts biological effects on tissues may be divided into : heat generation and mechanical effects, including acoustic cavitation, microstreaming and radiation pressure force.   There is currently no experimental evidence to show that heating, cavitation, microstreaming or radiation pressure force produces any significant effect on human tissues under diagnostic ultrasound imaging conditions (Kremkau, 1983).

In clinical studies, no surveys have shown an association between the antenatal use of ultrasound and the incidence of either congenital abnormalities (Hellman et al, 1970; Scheidt et al, 1978; Stark et al, 1984), or intrauterine growth retardation (Wladimiroff & Laar, 1980). Furthermore, many reassuring statements have been issued on ultrasound safety e.g. by the American institute of Ultrasound in Medicine (AIUM, 1983), the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB, 1984), the British Medical Ultrasound

Society (BMUS, 1984) and the Report of the Royal College of Obstetricians and Gynaecologists (RCOG) Working Party on Routine Ultrasound Examination in Pregnancy (1984). While additional information regarding the safety of ultrasound is considered necessary and is still being sought, its clinical usefulness outweighs any hypothetical risk, and the use of ultrasound is recommended for the proper care of obstetric patients (RCOG Working Party on routine ultrasound examination in pregnancy, 1984).

1.1.5 Indications for diagnostic ultrasound in obstetrics

The use of diagnostic ultrasound in obstetrics has increased rapidly in the last decade. Although the utilisation of ultrasound in obstetrics has been based initially on the confirmation of pregnancy, diagnosis of multiple pregnancy, estimation of gestational age and diagnosis of placenta praevia, the most essential uses are the detection of IUGR and congenital malformation. Furthermore, there is a substantial body of literature which indicates that ultrasound is diagnostically helpful in many clinical situations. Report of the RCOG Working Party on routine ultrasound examination in pregnancy (1984) agreed on most of the 28 clinical situations described in the report of the National Institutes of

Health Consensus statement (NIH, 1984) where ultrasound could be of benefit in the resolution of antenatal problems. These are the following:-

1. Bleeding or pain in early pregnancy: to exclude ectopic pregnancy, to establish fetal viability and attempt to find the source of the bleeding.

2. Vomiting in early pregnancy: to diagnose hydatidiform mole, multiple pregnancy or other possible causes of the disorder.

3. Estimation of gestational age when mothers present with unreliable menstrual dates or have had bleeding in early pregnancy or have oral contraceptives within two months of the last menstrual period.

4. Detailed anatomical examination of the fetus when there is a strong family history of congenital abnormality, when there is an associated condition which increases the risk, such as diabetes or polyhydramnios or when maternal serum alphafetoprotein (AFP) levels are raised.

5. Adjunct to prenatal diagnostic invasive procedures, such as chorion biopsy, amniocentesis, fetoscopy or

prenatal surgical procedures such as the placement of a vesico-amniotic shunt.

6. A discrepancy between dates and fundal height of three or more weeks. If the fundus is 'large for dates' to exclude fetal macrosomy, multiple gestation, polyhydramnios, hydrops fetalis or associated tumours. If 'small for dates' to exclude fetal growth retardation and oligohydramnios which may be related to IUGR, fetal renal abnormalities, premature rupture of the membranes or postmaturity.

7. To monitor fetal growth with serial measurements when IUGR is clinically suspected or when there is a previous history of IUGR babies or stillbirths, or when there is a multiple pregnancy. Also in diabetic pregnancy, to diagnose acceleration of growth associated with macrosomy.

8. Antepartum haemorrhage: to diagnose placenta praevia and to assess the relationship of the lower edge of the placenta to the cervix which can change with the unfolding of the lower uterine segment. To identify retroplacental bleeding where there is a normally situated placenta.

9. Fetal weight assessment: this is valuable in circumstances where early delivery is contemplated due to

complications such as premature rupture of the membranes, severe hypertension or IUGR for it may give guidance as to the timing and method of delivery.

The accuracy of ultrasound scanning is very dependent on the skill of the doctor or technician performing the scan. This is more true for ultrasound diagnosis than for other types of investigation such as biochemistry, radiology or nuclear medicine where fairly standardised procedures are adopted. Ultrasound demands the ability to interpret images and adapt the scan technique, gain control and dynamic focus settings of the equipment, according to the position of the fetus, the size of the mother, the amount of amniotic fluid and many other variables.

In Scotland, the survey of the RCOG Working Party on routine ultrasound examination in pregnancy (1984) comprised 29 hospitals with an obstetric service responsible for the vast majority of the Scottish annual births. It showed that 53% of the hospitals performed one routine scan, 10% two routine scans and 3% three routine scans. Thus 66% of the hospitals surveyed performed at least one routine antenatal scan. Some hospitals performed a scan at the mother's first visit to the hospital while others delayed the scan to between the 16th and 18th week in order to obtain more information.

1.2 Objectives of the Study

The aims of this study are threefold:

1. To display the birthweight distribution as a function of gestational age for all women attending The Queen Mother's Hospital antenatal clinic, who had ultrasound dating of gestational age in early pregnancy and to compare it with the Scottish Standards.

2. To evaluate the effectiveness of various ultrasound measurements and combinations of measurements for the antenatal detection of IUGR. The measurements studied were biparietal diameter (BPD), head area (HA), head circumference (HC), abdominal area (AA), abdominal circumference (AC), femur length (FL), amniotic fluid volume (LV), the product of abdominal area and femur length (AAFL), the product of abdominal circumference and femur length (ACFL).

3. To study the association of intrauterine growth retardation with perinatal mortality and congenital malformation.

CHAPTER 2

MATERIALS AND METHODS

2. MATERIALS AND METHODS

2.1 Source of Data

All patients attending The Queen Mother's Hospital antenatal clinics are offered a scan at the time of booking to establish an accurate gestational age, and to diagnose multiple gestation and major fetal abnormalities. Further scans are carried out for a specific indication such as bleeding or suspected IUGR.

Since 1985, there has been an ongoing process of recording and verifying the data obtained by the Department of Ultrasound in the hospital. Data regarding each patient are classified in nine major categories: general history, current pregnancy history, booking data, early pregnancy failure, placentography, retained products of conception, prenatal diagnosis, fetal growth, pelvic masses and delivery details (Fig. 5). A data sheet for each pregnancy is completed by the ultrasonographer and taken to the Ultrasonic Technology Laboratory of the University Department of Midwifery at the hospital for storage in the University mainframe computer to provide a research data base. Following entry the validity of the data is checked using a programme written in COBOL. This applies an elaborate sequence of comparisons to check that

QMH ULTRASOUND STUDY

QMH No. [ ][ ][ ][ ][ ]1   US No. [ ][ ][ ][ ]2   Card No. [ ]3 Fetal No. [ ]4
Transfer [ ]5   US refused [ ]6   NO US [ ]7 No. of scans [ ]8
                                              Default No. [ ]9

Age [ ][ ]10   Parity [ ]11
Abortns.Sp1 [ ]12 2 [ ]13   Ther1 [ ]14   Ther2 [ ]15

PMH Rh/Ab [ ]16 BP [ ]17   Cardiac [ ]18   Diabetic [ ]19 Other [ ]20
POH SB [ ]21 NND [ ]22   FA *A [ ]23   PTD [ ]24 IUGR [ ]25

Current Pregnancy History   Threat1 [ ]26   Threat2 [ ]27 APH [ ]28
                             PRM [ ]29   BP [ ]30 Poly/oligo [ ]31
MSAFP 1st [ ][ ][ ]32   at [ ][ ] wks 33

      2nd [ ][ ][ ]34   at [ ][ ] wks 35   NO Result *K [ ]36 Serial [ ]37

Booking data   Viable [ ]38   No. of fetuses [ ]39

LMP [ ][ ][ ] 40 41 42   Certain [ ]43   OC<3/12 [ ]44 Cycle [ ][ ]45
Gest.dates [ ][ ][ ]46   US [ ][ ]47   Exam [ ]48
Dates OK [ ]49   US EDD [ ][ ][ ] 50 51 52   No. of US [ ]53

Early pregnancy failure/problems

Referral *B [ ]54   Diagnosis *C [ ]55   No. of US [ ]56
Yolk sac [ ]57   Second sac [ ]58   Serial growth, No. of US [ ]59

Placentography   Indication *D [ ]60

<28 weeks [ ]61   Area of bleeding [ ]62   No. of US [ ]63
1.low 2.normal   1.SCH 2.RP 3.other

>/28 weeks *E [ ]64   Subsequent move [ ]65 Site confirmed [ ]66 No. of US [ ]67

RPC *F [ ]68   Evac [ ]69   No. of US [ ]70

Prenatal diagnosis   Indication *G [ ]71 CVS/Fetoscopy [ ]72 No. of US [ ]73

Fetal abn. *A [ ]74   No. amnios [ ]75

Pres. no.US [ ]76   Pre/post ECV [ ]77 Multiple preg. [ ]78 When detected [ ][ ]79
                     no.US

Growth   Indication *H [ ][ ]80   No. of US [ ]81

	82 83 84		85 86 87		88 89 90		91 92 93	
Date	[ ][ ][ ]		[ ][ ][ ]		[ ][ ][ ]		[ ][ ][ ]	
Weeks		94		95		96		97
CRL		98		99		100		101
BPD		102		103		104		105
FL		106		107		108		109
HC		110		111		112		113
HA		114		115		116		117
TC		118		119		120		121
TA		122		123		124		125
EFW		126		127		128		129
H/T		130		131		132		133
LV		134		135		136		137
Plac.mat.		138		139		140		141
LSR		142		143		144		145

Pelvic masses   Fibroids [ ]146   Cysts [ ]147   IUCD [ ]148   Other [ ]149

Delivery   No. of fetuses [ ][ ]150 Date [ ][ ][ ] 151 152 153   Ind [ ]154   Mode *J [ ]155
            weeks [ ][ ]156 Weight [ ][ ][ ]157   Sex [ ]158   FA *A [ ]159
            PNEW [ ][ ]160   [*]161

Figure 5: The data recording sheet used for each patient.

each individual data item is within "an acceptable range "
and that the relationship of groups of data items was
"acceptable" e.g. given a gestational age is the BPD
reasonable for that age. The validated data were then
processed by a Statistical Package for Social Science
(SPSS^X) data definition programme which assigned variable
names (used for formal reference to the variables in the
processing commands), variable labels (used to give a
readily understood description of the output) and value
labels (to translate the code values assigned to a given
variable) (Fig. 6). The defined data were stored in a
SPSS^X system file for access by analysis programmes such
as those described in this study (programmes 1-81). The
arrangement of data in this file was not suitable for all
the analyses. Therefore rearranged files were generated
in which all measurements of one type are recorded under
one variable name e.g BPD1, BPD2, BPD3, BPD4 were combined
under the variable name BPD.

The computerised data bases provided by the Ultrasound
Department were used as a material for this study. Data
were programmed for selection of population and
statistically analysed using SPSS^X package on the
University Mainframe Computer (ICL 3980). Some
computations were performed using the MINITAB package for
graphic work (available in the Department of Midwifery on

Figure 6 (A, B, C & D)

Ultrasound data definition programme

(A) VARIABLE NAME   DETAILS(Codes are:$=0=NO,1=YES. #=NUMBER OF)   DATA ITEM
                                                                         NUMBER

GENERAL HISTORY

Variable	Details	Data Item Number
QMHNO	Queen Mother's Hospital Number	1
USNO	Ultrasound Number (used when no QMHNO)	2
CARDNO	Card Number	3
FETALNO	Fetal Number	4
TRANS	Transfer (from another hospital) $	5
REFUSED	Ultrasound Refused (by patient) $	6
NOUS	NO Ultrasound	7
TOTSCANS	Total Number of Scans in this pregnancy=	8
DEFAULT	# Defaults	9
AGE	Age (yrs)	10
PARITY	# Previous Pregnancies > 28 weeks	11
ABORTSP1/2	# Spontaneous Abortion in 1st/2nd Trimester	12-13
THER1/2	# Therapeutic Abortion in 1st/2nd Trimester	14-15

PAST MEDICAL HISTORY

Variable	Details	Data Item Number
RHAB	Rhesus or other Antibodies $	16
BP	Hypertension $	17
CARDIAC	Cardiac Disease $	18
DIABETIC	Diabetes $	19
OTHER	Other Medical Problem $	20

PAST OBSTETRIC HISTORY

Variable	Details	Data Item Number
SB	# Stillbirth	21
NND	# Neonatal Death	22
FA∂A	Fetal Abnormality Code A	23
	0 No Fetal Abnormality 1 Neural Tube Defect	
	2 Abdominal Wall Defect 3 Urinary Tract Defect	
	4 Skeletal Defect 5 Chromosome Defect	
	6 Rhesus Disease 7 Cardiac Defect 8 Other	
PTD	Preterm Delivery	24
IUGR	Intrauterine Growth Retardation	25

CURRENT PREGNANCY HISTORY

Variable	Details	Data Item Number
THREAT1/2	Threat in 1st/2nd Trimester $	26-27
APH	Antepartum Haemorrhage $	28
PRM	Premature Rupture of Membranes $	29
BPCPH	Hypertension $	30
POLY	Polyhydramnios Or Oligohydramnios $	31
MSAFP1/2	1st/2nd Maternal Serum Alphafetoprotein	32,34
ATWKS1/2	# Weeks 1st/2nd MSAFP Sample Taken	33,35
NORES∂K	No MSAFP Result Code K	36
	1 Declined 2 Missed 3 Done Elsewhere	
SERIAL	Serial MSAFP's $	37

(B) VARIABLE NAME   DETAILS(Codes are:✱=0=NO,1=YES. #=NUMBER OF)   DATA ITEM
                                                                      NUMBER

BOOKING DATA

VIABLE	Viable Fetus ✱	38
NOFETUS	# Fetuses	39
LMPD/M/Y	Last Menstrual Period((Day)/(Month)/(Year))	40-42
CERT	Certain of Dates ✱	43
OC	Oral Contraception Within 3 Months of Conception ✱	44
CYCLE	Length of Menstrual Cycle in Days	45
	0 Menstrual Cycle Irregular	
GESTDATE	Gestation by Dates (Weeks/Days)	46
US	Gestation by Ultrasound (Weeks/Days)	47
EXAM	Gestation by Clinical Examination (Weeks)	48
DATESOK	Gestation by Dates Confirmed by Ultrasound ✱	49
USEDDD/M/Y	Ultrasound Estimated Delivery Date(Day/Mth/Yr)	50-52
NOUSBK	# Scans for Gestational Age	53

EARLY PREGNANCY FAILURE/PROBLEMS

REFER⊃B	Referral Code B	54
	1 Booking,Ante Natal Clin. 2 Gen. Pratitioner	
	3 Self 4 Western Inf. Glasgow	
	5 Royal Samaritan Hosp 6 Brit. Preg. Advisory Serv.	
	/Family Planning Ass.	
	7 Ante Natal Clinic 8 Past History 9 Other	
DIAG⊃C	Diagnosis Code C	55
	1 Viable pregnancy 2 Not pregnant	
	3 Blighted ovum 4 Missed abortion	
	5 Complete/Incomp. abortion 6 Mole	
	7 Ectopic 8 Intra Uterine Death	
NOUSEPF	# Early Pregnancy Problems	56
YOLKSAC	Yolk Sac ✱	57
SECSAC	Second Sac Present ✱	58
NOUSSG	# Scans for Serial Growth	59

PLACENTOGRAPHY

INDIC⊃D	Indication Code D	60
	1 Antepartum Haemorrhage 2 Threat	
	3 Abnormal lie 4 Breech	
	5 High presenting part 6 Ultrasound coincidental	
	7 Abdominal pain 8 Raised Alphafetoprotein	
LT28WKS	< 28 Weeks	61
	1 Low 2 Normal	
AREABL	Area of Bleeding	62
	1 Sub Chorionic Haematoma 2 Retroplacental clot	
	3 Other	
NOUSLT28	# Scans at < 28 Weeks	63
GE28WK⊃E	>= 28 Weeks Code E re:Placenta Praevia	64
	1 diagnosed 2 excluded 3 site uncertain	
SUBMOVE	Subsequent Move Of Placenta ✱	65
SITECONF	Site Confirmed	66
NOUSGE28	# Scans at >=28 Weeks	67
RPC⊃F	Retained Products Of Conception Code F	68
	1 Uterus empty 2 Clot & tissue 3 Clot 4 Uncertain	
EVAC	Evacuation of Uterus ✱	69
NOUSRPC	# Scans for Retained Products Of Conception	70

PRENATAL DIAGNOSIS

Variable	Details	Data Item Number
INDIC@G	Indication Code G	71
	1 Past History 2 Family History 3 Age	
	4 Clinical suspicion 5 Ultrasound suspicion	
	6 Raised Or Missed Alphafetoprotein 7 Twins	
	8 Growth problem 9 Complex	
CVS	Chorion Villus Sampling or Fetoscopy *	72
NOUSPND	# Scans for Prenatal Diagnosis	73
FETABN@A	Fetal Abnormality Code A (See FA@A)	74
NOAMNIO	# Amniocenteses	75
NOUSPRES	# Scans for Presentation	76
NOUSECV	# Scans for External Cephalic Version	77
MULTPREG	Multiple Pregnancy *	78
WHENDET	When Multiple Pregnancy Detected (Weeks)	79

GROWTH

Variable	Details	Data Item Number
INDIC@H	Indication Code H	80
	1 Past History Intra Uterine growth retardation	
	/smallish baby 2 Past Hist. macrosomia	
	3 Past History/Current History of Fetal Abnormality	
	4 Clinically Small For Dates 5 Clin. Large For Dates	
	6 Raised Blood Presure 7 Diabetes	
	8 Antepartum Haemorrhage/Threat/Abdominal pain	
	9 Research 10 Twins 11 Spont. Rupture Of Membranes	
	12 Late date 13 Preterm labour 14 Rhesus 15 Breech	
	16 Raised Alphafetoprotein 17 Term/Post dates	
	18 Decreased fetal movements 19 Complex	
NOUSGR	# Scans for Growth	81
DATE1D-4Y	Day/Mth/Yr of 1st-4th Scan	82-93
WKS1-4	# Weeks Pregnancy at Scan1 - 4	94-97
CRL1-4	Crown Rump Length, mm "	98-101
BPD1-4	Biparietal Diameter, mm "	102-105
FL1-4	Femur Length, mm "	106-109
HC1-4	Head Circumference, mm "	110-113
HA1-4	Head Area, sq cm "	114-117
TC1-4	Abdominal Circumference, mm "	118-121
TA1-4	Abdominal Area, sq cm "	122-125
EFW1-4	Estimated Fetal Weight, g/10 "	126-129
HT1-4	Head Abdomen Ratio, x100 "	130-133
LV1-4	Liquor Volume, mm "	134-137
PLACMAT1-4	Placental Maturity, grade "	138-141
LSR1-4	Lethicin Sphyngomyelin Ratio, no longer used	142-145

PELVIC MASSES

Variable	Details	Data Item Number
FIBR	Fibroids *	146
CYSTS	Cysts *	147
IUCD	Intra Uterine Contraceptive Device *	148
ALLOTHER	Other *	149

(D)　　　VARIABLE NAME　　DETAILS(Codes are:‡=0=NO,1=YES. #=NUMBER OF)　DATA ITEM
　　　　　——　NUMBER

DELIVERY DATA
==============

NOFETUSD	# Fetuses Delivered	150
DATED/M/Y	Date of Delivery((Day)/(Month)/(Year))	151-153
IND	Induction of labour ‡	154
MODE@J	Mode of Delivery	155
	1 Spontaneous Vertex Delivery 2 Forceps	
	3 Ventouse 4 Breech	
	5 Elective Caesarian Section	
	6 Emergency Caesarian Section 7 Spontaneous Abortion	
	8 Termination Of Pregnancy 9 Evacuation	
WKS	# Complete Weeks of Pregnancy at Delivery	156
WGHT	Weight of Baby at Birth, g/10	157
SEX	Sex of Baby, M/F	158
FADEL@A	Fetal Abnormality at Birth Code A (See FA@A)	159
PNRW	Perinatally Related Wastage	160
EORMARK	End of Record Mark	161

VARIABLES ADDED LATER
=====================

| BRNALV | Born Alive | |
| | 1 Born Alive 2 Stillborn 9 No Data Available | |

VARIABLES GENERATED BY DATA DEFINITION PROGRAM
==

| BWCT1 | Birthweight centile codes based on | |
| BWCT2 | Smalls, M., Forbes, J.F. (1983) | |

an Amstrad 1640 Microcomputer). The t-test and chi-square test were applied where appropriate. Other statistical procedure as the Law of Total Probability and its variation were also used in this study.

2.2 Equipment

All examinations and the fetal measurements were carried out using: a/ Diasonics DRF400 which was fitted with 3.5 and 5 MHz mechanical sector tranducers (Fig. 7). The measuring facility was improved by the addition of a Diagnostic Sonar Ltd Echo-computer; b/ Dynamic Imaging "Concept" which was fitted with a 3.5 MHz linear array transducer (Fig. 8); c/ Dynamic Imaging "XLP" which was fitted with a 3.5 MHz linear array transducer (Fig. 9). The ultrasound velocity was 1540 m/second. Measurements were made on screen by the use of an electronic light pen.

2.3 Measurement Techniques

The ultrasound measurements performed were: biparietal diameter (BPD), head area (HA), head circumference (HC), abdominal area (AA), abdominal circumference (AC), femur length (FL) and amniotic fluid volume (LV).

Figure 7: The Diasonics DRF400 scanner in clinical use.

Figure 8: Dynamic imaging "Concept" scanner.

Figure 9: Dynamic imaging "XLP" scanner.

Biparietal diameter

A series of scans was performed to find the long axis of the fetus. The probe was then rotated by 90 degrees to this axis, and angled so that a transverse plane of the fetal head was imaged. A series of parallel sections were then imaged to identify the following land-marks: short midline, cavum septum pellucidum, thalami and basal cisterns. An adequate BPD measurement was obtained when the thalami and midline were visualised. However the inclusion of the other two features was necessary for the head area and head circumference measurements (Fig. 10). Having identified the correct section, a BPD measurement was made on a frozen image from the leading portion of echo from proximal skull surface to leading portion of echo from distal skull surface (Fig. 11). In this way error associated with changes in the position of the echo peak can be avoided. Measurements made across the beam axis are known to be less accurate than those along the beam axis. The measurement was repeated until three successive readings agreed to within 1 mm. The average of these was taken as the BPD reading (Evans et al, 1987).
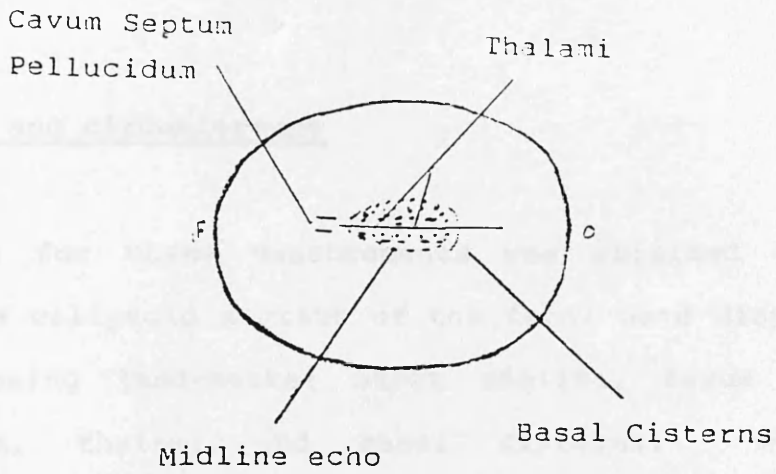
Figure 10: Diagrammatic representation of a transverse section of fetal head for measurement of BPD, HC and HA.

Figure 11: Ultrasonic image of the transverse section of the fetal head on which the BPD, HC and HA should be measured.

Head area and circumference

The plane for these measurements was obtained from a transverse ellipsoid section of the fetal head displaying the following land-marks: short midline, cavum septum pellucidum, thalami and basal cisterns. When a satisfactory image was obtained the circumference was measured by tracing along the the outer edge (Fig. 11). Using the same plane area measurements were obtained (Fig. 11).

Abdominal area and circumference

The long axis of the fetus was found by obtaining a longitudinal section through the fetal spine or aorta. The aorta is preferable to the spine as it is not as wide as the spine and consequently using the aorta will minimise the degree of obliquely to the true longitudinal plane. The transducer was then rotated through 90 degrees to obtain a transverse image of the fetus at the level of the umbilical vein. The transverse section should be circular in outline and show the portion of the umbilical vein situated almost centrally as it enters the portal system within the liver (Fig. 12). When a satisfactory image was obtained the circumference was measured by

Left
Portal
Vein

Spine
Aorta

Stomach
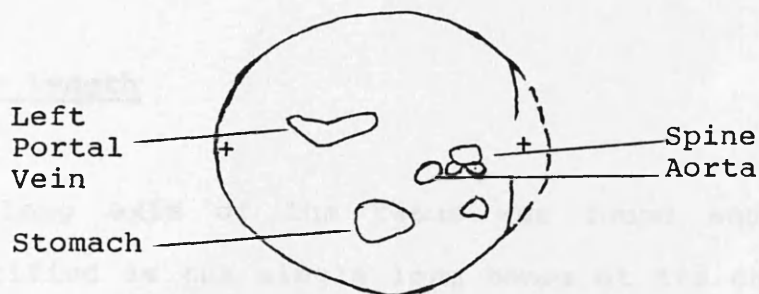
Figure 12: Diagrammatic representation of a transverse
section of fetal abdomen for measurement of
AC and AA.

Figure 13: Ultrasonic image of the transverse section
of the fetal abdomen for measurement of AC
and AA.

tracing along the outer edge (Fig. 13). Using the same plane area measurements were obtained (Evans et al, 1989).

Femur length

The long axis of the fetus was found and the femora identified as the single long bones at its caudal end. To ensure that the whole of the femur was measured and was not foreshortened, the transducer would have to be rotated until the longest possible image of the femur was obtained and the transducer was along the long axis of the femur. This image was then frozen. A straight line measurement between the two ends was made (Fig. 14). On occasions, the normal femur may have appeared slightly bowed but the measurement was still obtained as a straight line. This measurement was repeated until three within 1mm of each other were obtained and the largest of these was recorded (Evans, 1988).

Amniotic fluid volume

LV was measured as the maximum vertical depth (mm) of the deepest pool of fluid (pocket size) (Fig. 15).
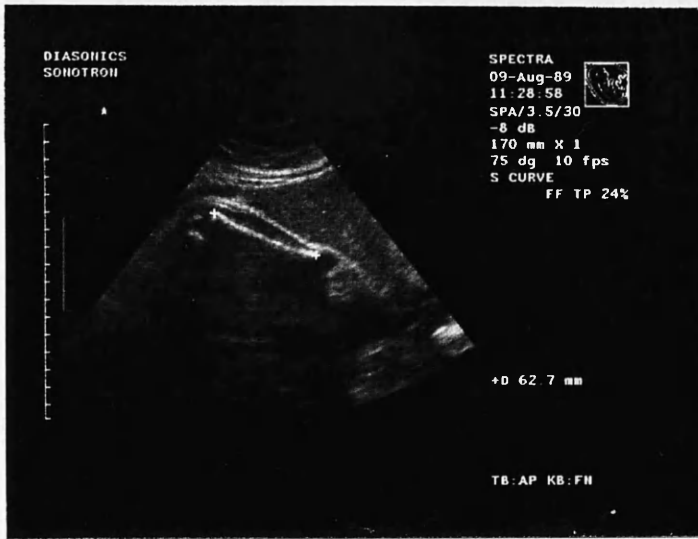
Figure 14: Image demonstrating straight line
measurement of FL.

Figure 15: Ultrasonic image of LV measurement.

CHAPTER 3

AN ANALYSIS OF BIRTHWEIGHT BY GESTATIONAL AGE OF INFANTS BORN IN THE QUEEN MOTHER'S HOSPITAL, GLASGOW, 1985-1987

3. AN ANALYSIS OF BIRTHWEIGHT BY GESTATIONAL AGE OF INFANTS BORN IN THE QUEEN MOTHER'S HOSPITAL, GLASGOW, 1985-87

3.1 Introduction

Birthweight is generally known as a most potent indicator of fetal growth and of the risk of both mortality and morbidity in the neonate. The importance of accurate and valid fetal growth standards which describe the distribution of birthweight for gestational age, has long been acknowledged. Such standards based on the analysis of data from live born infants have been used in three principal ways. First, they have provided widely adopted criteria for assessing fetal growth and development at birth (Lubchenco et al, 1963; Thomson et al, 1968; Miller & Richard, 1974). Secondly, they have been used to assess the validity and predictive value of antenatal screening tests for fetal growth retardation based on such techniques as fundal height measurement (Quaranta et al, 1981; Rosenberg et al, 1982) and ultrasound measurement (Campbell & Wilkin, 1975; Neilson et al, 1980). Thirdly they have been used to draw nomograms for precise determination of birthweight for gestational age (Altman & Coles, 1980).

Beginning with the early studies of Scammon and Calkins (1929), the need for accurate data to describe the relationship between birthweight and gestational age has generated numerous standards for a variety of populations. Most of these standards are unsatisfactory because of the inconsistencies in methodology, for example inclusion of both live and stillbirths in the analysis (McKeown & Gibson, 1951). Moreover, some of them described all births, irrespective of sex, parity or maternal size which have, later, been found to have an effect on birthweight (Thomson et al, 1968; Milner & Richards, 1974; Forbes & Smalls, 1982). Even when a sex difference was described, it was usually ignored. For example, Lubchenco and associates (1963) noted that sex differences were small compared with the range of weights at any gestation, and described the uses of an overall (both sexes) standards only. Standards based on Scottish populations have been reported for Aberdeen (Thompson et al, 1969), Scotland (Cole, 1981; Forbes & Smalls, 1982),and Glasgow (Forbes & Smalls, 1983). These studies relied on clinical estimation of gestational age which has been shown to be less accurate than ultrasound dating prior to 20 weeks (Campbell, 1974). Demographic, social, environmental and possibly biological factors characterising the reproductive experience of Scottish women have changed over the years and it is hoped that this study may provide

more accurate data of contemporary birthweight distribution according to gestational age as ascertained by ultrasound.

This study presents means, standard deviations and centile values of birth weight for gestational age, subdivided by the sex of infants and parity of mother, based on the analysis of live births occurring to women attending the Queen Mother's Hospital in Glasgow between 1985 and 1987. The basic purpose of this study is to provide the local standard for monitoring the birthweight of all infants born in the QMH.

3.2 Patients and methods

From the computerised ultrasound and perinatal data bases (Fig. 5 & 6), birthweight, gestational age and various demographic and clinical information were obtained by using programmes (1-6) and SPSS^X software.

The study population was selected by applying programmes (1-3). Ten thousand two hundred and fifty nine (10259) live singleton births occurring between 1985 and 1987 (QMH Group 1) were considered. This sample represented 26% of total live births in Greater Glasgow Health Board (GGHB) area and 5.2% of all live births in Scotland (Annual Report-Registrar General Scotland (1985, 1986 & 1987). Gestational age was confirmed by ultrasound prior to 20 weeks of gestation. Tables were prepared showing the mean, standard deviation and 5th, 10th, 25th, 50th, 75th, 90th and 95th smoothed centiles, of birthweight by gestational age for each week of gestation from 28 to 42 weeks gestation. Separate tables were provided for the following subgroups (1-6):-

1. All pregnancies with male infants.

2. All pregnancies with female infants.

3. All primiparae with male infants.

4. All primiparae with female infants.

5. All multiparae with male infants.

6. All multiparae with female infants.

To allow comparison with other reported standards and to provide a better representation of the pattern of fetal growth , the actual centile values were smoothed.

A similar analysis was repeated on a subset of 3919 births (QMH Group 2) selected from the above sample using programmes (4-6) written in SPSS[X]. Women included in this group had to meet the following criteria: (1) their babies were born without congenital malformation; (2) spontaneous onset of labour; (3) not on the contraceptive pill for the three months before pregnancy; (4) certain date of last menstrual period; (5) gestational age confirmed by ultrasound prior to 20 weeks. QMH Group 2 was subdivided in to six subgroups (7-12) corresponding to the subgroups of QMH Group 1.

Separate tables were prepared for each of the subgroups, from which the mean, standard deviation and the 5th, 10th, 25th, 50th, 75th, 90th and 95th smoothed centiles distribution of birthweights (in Kg), at each week were calculated.

Using the MINITAB statistical package, version 7.1 (available in the Department of Midwifery on an Amstrad

1640 microcomputer), curves of the 5th, 10th, 50th, 90th, and 95th centiles of the distribution from the 28th to 42nd weeks, for the subgroups (1-12) were constructed. These curves were super-imposed on the centiles curves derived from live births of Scotland 1975-79 (Smalls & Forbes, 1982) (Fig. 16-27 - following page 58).

The effect of the sex on birthweight for babies born to primiparae was examined. A t-test was performed on the difference between the mean birthweight of males and females (subgroups 3 & 4), so as to control for the influence parity might have on birthweight. Similarly, the effect of parity on birthweight was also examined. A t-test was performed on the difference between the mean birthweight of males born to primiparae and to multiparae (subgroups 3 & 5).

To determine the effect of induction of labour on the distribution of birthweight for gestational age, the QMH Group 1 (male infants) was divided into case and control groups. The cases comprised 989 women with induced labour, while the controls consisted of 4292 women with a spontaneous labour, so as to control for the influence baby's sex might have on birthweight. A t-test was performed on the difference between the mean birthweight of cases and controls.

```
FILE HANDLE A /NAME=´:GOUA02.US85.SPFQMH85´
FILE HANDLE B /NAME=´:GOUA13.US86.SPFQMH86´
FILE HANDLE C /NAME=´:GOUA07.US87.SPFQMH87´
ADD FILES FILE=A/FILE=B/FILE=C
SELECT IF NOFETUSD=1
SELECT IF WKS GT 27
SELECT IF PNRW EQ 0
TEMPORARY
SELECT IF SEX=´M´
   / TABLE = WKS BY WGHT
   / STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
        STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
        PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
        PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
        PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
        PTILE 95 (WGHT(F3.2))
TEMPORARY
SELECT IF SEX =´F´
   /TABLE = WKS BY WGHT
   /STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
        STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
        PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
        PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
        PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
        PTILE 95 (WGHT(F3.2))
```

Programme 1: SPSS[X] programme to calculate statistics
           for "all pregnancies" in QMH Group 1 (as
           defined on p 39) for a/ male infants and
           b/ female infants.

```
SELECT IF NOFETUSD=1
SELECT IF PARITY EQ 0
SELECT IF WKS GT 27
 SELECT IF PNRW EQ 0
 TEMPORARY
 SELECT IF SEX='M'
    / TABLE = WKS BY WGHT
    / STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
     STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
     PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
     PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
     PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
        PTILE 95 (WGHT(F3.2))
TEMPORARY
SELECT IF SEX ='F'
    /TABLE = WKS BY WGHT
    /STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
     STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
     PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
     PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
     PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
      PTILE 95 (WGHT(F3.2))
```

Programme 2: SPSS[x] programme to calculate statistics
            for "all primiparae" in QMH Group 1 (as
            defined on p39) for a/ male infants and
            b/ female infants.

```
SELECT IF NOFETUSD=1
SELECT IF WKS GT 27
SELECT IF PNRW EQ 0
 SELECT IF PARITY GT 0
 COMPUTE WGHT=WGHT/1000
 TEMPORARY
 SELECT IF SEX='M'
    / TABLE = WKS BY WGHT
    / STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
      STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
      PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
      PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
      PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
        PTILE 95 (WGHT(F3.2))
TEMPORARY
SELECT IF SEX ='F'
    /TABLE = WKS BY WGHT
    /STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
      STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
      PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
      PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
      PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
       PTILE 95 (WGHT(F3.2))
```

Programme 3: SPSS^{X} programme to calculate statistics for "all multiparae" in QMH Group 1 (as defined on p 39) for a/ male infants and b/ female infants.

```
SELECT IF NOFETUSD=1
SELECT IF WKS GT 27
SELECT IF PNRW EQ 0
 SELECT IF FADEL@A EQ 0
 SELECT IF IND EQ 0
 SELECT IF OC EQ 0
 SELECT IF CERT EQ 1
 SELECT IF DATESOK EQ 1
 TEMPORARY
 SELECT IF SEX='M'
    / TABLE = WKS BY WGHT
    / STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
     STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
     PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
     PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
     PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
        PTILE 95 (WGHT(F3.2))
 TEMPORARY
 SELECT IF SEX ='F'
    /TABLE = WKS BY WGHT
    /STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
     STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
     PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
     PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
     PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
      PTILE 95 (WGHT(F3.2))
```

Programme 4: SPSS[X] programme to calculate statistics
           for "all pregnancies" in QMH Group 2 (as
           defined on p 40) for a/ male infants and
           b/ female infants.

```
SELECT IF NOFETUSD=1
SELECT IF WKS GT 27
SELECT IF PNRW EQ 0
SELECT IF FADEL@A EQ 0
SELECT IF IND EQ 0
SELECT IF OC EQ 0
SELECT IF CERT EQ 1
SELECT IF DATESOK EQ 1
SELECT IF PARITY EQ 0
TEMPORARY
SELECT IF SEX='M'
   / TABLE = WKS BY WGHT
   / STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
    STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
    PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
    PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
    PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
       PTILE 95 (WGHT(F3.2))
TEMPORARY
SELECT IF SEX ='F'
   /TABLE = WKS BY WGHT
   /STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
    STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
    PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
    PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
    PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
     PTILE 95 (WGHT(F3.2))
```

Programme 5: SPSS[X] programme to calculate statistics
            for "all primiparae" in QMH Group 2 (as
            defined on p 40) for a/ male infants and
            b/ female infants.

```
SELECT IF NOFETUSD=1
SELECT IF WKS GT 27
SELECT IF PNRW EQ 0
 SELECT IF FADEL@A EQ 0
 SELECT IF IND EQ 0
 SELECT IF OC EQ 0
 SELECT IF CERT EQ 1
 SELECT IF DATESOK EQ 1
 SELECT IF PARITY GT 0
TEMPORARY
SELECT IF SEX='M'
 / TABLE = WKS BY WGHT
 / STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
    STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
    PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
    PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
    PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
      PTILE 95 (WGHT(F3.2))
TEMPORARY
SELECT IF SEX ='F'
/TABLE = WKS BY WGHT
/STATISTICS = COUNT (WGHT) MEAN (WGHT(F3.2))
    STDDEV (WGHT(F3.2)) RANGE (WGHT(F3.2))
    PTILE 5 (WGHT(F3.2)) PTILE 10 (WGHT(F3.2))
    PTILE 25 (WGHT(F3.2)) PTILE 50 (WGHT(F3.2))
    PTILE 75 (WGHT(F3.2)) PTILE 90 (WGHT(F3.2))
     PTILE 95 (WGHT(F3.2))
```

Programme 6: SPSS^X programme to calculate statistics for "all multiparae" in QMH Group 1 (as defined on p 40) for a/ male infants and b/ female infants.

3.3 RESULTS

3.3.1 Effect of sex and parity on birthweight

Tables 1A, B & C (pp 44-46) present means, standard
deviations and 5th, 10th, 25th, 50th, 75th, 90th, and 95th
smoothed centile values of birthweight in kilograms for
live births (QMH Group 1) classified according to sex and
parity. Of the very small number of births, from 28 weeks
till 32 weeks of gestation, the mean birthweights of male
and female are fairly similar. However, and in common
with other studies (Love & Kinch, 1965; Thomson et al,
1968), beyond 32 weeks males tend to be heavier than
females, with the greatest difference in the mean
birthweight (40 to 200 grams), occurring at 36-42 weeks
(Table 1A). The differences in mean birthweights between
males and females at 36 to 42 weeks were confirmed by
applying the t-test which was significant at $t = 2.13$, $p <$
0.02; $t = 2.42$, $p < 0.01$; $t = 5.96$, $p = 0.001$; $t = 3.50$, p
$= 0.001$; $t = 8.12$, $p = 0.001$; $t = 7.36$, $p = 0.001$; $t =$
5.00, $p = 0.001$, respectively.

In addition, for an accurate estimation of the effect of
sex on birthweight, a t-test was performed on the
difference between the mean birthweight of males and
females born to primiparae (Table 1B), so as to control

for the influence parity might have on birthweight. It was found to be significant between 38 and 42 weeks of gestation at t = 3.84, p = 0.001; t = 3.39, p = 0.001; t = 4.78, p = 0.001; t = 4.07, p = 0.001; t = 3.46, p = 0.001, respectively.

To determine the impact of parity on birthweight, a t-test was performed on the difference between the mean birthweight of males born to primiparae and to multiparae (Tables 1B & C). It was significant between 36 and 42 weeks of gestation at t = 3.55, p = 0.001; t = 1.88, p < 0.05; t = 3.53, p = 0.001; t = 3.65, p = 0.001; t = 9.04, p = 0.001; t = 6.78, p = 0.001; t = 2.54, p < 0.01, respectively.

The distributions of induced and non-induced births displayed no systematic difference at any gestational ages except at the 37th week (t = 3.02, p < 0.001) (Table 3).

Table 1: Means, standard deviations and smoothed centiles of birthweight (Kg), QMH Group 1

(A)

Males - All pregnancy numbers

| WKS | N | MEAN | SD | PERCENTILES | | | | | | |
				5	10	25	50	75	90	95
28	8	1.19	0.14	0.93	0.94	0.12	1.21	1.28	1.38	1.39
29	6	1.40	0.19	1.09	1.12	1.28	1.36	1.46	1.58	1.60
30	6	1.49	0.11	1.19	1.25	1.42	1.52	1.65	1.78	1.82
31	12	1.65	0.28	1.24	1.34	1.54	1.71	1.90	2.05	2.14
32	25	1.97	0.40	1.31	1.44	1.70	1.93	2.17	2.35	2.50
33	39	2.12	0.39	1.45	1.60	1.89	2.15	2.39	2.57	2.79
34	39	2.35	0.34	1.64	1.80	2.07	2.34	2.57	2.76	3.01
35	83	2.44	0.41	1.83	2.00	2.26	2.53	2.77	3.00	3.22
36	132	2.77	0.46	2.02	2.19	2.49	2.77	3.03	3.31	3.48
37	282	3.01	0.49	2.26	2.41	2.73	3.01	3.28	3.59	3.75
38	701	3.22	0.44	2.50	2.65	2.93	3.22	3.50	3.80	3.98
39	1148	3.40	0.44	2.70	2.85	3.12	3.39	3.69	3.98	4.17
40	1521	3.54	0.43	2.85	3.02	3.26	3.54	3.85	4.13	4.30
41	930	3.67	0.45	2.95	3.12	3.33	3.65	3.97	4.23	4.37
42	251	3.81	0.42	3.00	3.15	3.34	3.68	4.01	4.26	4.37

Females - All pregnancy numbers

| WKS | N | MEAN | SD | PERCENTILES | | | | | | |
				5	10	25	50	75	90	95
28	2	1.18	0.44	0.87	0.87	0.87	1.18	1.49	1.49	1.49
29	6	1.42	0.27	0.95	0.95	1.11	1.37	1.67	1.76	1.76
30	4	1.52	0.52	1.02	1.05	1.30	1.53	1.84	1.98	1.98
31	7	1.70	0.31	1.08	1.19	1.48	1.69	1.98	2.13	2.13
32	25	1.83	0.31	1.14	1.35	1.65	1.86	2.11	2.30	2.30
33	29	2.02	0.42	1.27	1.50	1.80	2.04	2.29	2.55	2.56
34	25	2.25	0.42	1.48	1.64	1.94	2.21	2.50	2.83	2.88
35	55	2.40	0.54	1.68	1.82	2.12	2.41	2.72	3.07	3.18
36	109	2.64	0.49	1.88	2.05	2.35	2.64	2.94	3.27	3.43
37	256	2.91	0.47	2.12	2.32	2.60	2.87	3.17	3.46	3.64
38	666	3.09	0.43	2.37	2.55	2.80	3.07	3.37	3.65	3.83
39	1133	3.26	0.43	2.57	2.74	2.97	3.25	3.54	3.82	3.99
40	1391	3.41	0.44	2.73	2.87	3.12	3.39	3.68	3.97	4.13
41	955	3.53	0.42	2.86	2.97	3.23	3.48	3.79	4.07	4.21
42	222	3.61	0.46	2.99	3.07	3.32	3.55	3.87	4.13	4.23

Table 1: (contd.)

(B)

Males - Primigravidae

WKS	N	MEAN	SD	PERCENTILES						
				5	10	25	50	75	90	95
28	6	1.15	0.13	0.94	0.93	1.10	1.18	1.24	1.35	1.32
29	5	1.42	0.21	1.10	1.09	1.22	1.36	1.44	1.51	1.49
30	3	1.45	0.14	1.20	1.20	1.31	1.51	1.61	1.66	1.65
31	4	1.51	0.22	1.23	1.29	1.44	1.68	1.86	1.88	1.92
32	12	1.94	0.43	1.26	1.45	1.64	1.90	2.19	2.21	2.28
33	15	2.17	0.40	1.37	1.68	1.86	2.12	2.46	2.52	2.57
34	22	2.31	0.36	1.58	1.87	2.05	2.26	2.60	2.74	2.78
35	41	2.37	0.38	1.77	1.97	2.20	2.40	2.74	2.97	3.04
36	67	2.64	0.46	1.94	2.12	2.39	2.61	2.95	3.23	3.33
37	113	2.88	0.42	2.17	2.35	2.61	2.87	3.19	3.47	3.62
38	265	3.17	0.43	2.43	2.60	2.83	3.11	3.40	3.66	3.87
39	493	3.30	0.42	2.64	2.78	3.03	3.29	3.58	3.82	4.04
40	706	3.44	0.40	2.79	2.93	3.17	3.46	3.75	3.99	4.17
41	445	3.57	0.43	2.89	3.05	3.25	3.59	3.89	4.12	4.27
42	152	3.76	0.40	2.97	3.11	3.27	3.64	3.94	4.17	4.31

Females - Primigravidae

WKS	N	MEAN	SD	PERCENTILES						
				5	10	25	50	75	90	95
29	2	1.32	0.43	0.99	1.02	0.99	1.32	1.63	1.63	1.63
30	3	1.57	0.62	1.01	1.05	1.04	1.51	1.80	1.87	1.88
31	3	1.44	0.26	1.05	1.13	1.18	1.66	1.94	2.04	2.10
32	12	1.73	0.40	1.10	1.26	1.41	1.83	2.06	2.19	2.34
33	14	2.02	0.39	1.18	1.44	1.63	2.01	2.20	2.34	2.61
34	11	2.06	0.38	1.30	1.62	1.83	2.19	2.39	2.58	2.92
35	32	2.40	0.58	1.48	1.79	2.05	2.40	2.63	2.90	3.25
36	58	2.64	0.51	1.74	2.00	2.30	2.63	2.88	3.18	3.49
37	105	2.81	0.46	2.02	2.24	2.55	2.84	3.10	3.39	3.65
38	258	3.04	0.43	2.30	2.46	2.76	3.02	3.30	3.58	3.78
39	485	3.21	0.41	2.52	2.66	2.92	3.18	3.47	3.74	3.91
40	593	3.33	0.43	2.70	2.82	3.05	3.32	3.60	3.88	4.03
41	467	3.46	0.40	2.84	2.94	3.18	3.43	3.72	4.00	4.10
42	138	3.59	0.45	2.98	3.04	3.30	3.52	3.84	4.09	4.14

Table 1: (contd.)

(C)

Males - Multiparae

WKS	N	MEAN	SD	PERCENTILES						
				5	10	25	50	75	90	95
28	2	1.32	0.08	1.26	1.26	1.26	1.31	1.37	1.37	1.35
29	1	1.34	*	1.31	1.31	1.34	1.39	1.45	1.46	1.44
30	3	1.53	0.08	1.35	1.36	1.42	1.55	1.64	1.69	1.68
31	8	1.72	0.29	1.39	1.42	1.53	1.75	1.90	2.04	2.07
32	13	2.00	0.37	1.43	1.50	1.70	1.95	2.15	2.38	2.49
33	24	2.09	0.38	1.52	1.63	1.93	2.15	2.36	2.60	2.80
34	17	2.40	0.32	1.69	1.83	2.16	2.36	2.56	2.79	3.03
35	42	2.51	0.42	1.91	2.07	2.38	2.61	2.80	3.05	3.30
36	65	2.91	0.43	2.14	2.31	2.61	2.87	3.07	3.37	3.62
37	169	3.10	0.51	2.34	2.52	2.82	3.10	3.34	3.66	3.90
38	436	3.25	0.45	2.55	2.72	3.01	3.29	3.57	3.87	4.10
39	655	3.48	0.45	2.77	2.93	3.18	3.46	3.76	4.04	4.27
40	815	3.63	0.44	2.94	3.10	3.34	3.62	3.92	4.20	4.42
41	485	3.76	0.45	3.00	3.15	3.43	3.71	4.03	4.34	4.48
42	99	3.90	0.45	3.00	3.15	3.45	3.75	4.13	4.43	4.49

Females - Multiparae

WKS	N	MEAN	SD	PERCENTILES						
				5	10	25	50	75	90	95
28	2	1.18	0.44	0.93	0.87	0.92	1.18	1.49	1.49	1.49
29	4	1.47	0.23	1.23	1.23	1.23	1.35	1.58	1.63	1.63
30	1	1.37	*	1.45	1.48	1.48	1.55	1.73	1.80	1.80
31	4	1.90	0.17	1.57	1.63	1.65	1.77	1.93	2.00	2.02
32	13	1.92	0.16	1.63	1.72	1.76	1.97	2.14	2.25	2.29
33	15	2.01	0.47	1.66	1.76	1.86	2.14	2.36	2.56	2.63
34	14	2.40	0.40	1.66	1.80	1.98	2.31	2.58	2.87	2.97
35	23	2.40	0.49	1.74	1.93	2.16	2.48	2.78	3.11	3.20
36	51	2.64	0.47	1.93	2.15	2.38	2.66	2.99	3.31	3.40
37	151	2.98	0.46	2.20	2.40	2.63	2.89	3.20	3.51	3.63
38	408	3.13	0.42	2.46	2.62	2.84	3.10	3.39	3.70	3.86
39	648	3.30	0.44	2.64	2.79	3.02	3.29	3.58	3.87	4.05
40	798	3.48	0.43	2.78	2.92	3.16	3.45	3.74	4.01	4.19
41	488	3.59	0.42	2.90	3.02	3.26	3.55	3.86	4.12	4.23
42	84	3.63	0.47	3.05	3.12	3.31	3.60	3.92	4.18	4.23

Table 2: Means, standard deviations and smoothed
centiles of birthweight (Kg), QMH Group 2

(A)

Males - All pregnancy numbers

WKS	N	MEAN	SD				PERCENTILES			
				5	10	25	50	75	90	95
28	4	1.17	0.20	0.93	0.93	1.01	1.17	1.32	1.38	1.38
29	4	1.37	0.23	1.11	1.12	1.17	1.33	1.47	1.55	1.55
30	1	1.51	*	1.24	1.30	1.32	1.52	1.63	1.72	1.74
31	3	1.63	0.31	1.35	1.45	1.46	1.73	1.85	1.93	2.03
32	11	1.90	0.35	1.48	1.59	1.63	1.94	2.09	2.18	2.44
33	13	2.12	0.33	1.68	1.75	1.83	2.12	2.33	2.43	2.81
34	13	2.37	0.31	1.88	1.90	2.06	2.31	2.58	2.72	3.07
35	26	2.54	0.44	2.02	2.06	2.29	2.54	2.85	3.07	3.28
36	48	2.82	0.47	2.17	2.25	2.53	2.82	3.12	3.39	3.50
37	102	3.09	0.45	2.38	2.49	2.76	3.08	3.36	3.62	3.73
38	272	3.26	0.41	2.58	2.71	2.96	3.27	3.55	3.81	3.96
39	476	3.41	0.45	2.74	2.89	3.13	3.41	3.72	4.00	4.16
40	642	3.56	0.42	2.89	3.05	3.28	3.54	3.85	4.14	4.30
41	354	3.68	0.43	3.03	3.19	3.40	3.64	3.92	4.18	4.34
42	73	3.80	0.44	3.10	3.24	3.44	3.67	3.92	4.16	4.30

Females - All pregnancy numbers

WKS	N	MEAN	SD				PERCENTILES			
				5	10	25	50	75	90	95
28	1	0.87	*	0.91	0.87	0.93	0.90	0.87	0.91	0.89
29	4	1.31	0.25	1.09	1.09	1.15	1.21	1.23	1.27	1.25
30	1	1.37	*	1.22	1.26	1.30	1.46	1.49	1.54	1.53
31	2	1.68	0.01	1.29	1.41	1.43	1.67	1.71	1.80	1.81
32	7	1.75	0.46	1.30	1.52	1.58	1.84	1.95	2.08	2.15
33	11	1.90	0.41	1.28	1.56	1.73	1.97	2.21	2.36	2.46
34	7	2.13	0.29	1.35	1.64	1.89	2.15	2.50	2.67	2.77
35	15	2.39	0.62	1.55	1.86	2.11	2.41	2.84	3.01	3.12
36	34	2.75	0.47	1.82	2.19	2.38	2.70	3.11	3.31	3.44
37	93	3.00	0.49	2.16	2.46	2.64	2.93	3.30	3.52	3.68
38	251	3.11	0.41	2.46	2.64	2.85	3.11	3.44	3.69	3.88
39	422	3.30	0.44	2.66	2.78	3.00	3.27	3.57	3.86	4.05
40	579	3.42	0.43	2.78	2.90	3.13	3.40	3.68	3.97	4.17
41	363	3.54	0.42	2.88	3.01	3.24	3.48	3.73	4.01	4.21
42	74	3.53	0.42	3.03	3.14	3.33	3.51	3.73	3.99	4.18
43	5	3.74	0.33	3.24	3.30	3.41	3.51	3.71	3.93	4.03
44	1	3.43	*	3.43	3.45	3.45	3.51	3.66	3.83	3.78

Table 2: (contd.)

(B)

Males - Primigravidae

WKS	N	MEAN	SD				PERCENTILES			
				5	10	25	50	75	90	95
28	2	1.01	0.12	0.93	0.93	0.93	1.01	1.13	1.10	1.12
29	3	1.38	0.28	1.15	1.14	1.21	1.36	1.62	1.68	1.68
32	5	1.79	0.39	1.41	1.41	1.52	1.71	2.01	2.16	2.15
33	4	2.03	0.32	1.70	1.70	1.82	2.01	2.32	2.53	2.52
34	7	2.45	0.35	1.91	1.94	2.07	2.23	2.56	2.83	2.85
35	11	2.42	0.31	2.02	2.07	2.26	2.41	2.77	3.09	3.13
36	19	2.63	0.45	2.12	2.21	2.44	2.62	2.98	3.29	3.37
37	32	2.92	0.36	2.26	2.40	2.67	2.90	3.20	3.48	3.62
38	88	3.20	0.46	2.44	2.60	2.89	3.14	3.41	3.66	3.89
39	189	3.28	0.42	2.63	2.76	3.05	3.31	3.59	3.87	4.10
40	270	3.46	0.41	2.81	2.92	3.19	3.47	3.76	4.04	4.22
41	155	3.60	0.44	2.98	3.05	3.31	3.59	3.88	4.11	4.24
42	48	3.72	0.40	3.10	3.12	3.35	3.63	3.92	4.09	4.21

Females - Primigravidae

WKS	N	MEAN	SD				PERCENTILES			
				5	10	25	50	75	90	95
29	2	1.32	0.43	1.16	1.15	1.02	1.33	1.63	1.63	1.62
31	1	1.69	*	1.20	1.19	1.27	1.61	1.78	1.84	1.84
32	6	1.72	0.49	1.24	1.23	1.47	1.80	1.95	2.07	2.06
33	8	1.83	0.41	1.28	1.31	1.65	1.91	2.11	2.30	2.29
34	3	2.04	0.07	1.38	1.51	1.84	2.02	2.33	2.60	2.64
35	9	2.20	0.62	1.58	1.84	2.06	2.28	2.68	2.99	3.12
36	11	2.84	0.56	1.82	2.15	2.31	2.65	3.05	3.31	3.53
37	31	2.93	0.48	2.07	2.35	2.55	2.93	3.29	3.50	3.75
38	83	3.01	0.42	2.35	2.51	2.75	3.08	3.42	3.65	3.88
39	157	3.26	0.46	2.58	2.67	2.91	3.20	3.53	3.81	4.01
40	227	3.33	0.40	2.73	2.80	3.04	3.33	3.63	3.94	4.10
41	155	3.47	0.42	2.86	2.92	3.16	3.43	3.69	3.98	4.13
42	40	3.54	0.45	3.06	3.11	3.29	3.47	3.71	3.95	4.07

Table 2: (contd.)

(C)

Males - Multiparae

WKS	N	MEAN	SD	PERCENTILES						
				5	10	25	50	75	90	95
28	2	1.32	0.08	1.27	1.26	1.28	1.30	1.36	1.36	1.36
29	1	1.34	*	1.32	1.31	1.32	1.38	1.42	1.42	1.42
30	1	1.51	*	1.39	1.38	1.40	1.52	1.58	1.60	1.60
31	3	1.63	0.31	1.50	1.49	1.54	1.72	1.82	1.96	1.96
32	6	1.99	0.32	1.61	1.61	1.69	1.93	2.09	2.37	2.37
33	9	2.16	0.35	1.72	1.75	1.85	2.13	2.33	2.69	2.71
34	6	2.28	0.27	1.83	1.93	2.04	2.35	2.59	2.95	3.07
35	15	2.61	0.50	1.95	2.14	2.31	2.62	2.90	3.22	3.47
36	29	2.94	0.46	2.13	2.36	2.61	2.91	3.20	3.48	3.75
37	70	3.16	0.47	2.38	2.58	2.86	3.15	3.43	3.69	3.90
38	184	3.29	0.39	2.61	2.77	3.05	3.32	3.61	3.88	4.03
39	287	3.50	0.45	2.79	2.95	3.21	3.47	3.77	4.05	4.20
40	372	3.63	0.41	2.97	3.11	3.34	3.59	3.92	4.21	4.35
41	199	3.75	0.42	3.16	3.26	3.41	3.71	4.09	4.34	4.43
42	25	3.96	0.49	3.33	3.37	3.44	3.91	4.27	4.43	4.45

Females - Multiparae

WKS	N	MEAN	SD	PERCENTILES						
				5	10	25	50	75	90	95
28	1	0.87	*	0.93	0.93	0.92	0.88	0.87	0.87	0.87
29	2	1.30	0.01	1.23	1.23	1.23	1.19	1.18	1.18	1.18
30	1	1.37	*	1.47	1.47	1.47	1.45	1.42	1.42	1.42
31	1	1.68	*	1.62	1.62	1.62	1.68	1.67	1.67	1.67
32	1	1.93	*	1.70	1.70	1.73	1.91	1.99	1.99	1.99
33	3	2.08	0.43	1.72	1.72	1.85	2.13	2.33	2.36	2.36
34	4	2.20	0.38	1.77	1.77	2.00	2.35	2.63	2.74	2.74
35	6	2.67	0.55	1.91	1.93	2.22	2.60	2.90	3.08	3.11
36	23	2.70	0.42	2.16	2.21	2.46	2.79	3.11	3.35	3.44
37	62	3.03	0.50	2.41	2.49	2.69	2.96	3.26	3.54	3.70
38	168	3.16	0.40	2.59	2.68	2.89	3.13	3.41	3.71	3.92
39	265	3.33	0.44	2.71	2.84	3.05	3.30	3.59	3.86	4.08
40	352	3.48	0.43	2.82	2.97	3.18	3.43	3.72	3.97	4.18
41	208	3.60	0.42	2.93	3.08	3.27	3.49	3.82	4.04	4.21
42	34	3.53	0.38	3.10	3.19	3.31	3.50	3.95	4.10	4.19

Table 3: Birthweight means and standard deviation by
         gestational age for cases (all women with
         an induced male births) and controls (all
         women with non-induced male births)

Group	Week	Number	Mean	Standard Deviation
Cases	32	2	2.35	0.52
	33	2	1.72	0.44
	34	2	2.59	0.19
	35	12	2.38	0.54
	36	25	2.63	0.62
	37	45	2.82	0.47
	38	115	3.15	0.51
	39	164	3.39	0.47
	40	269	3.58	0.47
	41	246	3.68	0.45
	42	99	3.83	0.40
Controls	32	26	1.97	0.39
	33	37	2.14	0.38
	34	39	2.33	0.34
	35	71	2.45	0.39
	36	109	2.80	0.41
	37	239	3.05	0.48
	38	597	3.23	0.43
	39	998	3.40	0.44
	40	1271	3.53	0.42
	41	697	3.67	0.45
	42	157	3.81	0.43

3.3.2 Comparison with other standards

Tables 4 & 5 compare the 10th centile values of birthweight for QMH Group 1 and 2 for males and females with similar values derived from four studies based on the Scottish population. The Aberdeen centiles are those reported by Thomson and associates (1968) in their analysis of 46,703 births which occurred between 1948 and 1964 in the city of Aberdeen. The centile values reported by Cole (1981) were based on data derived from the Scottish neonatal discharge record, SMR11, on approximately 169,631 babies amounting to 40% of all live births in Scotland occurring between 1973 and 1979. The Glasgow standard (Forbes and Smalls, 1983) was estimated using data from the SMR2 maternity discharge records relating to 55,387 births to women resident in the Greater Glasgow Health Board area during 1975-79. The Scottish Standard (Forbes and Small, 1982) was obtained from the Scottish Maternity Discharge Record SMR2 relating to 303,056 births from 1975-79.

Comparison between the figures of QMH Group 1 and 2 (Table 4) shows that the centile values of QMH Group 2 are generally greater throughout the gestational weeks, with the largest difference occurring at 32 weeks of gestation (150 grams). The QMH Group 1 centile values are generally

higher, later in pregnancy, than those recorded for Scotland (1973-79), Glasgow (1975-79) and Scotland (1975-79), with the largest differences occurring at 40-42 weeks gestation (70-130 grams; 120-160 grams and 100-140 grams) respectively. The Aberdeen centile values tend to be greater between 33-38 weeks, but beyond 38 weeks they are lower than QMH Group 1. The greatest difference is 140 grams at 42 weeks. QMH Group 2 centile values are greater than almost all of the other standards. They are greater than those for Scotland (1973-79) with the largest differences occurring at 32-33 weeks of gestation (220-200 grams), for Scotland (1975 -79) at 32-42 (260-230 grams), and for Glasgow (1975-79) at 33-42 weeks of gestation (230-250 grams). Although the Aberdeen centile values are greater between 33-37 weeks, beyond 38 weeks the QMH Group 1 and 2 values are greater with a difference of 140 and 230 grams at 42 weeks respectively.

In general the figures in table 4 closely resemble those in table 5. Throughout gestational weeks the centile values of QMH Group 2 are greater than QMH Group 1 with the largest difference at 32 weeks (170 grams). At many gestational ages, particularly after 37 weeks, the 10th centile values of QMH Group 1 are greater than those recorded for Scotland (1973-79), Scotland (1975-79) and Glasgow (1975-79) with the largest differences at 42 weeks

(160 grams; 180 grams and 220 grams respectively).
Similarly the QMH Group 2 centile values stay greater than
those of Scotland (1973-79), Scotland (1975-79) and
Glasgow (1975-79) , with the largest differences at 42
weeks of gestation (20-30 grams; 30-30 grams and 90-70
grams respectively). Beyond 38 weeks QMH Group 1 and 2
centile values are greater than Aberdeen centile values
with the largest differences at 42 weeks (290 and 220
grams respectively).

Table 4: Birthweight for gestational age standards compared with the Queen Mother's Hospital standards (1985-1987) at the 10th centile for males-all pregnancies

MALE Gestation (Weeks)	Aberdeen 1948-64 (A) Kg.	Scotland 1973-79 (B) Kg.	Glasgow 1975-79 (C) Kg.	Scotland 1975-79 (D) Kg.	QMH Group 1 1985-87 (E) Kg.	QMH Group 2 1985-87 (F) Kg.
32	1.36	1.37	1.29	1.33	1.44	1.59
33	1.66	1.55	1.52	1.52	1.60	1.75
34	1.93	1.76	1.75	1.74	1.80	1.90
35	2.17	1.98	1.99	1.97	2.00	2.06
36	2.38	2.21	2.22	2.20	2.19	2.25
37	2.56	2.44	2.43	2.42	2.41	2.49
38	2.71	2.64	2.62	2.62	2.65	2.71
39	2.83	2.82	2.78	2.79	2.85	2.89
40	2.92	2.95	2.90	2.92	3.02	3.05
41	2.98	3.02	2.97	3.00	3.12	3.19
42	3.01	3.02	2.99	3.01	3.15	3.24

(A) Thomas et al, 1968
(B) Cole, 1981
(C) Forbes & Small, 1983
(D) Forbes & Small, 1982
(E) The Queen Mother's Hospital (Group 1), 1989
(F) The Queen Mother's Hospital (Group 2), 1989

Table 5: Birthweight for gestational age standards compared with the Queen Mother's Hospital standards (1985-1987) at the 10th centile for males-all pregnancies

FEMALE Gestation (Weeks)	Aberdeen 1948-64 (A) Kg.	Scotland 1973-79 (B) Kg.	Glasgow 1975-79 (C) Kg.	Scotland 1975-79 (D) Kg.	QMH Group 1 1985-87 (E) Kg.	QMH Group 2 1985-87 (F) Kg.
32	1.27	1.26	1.39	1.27	1.35	1.52
33	1.57	1.45	1.55	1.46	1.50	1.56
34	1.83	1.66	1.73	1.67	1.64	1.64
35	2.07	1.89	1.93	1.89	1.82	1.86
36	2.27	2.12	2.14	2.11	2.05	2.19
37	2.44	2.34	2.34	2.33	2.32	2.46
38	2.59	2.54	2.52	2.52	2.55	2.64
39	2.70	2.71	2.68	2.68	2.74	2.78
40	2.78	2.83	2.79	2.81	2.87	2.90
41	2.83	2.90	2.85	2.88	2.97	3.01
42	2.85	2.91	2.85	2.89	3.07	3.14

(A) Thomas et al, 1968
(B) Cole, 1981
(C) Forbes & Small, 1983
(D) Forbes & Small, 1982
(E) The Queen Mother's Hospital (Group 1), 1989
(F) The Queen Mother's Hospital (Group 2), 1989

3.3.3 Comparison with the Scottish standard 1975-79

(Forbes & Smalls, 1982)

Comparison of the 10th centile values of the QMH groups with those based on Scottish population (Forbes & Smalls, 1982), shows that, beyond 38 weeks of gestation, the QMH centile values are higher than the Scottish (Tables 4 & 5). The difference was confirmed statistically by a chi-square test which was significant at the 95% level of confidence except for few isolated cases (Table 6). Similarly, beyond 35 weeks of gestation the 10th centile lines of QMH curves (figures 16-27) are constantly parallel and above the Scottish lines.

Table 6: Summary of chi-square value of 10th centile birthweight difference between the QMH Groups 1 & 2 and Scotland 1975-79 (Forbes & Smalls, 1982), for male and female between 38 and 42 weeks of gestation

	Male					Female				
	Weeks of gestation					Weeks of gestation				
	38	39	40	41	42	38	39	40	41	42
Group 1	4.62 (S)	4.71 (S)	18.04 (S)	22.08 (S)	20.24 (S)	2.07 (NS)	9.49 (S)	9.53 (S)	26.00 (S)	25.00 (S)
Group 2	6.63 (S)	3.33 (NS)	11.50 (S)	13.70 (S)	6.15 (S)	36.82 (S)	11.75 (S)	8.90 (S)	6.78 (S)	2.90 (NS)

3.3.4 Centiles growth curves for the QMH 1985-87

Figures 16-27 present curves of the 5th, 10th, 50th, 90th and 95th smoothed centiles of the distribution from 28th to 42nd weeks, for the QMH subgroups (1-12), super-imposed on the Scottish centiles curves (Forbes & Smalls, 1982). All QMH lines (5th, 10th, 50th, 90th, 95th) are evenly distributed with gestational age except between 28 to 35 weeks where fluctuations occur due to a small sample size. The 50th centiles lines are changing smoothly with gestational age. As can be seen by comparing QMH lines with those of the Scottish, between 35 to 38 weeks of gestation, the QMH lines are consistently parallel to the Scottish lines and beyond 38 weeks of gestation they are markedly above the Scottish lines.

Figure 16. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 1 curves 1985-87. Males – All pregnancies

Legend (within figure):

QMH Group 1 . : . solid line
Forbes & Smalls . : . dashed line
Orange . . . : . 95th centile
Blue . . . : . 90th centile
Green . . . : . 50th centile
Red . . . : . 10th centile
Black . . . : . 5th centile

Axis labels: Gestation in weeks (x-axis: 30.0, 32.5, 35.0, 37.5, 40.0); Birthweight in kg (y-axis: 0.0, 1.6, 3.2)

Figure 17. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 1 curves 1985-87. Females - All pregnancies

Figure 18. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 1 curves 1985-87. Males - Primigravidae

Figure 19. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 1 curves 1985-87. Females - Primigravidae
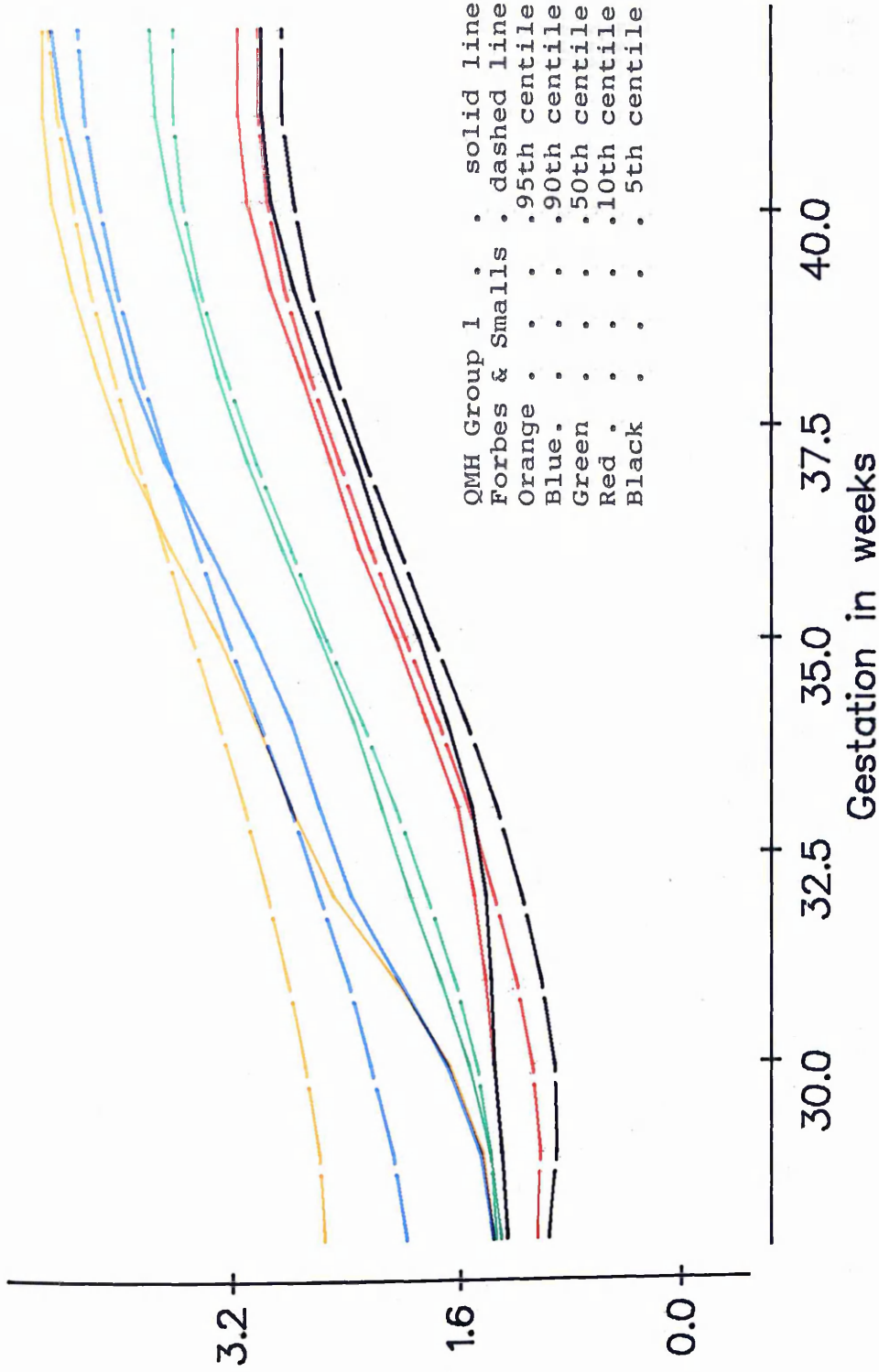
Figure 20. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 1 curves 1985-87. Males - Multiparae

Legend (within figure):

QMH Group 1 . . . . solid line
Forbes & Smalls . . . dashed line
Orange . . . . . .95th centile
Blue . . . . . . .90th centile
Green . . . . . .50th centile
Red . . . . . . .10th centile
Black . . . . . . 5th centile

Axis labels: Gestation in weeks (30.0, 32.5, 35.0, 37.5, 40.0)

Y-axis: Birthweight in kg (0.0, 1.6, 3.2)
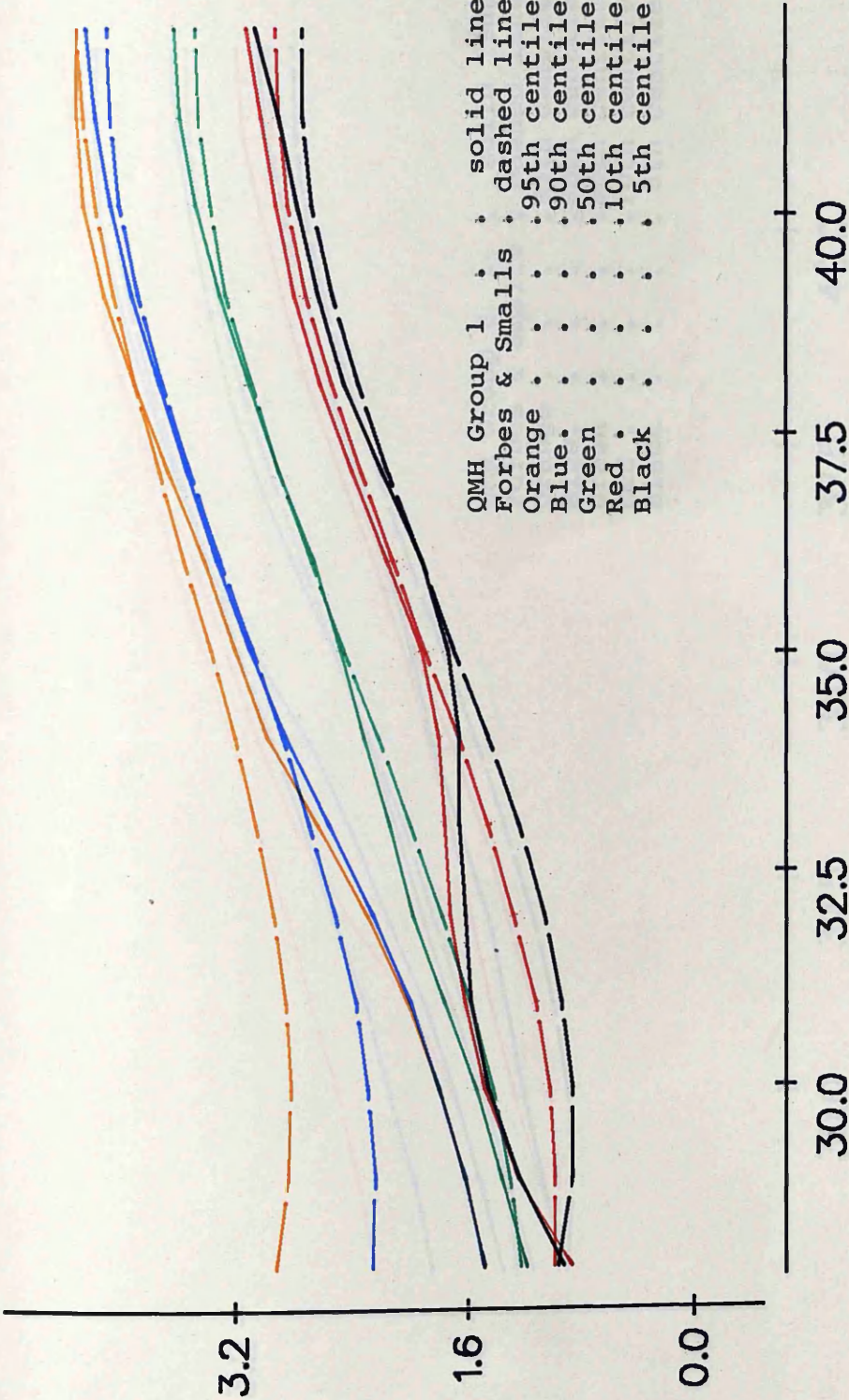
Figure 21. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 1 curves 1985-87. Females - Multiparae

Legend (within figure):

QMH Group 1 : ; solid line
Forbes & Smalls : ; dashed line
Orange . : . ;95th centile
Blue. . : . ;90th centile
Green . : . ;50th centile
Red . . : . ;10th centile
Black . . : . ; 5th centile

Axis labels: Gestation in weeks (x-axis: 30.0, 32.5, 35.0, 37.5, 40.0)
Birthweight in kg (y-axis: 0.0, 1.6, 3.2)
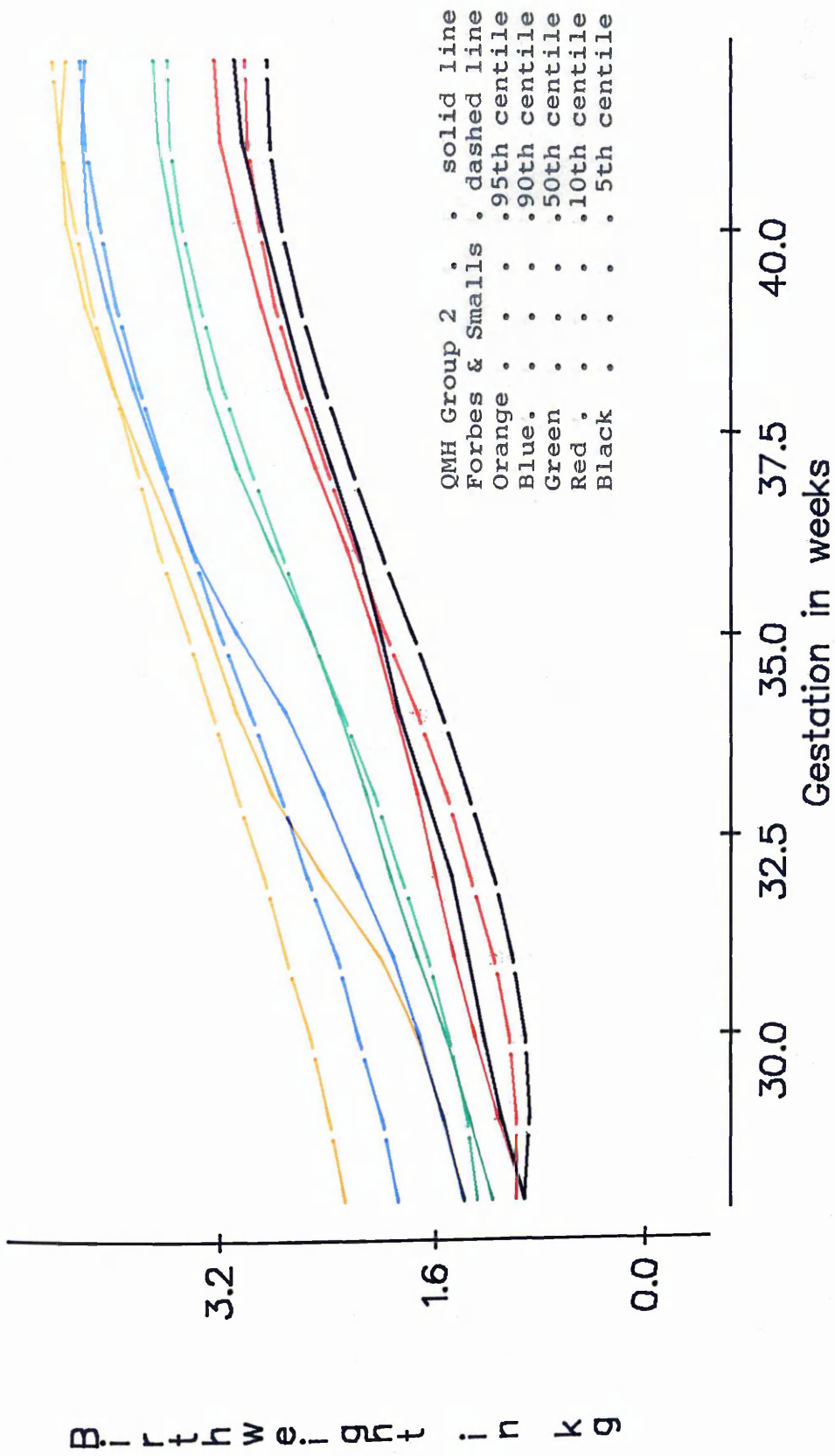
Figure 22. Centile growth curves for Scotland 1975–79 (Forbes & Smalls, 1982) compared with the QMH Group 2 curves 1985–87.
Males – All pregnancies

Legend:
QMH Group 2 . . solid line
Forbes & Smalls . dashed line
Orange . . . .95th centile
Blue. . . . .90th centile
Green . . . .50th centile
Red . . . .10th centile
Black . . . 5th centile

Axis labels:
Gestation in weeks (30.0, 32.5, 35.0, 37.5, 40.0)
Birthweight in kg (0.0, 1.6, 3.2)
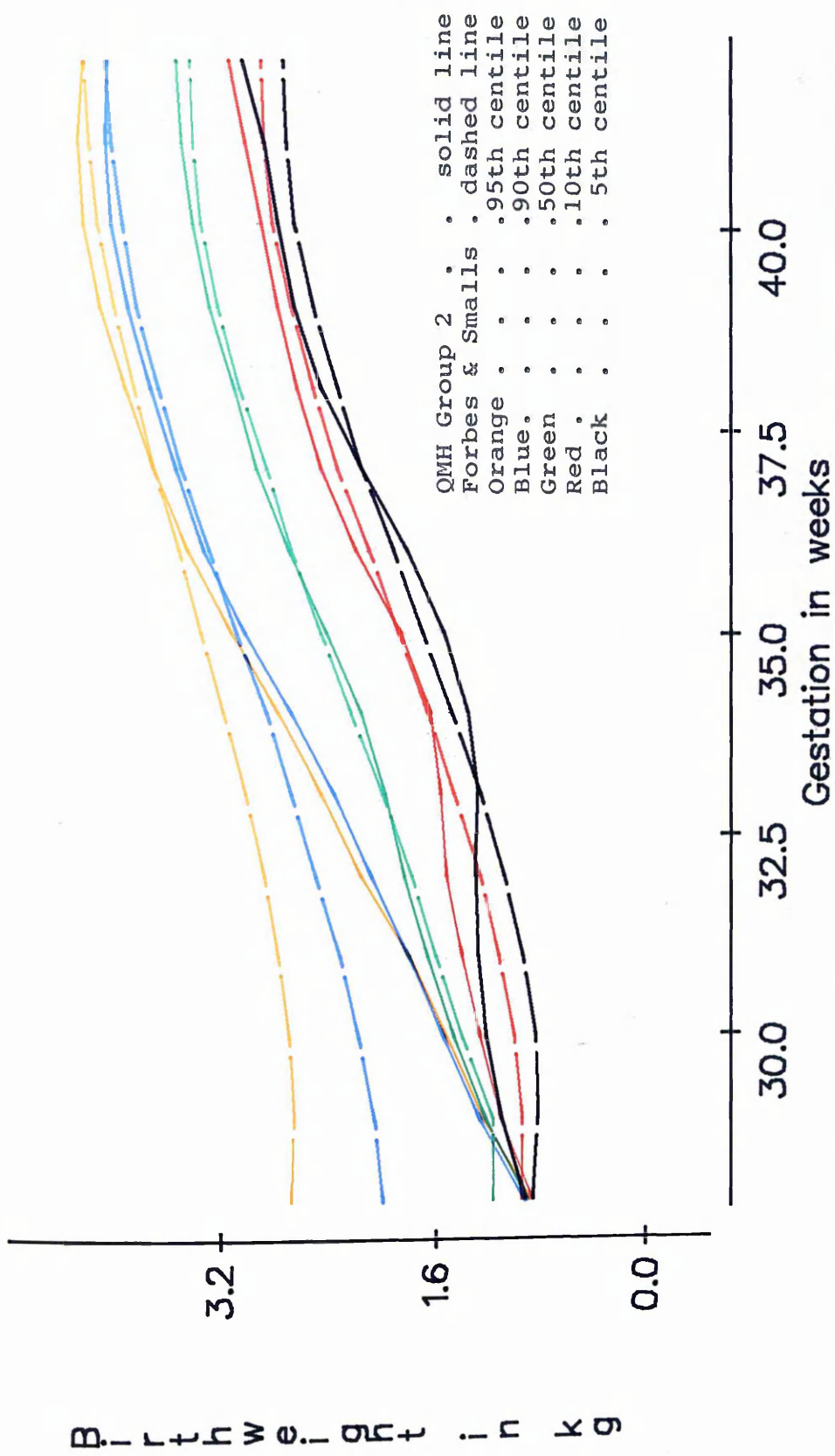
Figure 23. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 2 curves 1985-87. Females - All pregnancies

Legend (within figure):

QMH Group 2 . . solid line
Forbes & Smalls . dashed line
Orange . . . .95th centile
Blue. . . . .90th centile
Green . . . .50th centile
Red . . . . .10th centile
Black . . . . 5th centile

Y-axis: Birthweight in kg (3.2, 1.6, 0.0)

X-axis: Gestation in weeks (30.0, 32.5, 35.0, 37.5, 40.0)
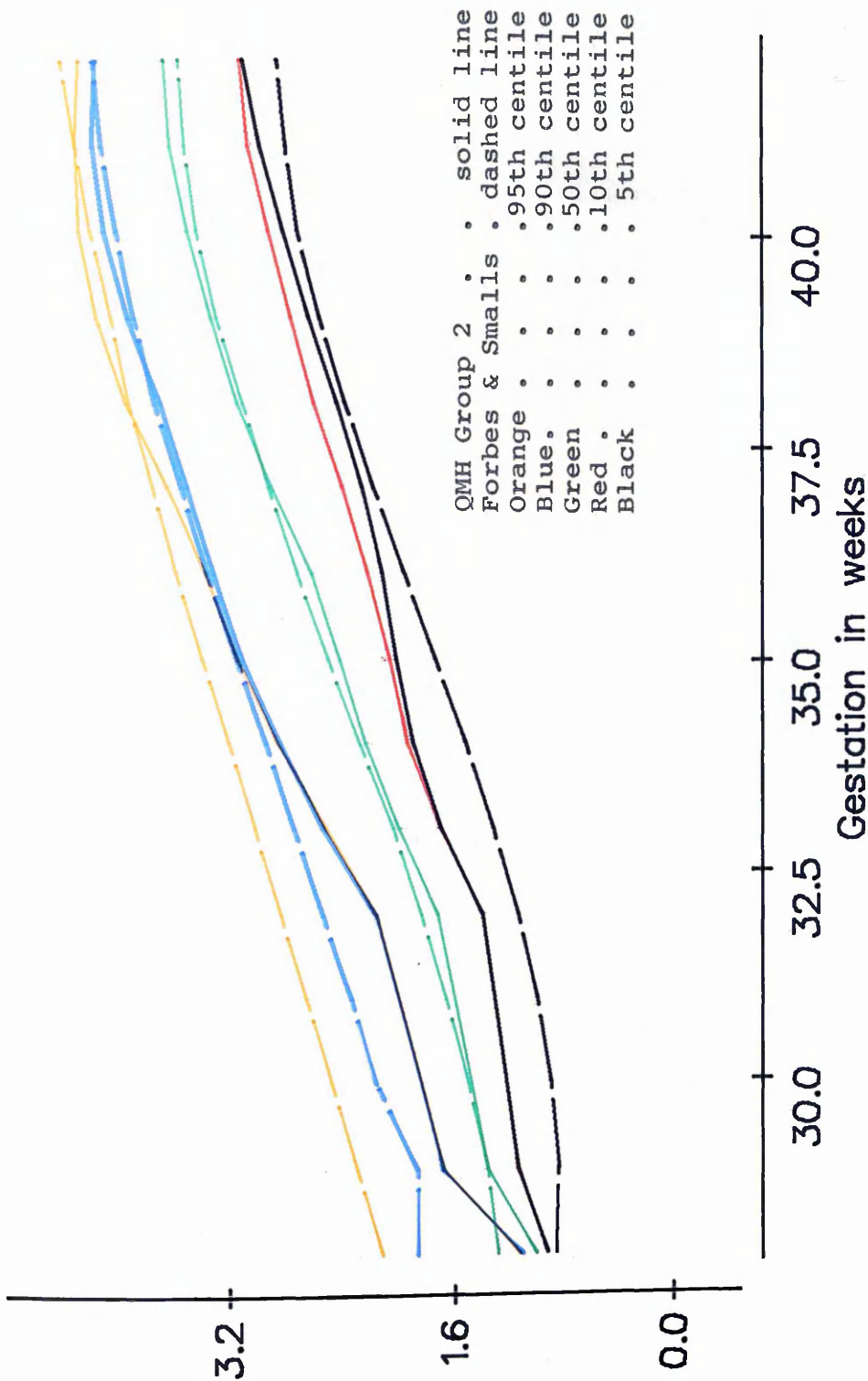
Figure 24. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 2 curves 1985-87. Males - Primigravidae
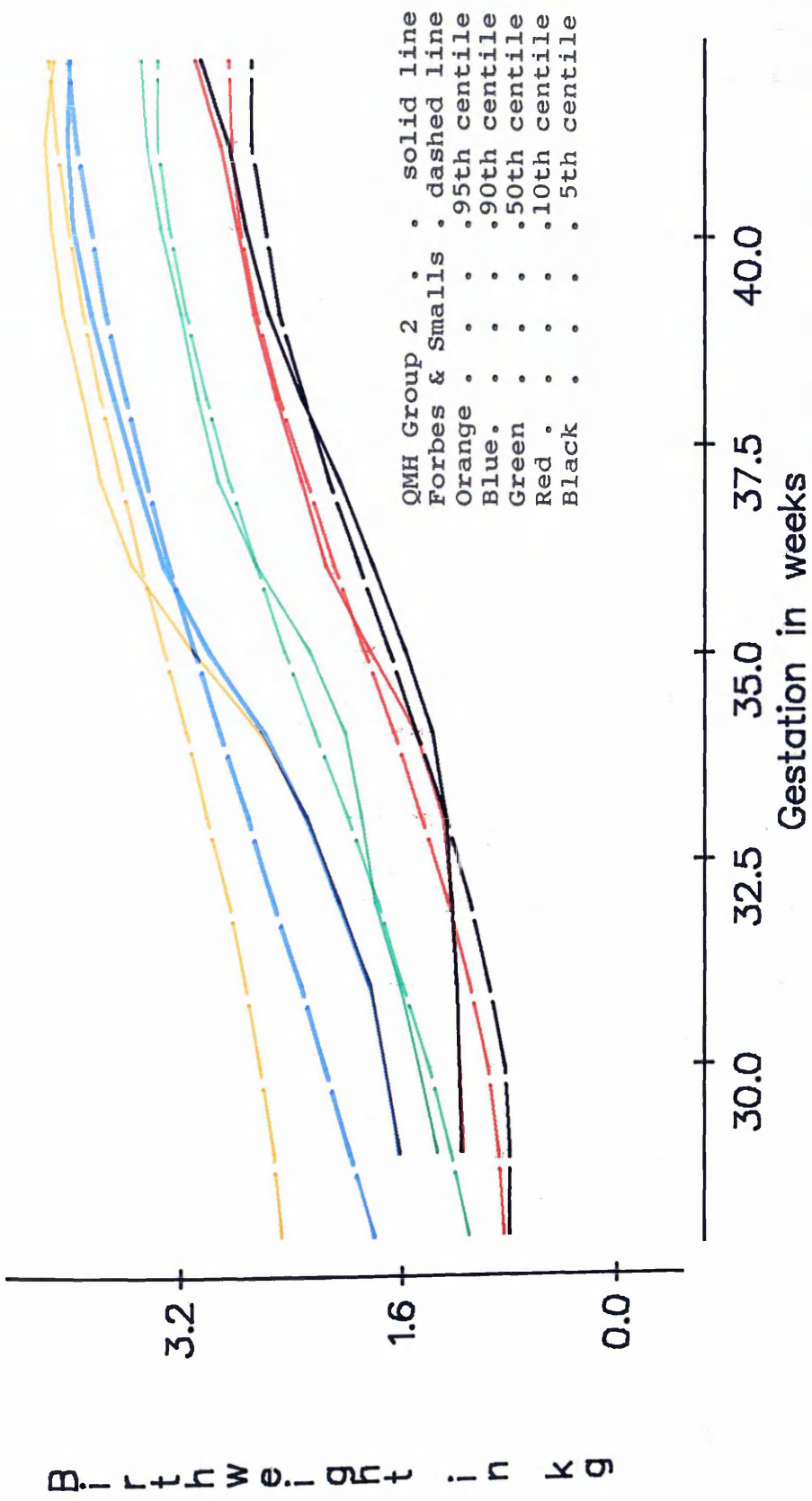
Figure 25. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 2 curves 1985-87.
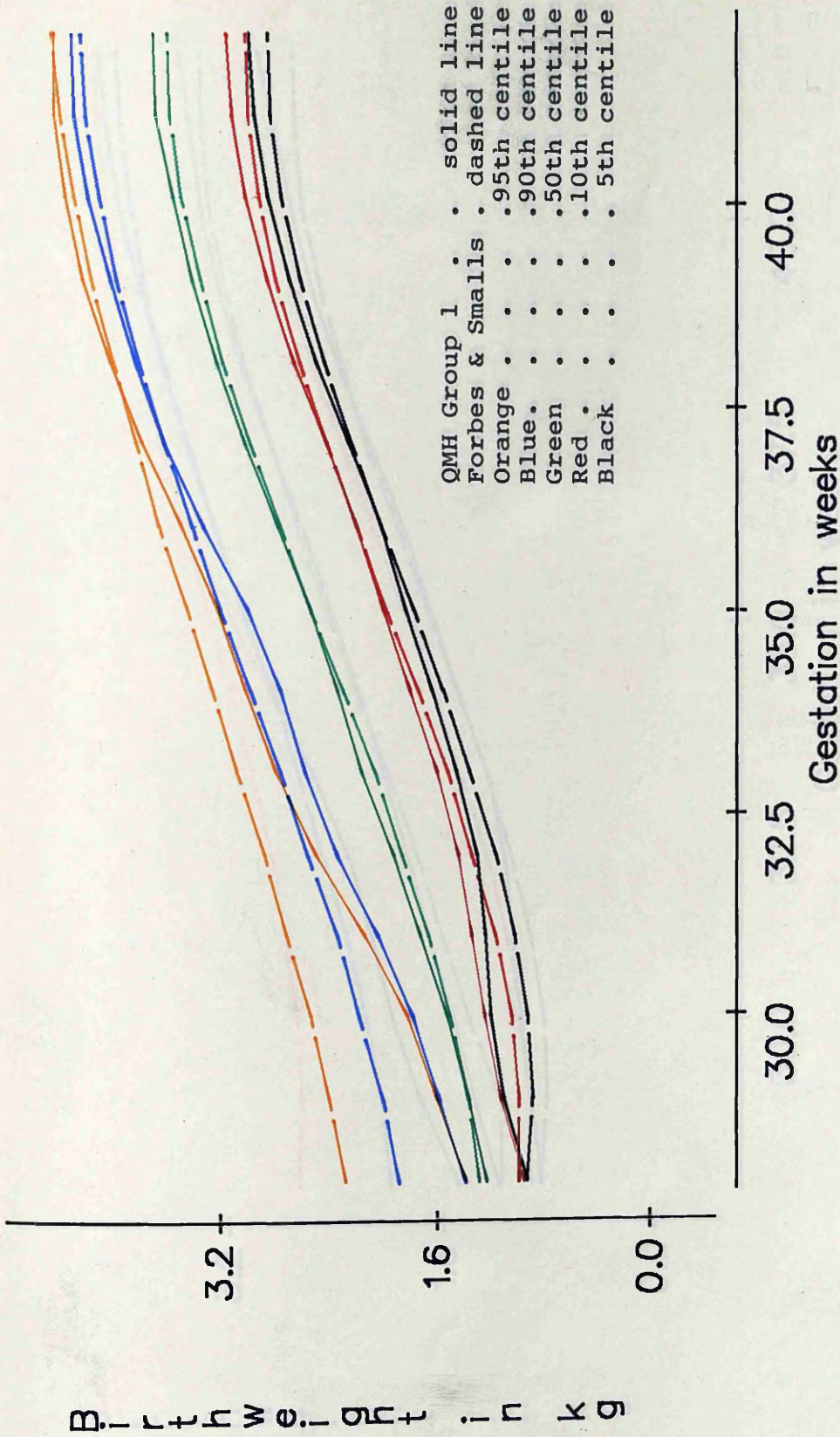Females - Primigravidae
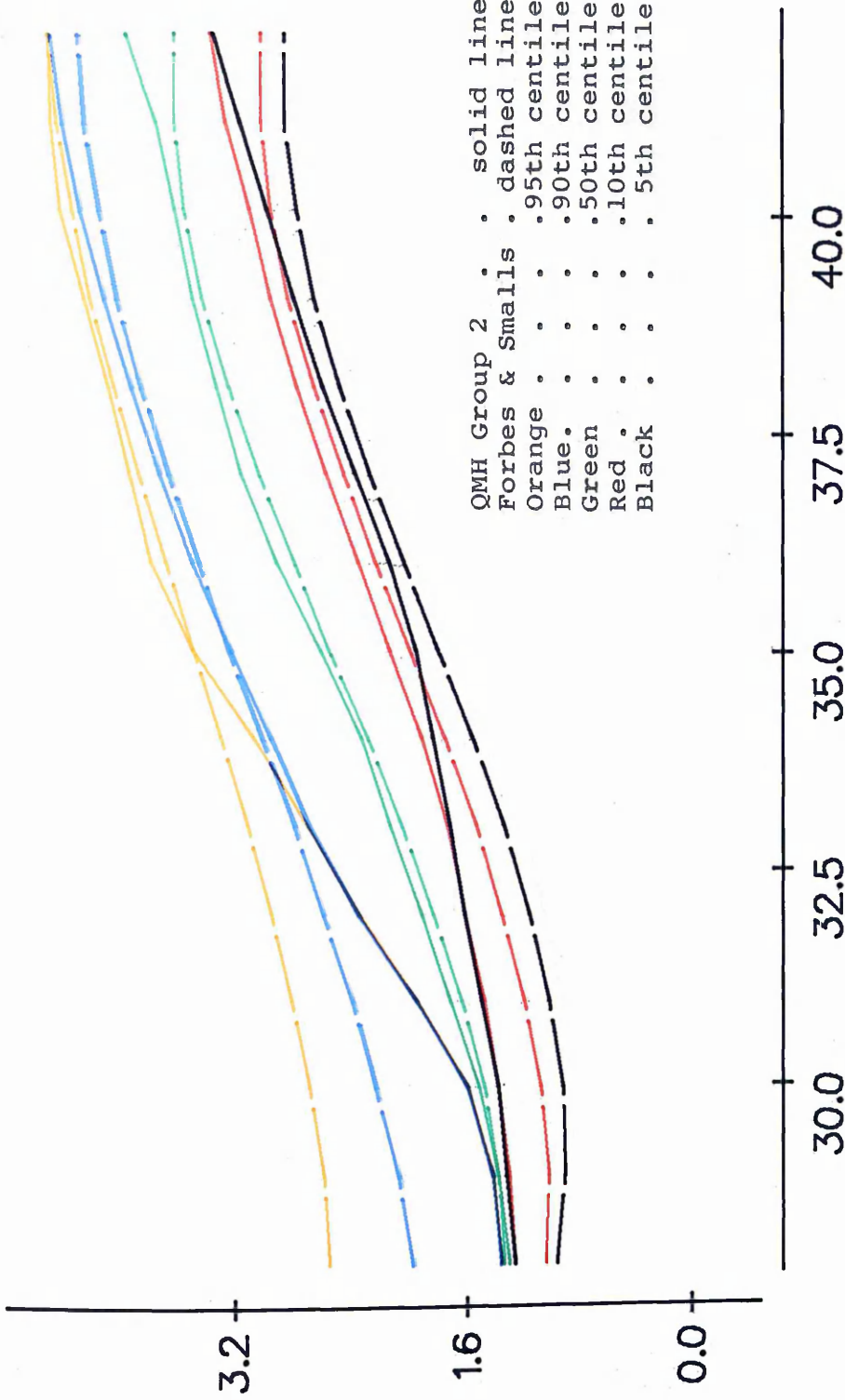
Figure 26. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 2 curves 1985-87. Males - Multiparae
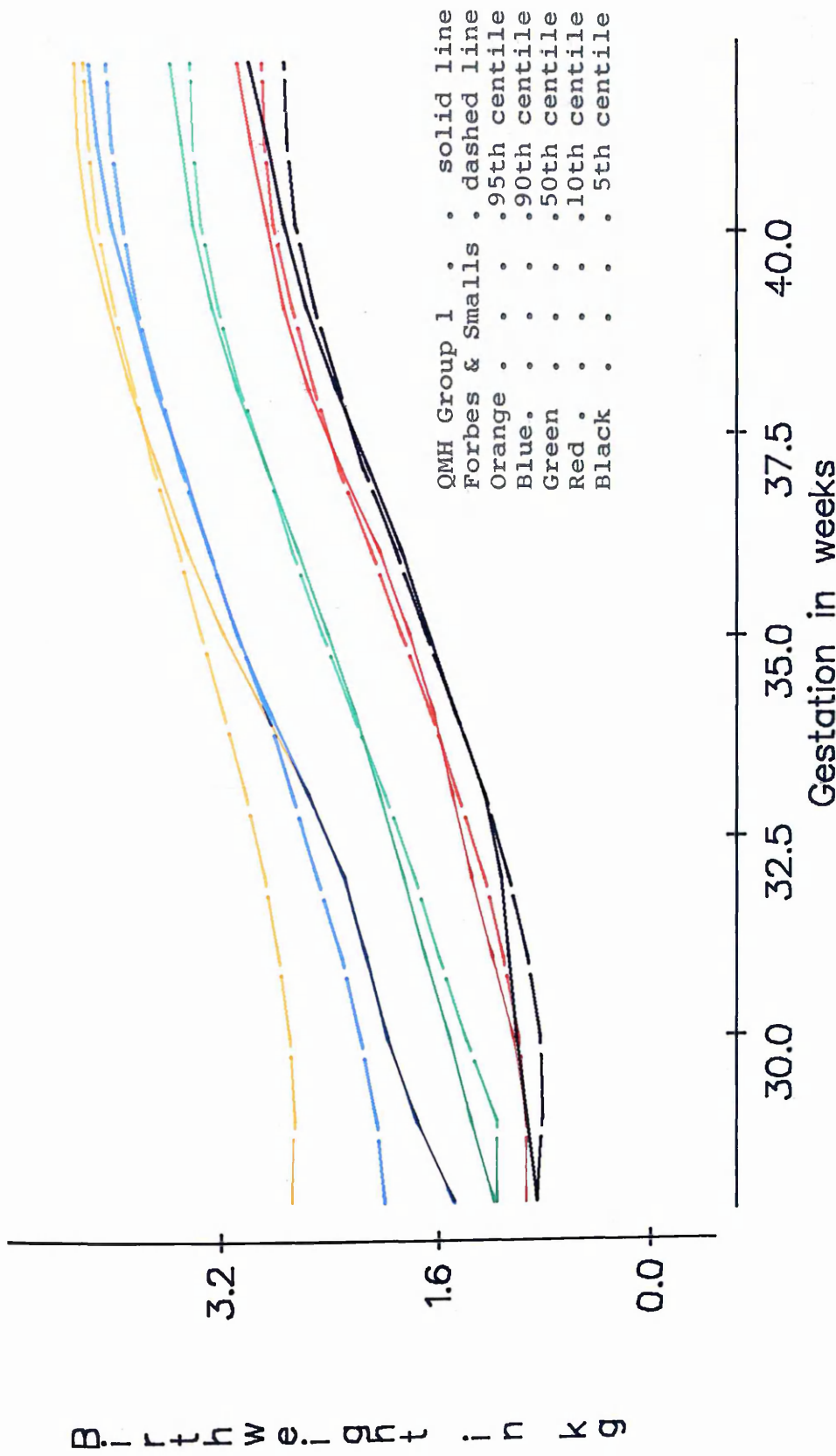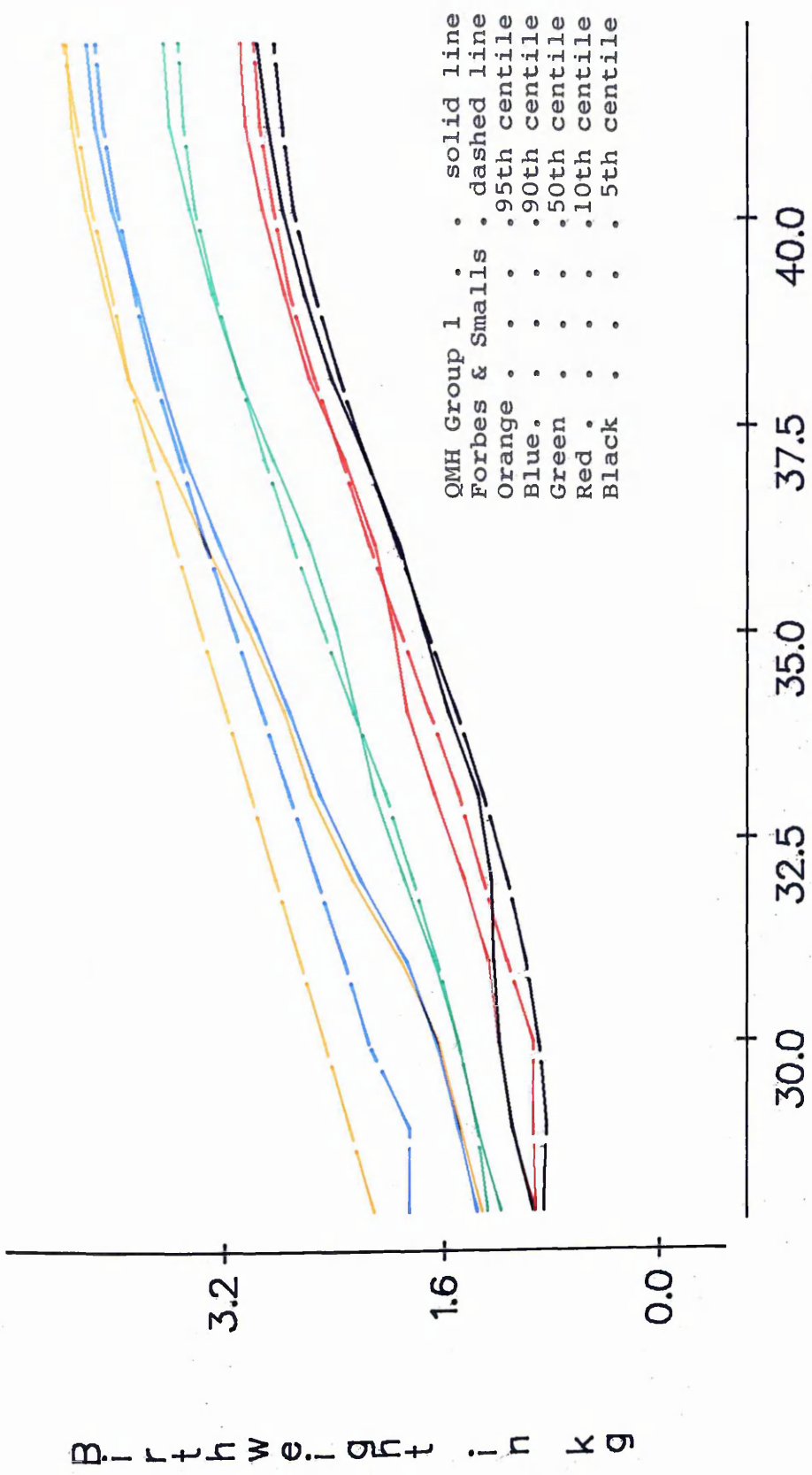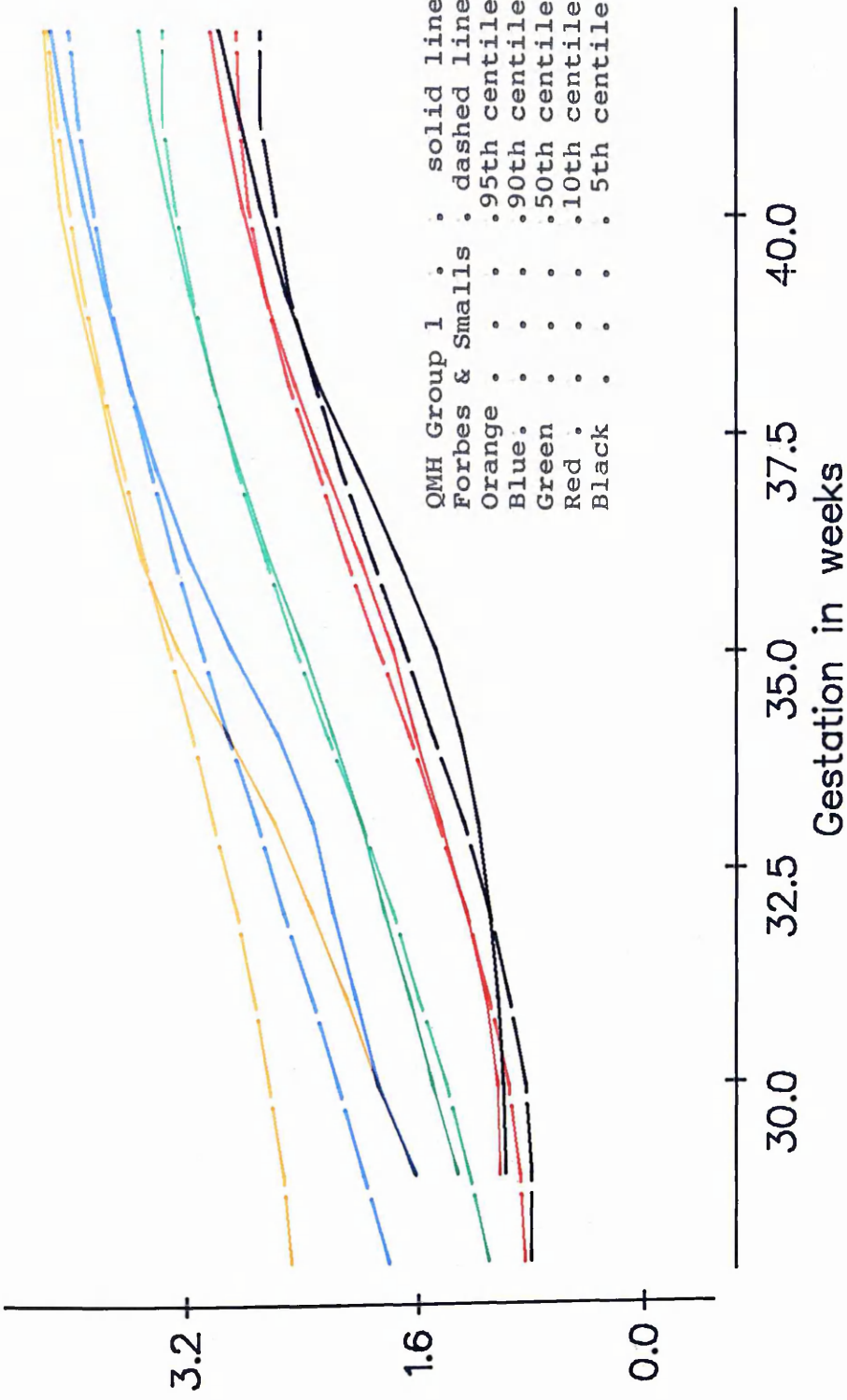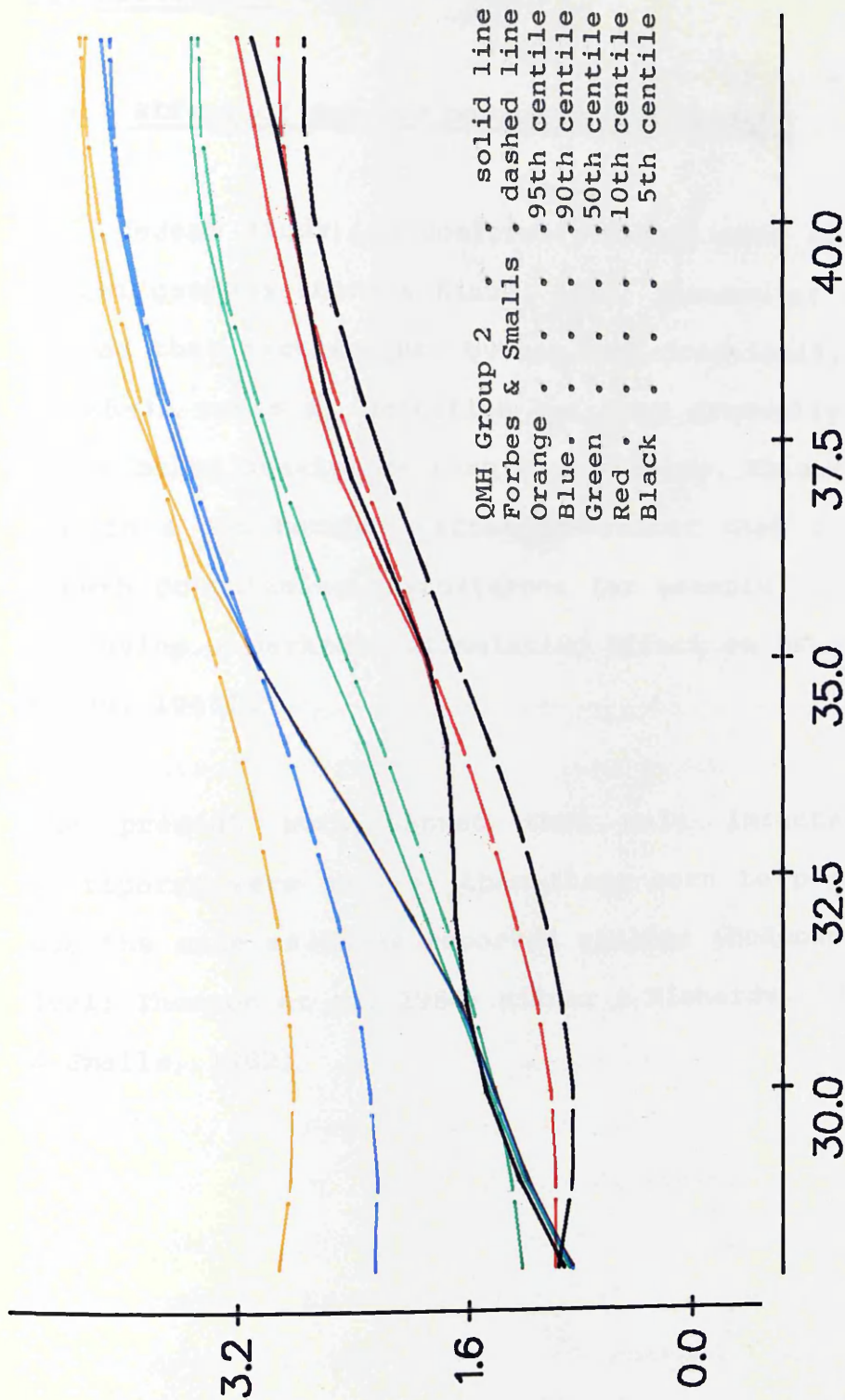
Figure 27. Centile growth curves for Scotland 1975-79 (Forbes & Smalls, 1982) compared with the QMH Group 2 curves 1985-87. Females - Multiparae

3.4 DISCUSSION

3.4.1 Effect of sex and parity on birthweight

The present study, in conformity with almost all previous investigations (Love & Kinch, 1965; Thomson et al, 1968), showed that birthweights by sex were practically identical at 28-33 weeks of gestation but then gradually diverged; males being heavier at term than females. This is possibly due to a sex hormone difference rather than to different growth potentials; testosterone for example is recognised as having a markedly stimulating effect on growth (Love & Kinch, 1965).

The present work showed that male infants born to multiparae were heavier than those born to primparae and was the same as those reported earlier (McKeown & Gibson, 1951; Thomson et al, 1986; Milner & Richards, 1974; Forbes & Smalls, 1982)

3.4.2 Fetal Growth Standards

General consideration

Appropriate fetal growth standards usually describe mean, standard deviation and percentile values of birthweight for each length of gestation subdivided by the sex, parity and maternal size. Some investigators (Lubchenco et al, 1963) described the uses of common (all pregnancies, both sexes) standard only. But the matter is not so straight forward. Suppose that a common standard was used to study the effect of pre-eclampsia on birthweight. Any depression of fetal growth associated with pre-eclampsia would be exaggerated, because most cases of pre-eclampsia occur in first pregnancies, which have relatively low birthweight for gestation. In fact, a 'false positive' result might be obtained merely because of the association between pre-eclampsia and primiparity. In such comparison, the use of parity-specific standards is essential. The same sort of problems would arise in any comparison which might imply differences of maternal height and weight; for example, a comparison between ethnic groups, social classes, or even different regions of a country. The effect of maternal size was not considered in this study because the relevant data was not available. Nevertheless, fetal growth standards of this

study have given smoothed percentiles values of birthweight by gestation for all live born fetuses subdivided by sex and parity. These results are comparable with most previously published standards.

Comparison with other standards

Since 1968, Aberdeen standards have been widely adopted in Scotland and elsewhere. Clearly they are still appropriate in clinical and research applications if the population to which they are applied exhibits the same underlying pattern of fetal growth inherent in Aberdeen population. However, it may be reasonable to assume that the reproductive experience of the Aberdeen population was and remains different from that in both local population and the general Scottish population. As such, the differences in birthweight for gestational age standards reported in this study are, perhaps, not unexpected.

In this study, The QMH Group 1 and 2 standards were generally greater, later in pregnancy, than the previous Scottish standards and Aberdeen standards. The reasons for the discrepancies among the standards are complex. One possible explanation can be traced to differences in demographic, social, ethnic and environmental character-istics of the population. Recent shifts in the maternal

age, parity and social class distribution of births in
Scotland (Baird, 1980; Forbes et al,1982) may explain some
of the differences between the Aberdeen and Scottish
standards. For example, the proportion of women in the
Aberdeen sample who had three or more previous pregnancies
was 35%, whereas since 1975 this proportion was only 7% in
Scotland. The social class distribution of births has
also changed with a relative increase in social class I
and II births accompanied by a decline in social class IV
and V births.

Improvements in obstetric care and changes in obstetric
management and intervention over the past 10-20 years may
have also affected the observed relation between
birthweight and gestational age. One influence,
attributable to a number of factors including more
effective obstetric care, is the decline in stillbirth
rates at all birthweights. Improved chances of survival
will increase the number of infants being included in the
sample of live births and thus altering the centile curves
of birthweight for gestational age. The overall effect of
falling stillbirth rates on birthweight distribution
appears to be greater between 28 and 36 weeks gestation
where low birthweight infants predominate and the number
of births are small whereas at 36-40 weeks the birthweight
distribution of live births is largely independent of

changes in stillbirth rate due to a large number of births at these gestational ages (Forbes & Smalls, 1983). Nevertheless, the improvements in obstetric care offer only a partial explanation for the observed differences between QMH Groups and the various growth standards.

Changes in obstetric practice in terms of the proportion of induced deliveries may also influence the relation between birthweight and gestational age. Induced deliveries of infants with suspected growth retardation may tend to increase the number of "light" birthweight infants at short gestation and depress the corresponding birthweight distribution as growth retarded live born infants are redistributed from, say, 39 to 38 weeks gestation. This proposition was tested in this study and the distributions of induced and non-induced births displayed no systematic differences. It was only significant at the 37th week of gestation which may have occurred, most probably, by chance. These changes in obstetric practice thus appear to have no impact on the distribution of birthweight and provide no explanation for the greater centiles values of QMH Group 1 and 2, in which the percentage of non-induced labour were 82% and 100% respectively.

Since the Scottish standard 1975-79 (Forbes & Smalls, 1982) and that of the QMH Group1 (subgroups 1-6) are based on the analysis of all live singleton births with the exception that the QMH Group1 has included all women with an accurate ultrasound dating early in pregnancy, it is justifiable to consider the Scottish population as a control group. Having not forgotten the difference in the respective population sizes, nevertheless, the QMH 10th centile values are significantly higher later in pregnancy than the Scottish values. This finding could be attributed to the ultrasound dating early in pregnancy which is a routine at the time of first booking at the Queen mother's Hospital.

3.5 Conclusions and Recommendations

The accurate assessment of fetal growth in a population
requires growth standards ideally reflecting the pattern
of growth and development characteristic of that
population. This study provides local growth standards.
Tables and curves are prepared, showing the mean,
standard deviation and 5th, 10th, 25th, 50th, 75th, 90th
and 95th smoothed centile values of birthweight by
gestational age for each week of gestation from 28 to 42
weeks, subdivided by sex of infant and parity of the
mother. It appears that between 35 and 38 weeks of
gestation, the 10th centile values of QMH groups are
comparable with those recorded for Scotland (1975-9), but
beyond 38 weeks of gestation, they are significantly
higher.

The growth curves show that, between 35 and 38 weeks of
gestation, all centile lines (5th, 10th, 50th, 90th and
95th) are comparable with the Scottish centile lines
(Forbes & Smalls, 1982), but beyond 38 weeks they are
higher.

The study shows that sex of the baby and parity of the
mother have an effect on the birthweight.

Beyond 32 weeks of gestation male infants are heavier than females. Likewise infants of multiparae are heavier than infants of primiparae at most gestational ages.

The distributions of induced and non-induced births display no systematic differences and was only statistically significant at the 37th week of gestation.

Although the number of live births involved in this study was small, the results were encouraging as they were achieved by relying on groups of women with accurate ultrasound dating. This could be of great value in improving the accuracy of the growth standard. Therefore, further studies based on a large population of live births born to women with accurate ultrasound dating early in pregnancy would be ideal for a growth standard.

It is hoped that the QMH centile values will prove useful in monitoring birthweights of infants born in the QMH.

CHAPTER 4

INTRAUTERINE GROWTH RETARDATION

4. INTRAUTERINE GROWTH RETARDATION

4.1 Introduction

Intrauterine growth retardation is the term applied to an infant whose growth as a fetus was less than expected (Chudleigh & Pearce, 1986). One criterion for identifying these infants is the birthweight centile (Deter et al, 1982), and end-points on or below the 10th, 5th or 3rd centiles have been used to define small for gestational age (SGA) babies who are at increased risk of being growth retarded (Chudleigh & Pearce, 1986) and have been shown to have a high incidence of somatic and intellectual sequelae (Commey & Fitzhardinge, 1979). IUGR is commonly used incorrectly as an interchangeable term with SGA. Not all SGA fetuses are cases of IUGR. For example, most cases of symmetrical IUGR (in which there is symmetrical reduction in the size of all organs) have no demonstrable cause and probably represent the lower end of the normal range. These infants should not, therefore, be looked upon as growth retarded. On the other hand, not all cases of IUGR are SGA. For instance, if the infant was genetically" programmed" to be 4.5 kg at delivery and was only 3.7 kg it would not be SGA but would be growth retarded and could be expected to have all the problems associated with IUGR (Chudleigh & Pearce, 1986).

4.1.1 <u>Intrauterine growth retardation and fetal mortality and morbidity</u>

The intrauterine growth retarded infant is at greater risk of perinatal death , neonatal morbidity and long term physical and mental handicap (Lubchenco et al, 1963; Van den Berg & Yerushalmy, 1966; Fitzhardinge & Steven et al, 1972). In studies of perinatal mortality conducted both in this country and abroad, it has been found that a sizable proportion of perinatal loss is associated with IUGR. The report of Forbes and associates (1982) of the perinatal mortality in Scotland: 1970-1979, showed a high rate of perinatal mortality in low birth weight infants. The Scottish perinatal mortality survey for 1977 showed that 34% of perinatal deaths in singleton pregnancies occurred in association with IUGR in the absence of fetal abnormality, maternal diseases and other complications of pregnancy. The majority of these deaths occurred in utero; 45% occurred after the 36th week and most of these could probably have been prevented by planned early delivery had the diagnosis of growth retardation been established in time (McIlwaine et al, 1979). To reduce perinatal mortality, morbidity and long term handicap, there is thus a vital need for an effective method of detecting such fetuses early enough to permit intensive monitoring of fetal wellbeing during the last months of

pregnancy and during labour upon which decisions on optimal timing and mode of delivery should be based (Brook, 1983).

4.1.2 **Types of intrauterine growth retardation**

It is recognized that babies with IUGR are not a homogenous population and that at least two morphological groups can be distinguished: one in which there is symmetrical reduction in the size of all organs (symmetrical growth retardation) and the second in which the baby has a long wasted body and a relatively large brain which has been preferentially protected from the full effects of the growth retarding mechanism (asymmetrical growth retardation). The aetiological mechanisms, perinatal risks and long term prognosis appear to differ between the two groups (Campbell, 1974a).

4.1.3 Aetiology of impaired intrauterine growth

The aetiology of IUGR is complex, and will be considered
in relation to three groups of factors (Hohler, 1985)
(Fig.28): (1) Maternal (2) Placental (3) Fetal

```
┌─────────────┐
│ Maternal    │┐
│ Disease     │├┐        ┌─────────────────┐         ┌──────────────────┐
└─────────────┘││ -----> │ Poor Placental  │ -----> │ Uteroplacental   │
              ││        │ Perfusion       │         │ Insufficiency    │
┌─────────────┐││        └─────────────────┘         └──────────────────┘
│ Primary     ││┘                                             │
│ Placental   │┘                                              │
│ Pathology   │                                               ▼
└─────────────┘
┌─────────────┐
│ Congenital  │
│ Anomaly or  │ --------------------------------------> │ Fetal IUGR │
│ Infection   │
└─────────────┘
```
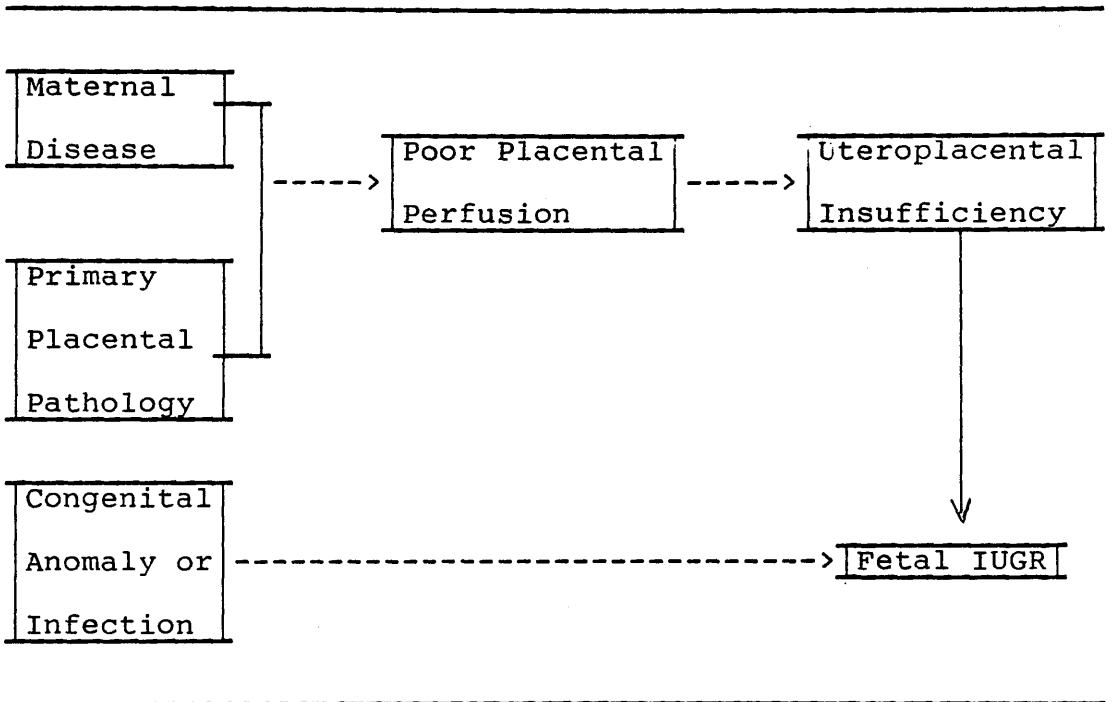
Figure 28: Categories of pathology that may lead to fetal
          IUGR are grouped into those that cause poor
          placental perfusion and those which cause
          primary anomalies, chromosomal abnormalities,
          or infection in the fetus.

1. Maternal factors

Maternal disease states, such as severe diabetes mellitus, chronic hypertension, chronic renal disease, sickle cell disease, cyanotic heart disease and some collagen diseases such as systemic lupus erythematosus, can cause vascular damage in the uteroplacental bed leading to reduced placental perfusion, which, in turn deprives the fetus of oxygen and/or vital nutrients especially glucose. Such reduced placental support of the growing fetus is broadly termed "uteroplacental insufficiency" (UPI).

2. Placental factors

Placental abnormalities such as circumvallate placenta, chronic retroplacental bleeding, placenta praevia, placenta accreta, and placental infarction, can also lead to UPI, but this is not as common as decreased placental perfusion secondary to maternal vascular disease.

3. Fetal factors

Fetal abnormalities such as cardiac malformations, a variety of anomalies of the genitourinary and central nervous systems, as well as many chromosomal abnormalities, such as trisomies 13, 18, and 21, are

frequently associated with IUGR.   In addition, certain congenital viral infections such as rubella or cytomegalic virus can also cause IUGR.

These factors can lead to two groups of growth retarded fetuses, some becoming symmetrically retarded others asymmetrically. In symmetrical retardation, occurring when there are intrinsic fetal abnormalities such as anomalies or infection, growth of the fetal head, the trunk, body length and all fetal organs are proportionately reduced compared with normal expected values.   Measurement of various parts of the fetus will, therefore, show no change in the symmetry of the fetal body.   Hence, this type of IUGR is called symmetrical or "low profile" type IUGR.   On the other hand, intrauterine growth retardation caused by uteroplacental insufficiency affects various fetal organs at different rates and to varying degrees.   This leads to an asymmetry of organ sizes.   Hence, this type is called asymmetrical or "late flattening" type of IUGR (Campbell, 1974).

4.1.4 <u>Detection of intrauterine growth retardation</u>

Although various methods have been used for prenatal detection of intrauterine growth retarded fetuses, accurate detection remains difficult. Clinical techniques of fundal height measurement for its detection have been disappointing (Beazley & Underhill, 1970). Hall and associates (1980) reported only a 44% detection rate of growth retarded fetuses, while in another study Rosenberg and associates (1982) found a 50% unsuspected rate by clinical parameters in 226 growth retarded fetuses. Only 73 of 226 were detected by palpation and 13 of 226 by poor weight gain. Ultrasonography with the ability to visualize the fetus and measure fetal body parameters and growth has potential for detection of the growth retarded fetus.

The two types of IUGR may be recognized by serial ultrasonic measurements. A late flattening growth curve detected by serial measurement of the BPD reflects asymmetrical IUGR; the BPD is within the normal range until after 30 weeks of gestation when its rate of growth slows or stops and comparisons of head and trunk growth have revealed a disproportionate decrease in the latter (Campbell & Thoms, 1977; Crane & Kipta, 1979). The second type of growth retardation, i.e low profile or

symmetrical, is characterized by a BPD that grows consistently slower than normal from as early as 20 weeks, and comparisons of head and trunk growth have revealed a proportionate decrease in trunk growth (Campbell & Thoms 1977).

Over the years several fetal parameters have been measured with ultrasound in an attempt to detect IUGR. These include:-

1. Head (Biparietal diameter 'BPD'; head area 'HA'; head circumference 'HC'; cerebellar diameter).

2. Trunk (abdominal area 'AA'; abdominal circumference 'AC'; thorax; liver; kidney; adrenal).

3. Limb (femur length 'FL'; tibia length 'TL'; feet).

4. Other measurements (crown rump length 'CRL'; total intrauterine volume 'TIUV'; qualitative amniotic fluid volume 'LV'; placental grading).

The choice of measurement depends on several factors, including the equipment, personnel and time available, in addition to fetal attitude and position.

Since the introduction of diagnostic ultrasound in obstetrics, cephalometery has been used for the assessment of gestational age and fetal growth. BPD was the first to be intensively investigated, serial BPD measurements were first introduced by Willocks (1962b) as a means of detecting placental insufficiency. However it was useful in identifying only 60-70% of cases of IUGR. Other investigators have found that BPD alone was a poor indicator, with a detection rate of only (50-60%) (Queenan et al, 1976; Sabbaga, 1978). Kurjak and associates (1980) found that both single or serial BPD determinations showed only about a 50% positive diagnostic accuracy. These results are disappointing but not surprising because measurement of the head alone ignores brain sparing which lead to asymmetrical or late flattening type of IUGR that comprises two thirds of these cases.

The cerebellum, which is housed in the posterior fossa, represents an area of the brain that is easily visualized sonographically yet has been poorly studied. Early sonographic visualization of the cerebellum occurred as early as 10 to 11 weeks' gestation. The sonographic evaluation of cerebellar growth reveals a linear relationship during the second trimester, thus the measurements in millimetres are approximately equal to the gestational age in weeks during this period (Goldstein et

al, 1987). It was found that the measurement of transverse diameter of cerebellum permits the estimation of gestational age independent of the shape of the fetal head or presentation of the fetus and also may offer more precise information regarding fetal growth than would bony measurement of the fetal head have offered (McLeary et al, 1984; Goldstein et al, 1987). Reece and associates (1987) findings indicate that growth of the transverse cerebellar diameter is unaffected by IUGR, and this measurement represents a parameter that is not affected by alteration in fetal growth and therefore could be used as a standard for gestational age against which all other biometric parameters could be compared (Reece et al, 1987). At present assessment of head size alone, using BPD, HA or HC, has been recognized as inappropriate and superseded by ultrasonic measurement of fetal trunk.

Abnormalities of fetal trunk dimension should relate well to IUGR because animal and human studies have consistently shown severely reduced hepatic glycogen stores and liver mass with IUGR (Evans et al, 1983). The best predictor of intrauterine growth retarded fetus was the AC alone or in conjunction with HC in HC/AC ratio (Wittmann et al, 1979; Kurjak et al, 1980). The HC/AC ratio was first described in 1977 (Campbell & Thoms, 1977)) and was used to distinguish between symmetrical and asymmetrical IUGR,

since a high ratio would be expected if the head was of normal size and the abdomen small because of reduced liver size. Taken in conjunction with other parameters, this is a useful measurement, but, alone it cannot be relied on since patterns of growth are so variable.

Femur length adds a relatively new easily reproducible measurement of the fetus that can be made throughout pregnancy. It has two important roles in relation to IUGR. It provides an antenatal measurement of length which can also be followed through postnatal life. Moreover, it defines another parameter for identifying symmetrical IUGR (Gregory, 1982).

As a further diagnostic possibility, ultrasonic measurement of total intrauterine volume (TIUV) has been advocated as a useful early predictor of IUGR (Gohari et al, 1977; Geirsson et al, 1985; Hobbins et al, 1987). Because of the necessity to use a contact B-Scanner, TIUV measurement has recently decreased in popularity (Grossman et al, 1982; Seed, 1984; Hohler, 1985). The qualitative assessment of amniotic fluid (amniotic fluid volume'LV') has been confirmed as a gestational age independent method for the detection of IUGR (Manning et al, 1981). The presence of a pocket of amniotic fluid less than 2.0 cm in depth is highly suggestive of SGA fetus. However, the

presence of a pocket of amniotic fluid more than 2.0 cm
does not guarantee an appropriate for gestational age
fetus (Chamberlain et al, 1984a).

Subsequent work confirms that fetal growth is best
assessed by a combination of two or more measurements.
Wittman and associates (1979), followed by Neilson and
associates (1980), compared head, abdominal and CRL
measurements as predictors of IUGR. The product of CRL and
AA gave a sensitivity of (94%) and a specificity of (90%)
in predicting IUGR at 34-36 weeks. Other investigators
suggested that FL/AC is the best indicator in the patients
with inaccurate gestational dating (Vintzileos et al,
1985).

The proper use of all these parameters, requires precise
knowledge of the duration of gestation, which is unknown
or unavaialable in 20-40% of the cases (Dewhurst &
Campbell, 1972). When the last menstrual period is
unknown or uncertain, the use of a date-independent fetal
parameter or ratio has been shown to be of great benefit
(Hadlock et al, 1983). Many studies have outlined the
roles of AC, FL/AC ratio, TL/AC ratio and qualitative
determination of amniotic fluid volume as age independent
indices in identifying intrauterine growth retarded fetus

(Dewhurst & Campbell, 1972; Gohari et al, 1977; Vintzileos et al, 1985; Divon et al, 1986).

It was the main aim of this study to identify which single measurement or combination of measurements would best discriminate the growth retarded fetus, and to assess the predictive ability by evaluating the sensitivity, specificity, predictive value of positive and negative test, of these measurements throughout gestation. In addition the associations between IUGR and perinatal mortality and morbidity are studied.

4.2 Patients and methods

4.2.1 Evaluation of the various ultrasound measurements

Applying programmes (7-15) on the computerised ultrasound and perinatal data bases, a total of 14791 measurements were obtained from 2810 women at 28 to 36 weeks gestation. All the women included in this group (group 1) had singleton pregnancies and had an ultrasound examination before 20 completed weeks of pregnancy to establish or confirm gestational age. They had a second examination at 28 to 36 weeks' gestation to assess fetal growth. For practical purposes of this thesis, birthweight below the 10th centile line on the Scottish birth weight for gestation nomogram (Forbes & Smalls, 1982) was used as a criterion to identify the growth retarded fetus. This work included some babies genetically predetermined to be small and whose intrauterine growth not subsequently retarded.

Seven different single ultrasound parameters and two pairs of combined measurements were evaluated for their ability to detect growth retarded fetuses (Table 7).

Table 7: Nine ultrasound parameters

Biparietal diameter (BPD)

Head area (HA)

Head circumference (HC)

Abdominal area (AA)

Abdominal circumference (AC)

Femur Length (FL)

Amniotic fluid volume (LV)

Abdominal area x femur length (AAFL)

Abdominal circumference x femur length (ACFL)

The equipment used and measurement techniques were described in chapter 2 (para 2.2 & 2.3).

AAFL was calculated from the product of abdominal area and femur length and ACFL from the product of abdominal circumference and femur length. Values below the 10th percentile for the various measurements were used to indicate the possibility of a fetus being growth retarded and compared with a birth weight of less than 10th centile.

<u>Programmes 7-42:</u>

Programmes 7-15: SPSS^X programmes to calculate
                  sensitivity and specificity for BPD,
                  HA, HC, AA, AC, FL, LV, AAFL & ACFL
                  for a women with a singleton
                  pregnancy and confirmed ultrasound
                  date prior to 20 weeks. (group 1)

Programmes 16-24: Same as programmes 7-15, for 14 days
                  before delivery.

Programmes 25-33: Same as programmes 7-15, 7 days before
                  delivery. (group 2)

Programmes 34-42: Same as programmes 7-15, for 2 days
                  before delivery.

The following page shows programme 10 as an example of the
programmes 7-15. This example relates to AA (group 1).
Note the programmes use the variable names TA and TC
(trunk area and trunk circumference) to denote the
measurements of abdominal area(AA) and abdominal
circumference (AC).

```
FILE HANDLE ALPHA / NAME = ":GOUA02.US85.SPFALLUM85"
FILE HANDLE BETA / NAME =":GOUA13.US86.SPFALLUM86"
FILE HANDLE GAMMA / NAME =":GOUA07.US87.SPFALLUM87"
ADD FILES FILE =ALPHA / FILE =BETA / FILE =GAMMA
SELECT IF TA GT 0
        AND NOFETUSD EQ 1 AND US LE 200 AND (WKSM GT 27 AND WKSM LT 37)
(SELECTION REPEATED FOR 14 DAYS BEFOR DELIVERY "TIMEDIFF LE 14",
        7 DAYS BEFOR DELIVERY "TIMEDIFF LE 7" OR 2 DAYS BEFOR
        DELIVERY "TIMEDIFF LE 2")
SORT CASES BY QMHNO WKSM
MATCH FILES FILE = */BY = QMHNO / FIRST= FST/LAST=LAST
VARIABLE LABELS FST ´1= FIRST RECORD FOR THIS PATIENT´
                LAST ´1= LAST RECORD FOR THIS PATIENT´
SELECT IF FST = 1
COMPUTE TACT2 = 0
MISSING VALUES TACT2 (0)
DO IF (WKSM = 15 )
RECODE TA (LO THRU  70.1 = 5)
           (  70.2 THRU  71.9 = 10)(  72.0 THRU HI = 11) INTO TACT2
           ( 778.8 THRU 809.6 = 10)( 809.7 THRU HI = 11) INTO TACT2
(PROCEDURE REPEATED FOR EACH WEEK, 15 THROU 43)
ELSE IF (WKSM = 43 )
RECODE TA (LO THRU 877.3 = 5)
           ( 877.4 THRU 877.4 = 10)( 877.5 THRU HI = 11) INTO TACT2
END IF
COMPUTE NUM = 1
COMPUTE TP=0
COMPUTE TN=0
COMPUTE FP=0
COMPUTE FN=0
DO IF (BWCT2 LE 10 AND TACT2 LE 10)
COMPUTE TP = 1
END IF
DO IF (BWCT2 GT 10 AND TACT2 LE 10)
COMPUTE FP = 1
END IF
DO IF (BWCT2 GT 10 AND TACT2 GT 10)
COMPUTE TN = 1
END IF
DO IF (BWCT2 LE 10 AND TACT2 GT 10)
COMPUTE FN = 1
END IF
SORT CASES BY WKSM
```

Programmes 7-42:

```
AGGREGATE OUTFILE = *
    / BREAK = NOFETUSD / SUMNUM SUMTP SUMFP SUMTN SUMFN = SUM (NUM TP F
                                                              P TN FN )
COMMENT *** CALCULATE SENSITIVITY AND SPECIFICITY
COMPUTE AB = SUMTP + SUMFN
DO IF (SUMTP = 0 AND SUMFN = 0)
COMPUTE AB = -1
END IF
MISSING VALUES AB (-1)
COMPUTE SENS = SUMTP / AB
COMPUTE CD = SUMTN + SUMFP
DO IF (SUMTN = 0 AND SUMFP = 0)
COMPUTE CD = -1
END IF
MISSING VALUES CD (-1)
COMPUTE SPEC = SUMTN / CD
VARIABLE LABELS SENS 'SENSITIVITY OF TEST'
                SPEC 'SPECIFICITY OF TEST'
COMMENT *** CALCULATE PREDICTED VALUE OF POSITIVE RESULT AND
COMMENT *** PREDICTED VALUE OF NEGATIVE RESULT.
COMPUTE AB = SUMTP + SUMFP
DO IF (SUMTP = 0 AND SUMFP = 0)
COMPUTE AB = -1
END IF
MISSING VALUES AB (-1)
COMPUTE PVPR = SUMTP / AB
COMPUTE CD = SUMTN + SUMFN
DO IF (SUMTN = 0 AND SUMFN = 0)
COMPUTE CD = -1
END IF
MISSING VALUES CD (-1)
COMPUTE PVNR = SUMTN / CD
VARIABLE LABELS PVPR 'PRED. VAL OF + RESULT'
                PVNR 'PRED. VAL OF - RESULT'
COMPUTE PERCTP = (SUMTP/SUMNUM) * 100
COMPUTE PERCFP = (SUMFP/SUMNUM) * 100
COMPUTE PERCTN = (SUMTN/SUMNUM) * 100
COMPUTE PERCFN = (SUMFN/SUMNUM) * 100
LIST VARIABLES  SUMNUM SUMTP PERCTP SUMFP PERCFP SUMTN
        PERCTN SUMFN PERCFN SENS SPEC PVPR PVNR
FINISH
```

Programmes 7-42: (contd.)

The indications for a second scan were as shown in table
(8). By far the commonest indication was the clinical
suspicion that the fetus was growth retarded (585
pregnancies, or 26.8%)

Table 8: Indications for referral for the second scan

Indication	No.	%
Clinical suspicion of IUGR	585	26.8
Previous history of IUGR	182	8.3
Hypertension	335	15.4
Diabetes	23	1.1
Antepartum haemorrhage/Abdominal pain	266	12.2
Miscellaneous	740	33.9
Total	2180	100.0

Data analysis was performed using the SPSS[x] package. The
predictive ability of the different parameters was
assessed by calculating the sensitivity, (i.e. the

probability of obtaining an abnormal test result in babies eventually having an abnormal birthweight), specificity, (i.e. the probability of obtaining a normal test result in babies eventually having a normal birthweight) and predictive value of a positive and negative tests (i.e. probability of being abnormal/normal if the test is positive/negative). A chi-square test was used to analyse the differences.

Similar calculations and methods were followed in a subgroup of women (group 2) selected by using programmes (25-33) from group 1 who delivered within one week of the second ultrasound examination. Furthermore, analysis was repeated on a subgroup of women (group 3) selected by using programmes (34-51) from group 1, who had undergone the second ultrasound examination at 35 weeks gestation.

With regard to AA, AC, AAFL and ACFL measurements, the efficacy was calculated by using programmes [(43-51),(52-60), (61-69) & (70-78)] in different subgroups of women (group 4, 5, 6 & 7), who had undergone the second examination at 34 weeks gestation and within two weeks, one week, and two days of delivery respectively. The size of the 'at risk' group (%) selected by the test was found by dividing the 'true-positive' + 'false-positive' tests by the total number tested x 100.

Programmes 43-78:

Programmes 43-51: Same as programmes 7-15, for each week
                   of gestation from 28 to 36, [at 35th
                   week of gestation (group 3)].

Programmes 43-51: Same as programmes 7-15, for each week
                   of gestation [at 34th week (group 4)].

Programmes 52-60: Same as programmes 43-51, for 14 days
                   before delivery (group 5).

Programmes 61-69: Same as programmes 43-51, for 7 days
                   before delivery (group 6).

Programmes 70-78: Same as programmes 43-51, for 2 days
                   before delivery (group 7).

The following page shows programme 46 as an example of the
programmes 43-78. This example relates to AA (group 3).

```
FILE HANDLE ALPHA / NAME = ":GOUA02.US85.SPFALLUM85"
FILE HANDLE BETA / NAME =":GOUA13.US86.SPFALLUM86"
FILE HANDLE GAMMA / NAME =":GOUA07.US87.SPFALLUM87"
ADD FILES FILE =ALPHA / FILE =BETA / FILE =GAMMA
SELECT IF TA GT 0
      AND NOFETUSD EQ 1 AND US LE 200 AND (WKSM GT 27 AND WKSM LT 37)
(SELECTION REPEATED FOR 14 DAYS BEFOR DELIVERY "TIMEDIFF LE 14",
      7 DAYS BEFOR DELIVERY "TIMEDIFF LE 7" OR 2 DAYS BEFOR
      DELIVERY "TIMEDIFF LE 2")
SORT CASES BY QMHNO WKSM
MATCH FILES FILE = */BY = QMHNO / FIRST= FST/LAST=LAST
VARIABLE LABELS FST ´l= FIRST RECORD FOR THIS PATIENT´
                LAST ´l= LAST RECORD FOR THIS PATIENT´
SELECT IF FST = 1
COMPUTE TACT2 = 0
MISSING VALUES TACT2 (0)
DO IF (WKSM = 15 )
RECODE TA (LO THRU  70.1 = 5)
          (  70.2 THRU  71.9 = 10)(  72.0 THRU HI = 11) INTO TACT2
          ( 778.8 THRU 809.6 = 10)( 809.7 THRU HI = 11) INTO TACT2
(PROCEDURE REPEATED FOR EACH WEEK, 15 THROU 43)
ELSE IF (WKSM = 43 )
RECODE TA (LO THRU 877.3 = 5)
          ( 877.4 THRU 877.4 = 10)( 877.5 THRU HI = 11) INTO TACT2
END IF
COMPUTE NUM = 1
COMPUTE TP=0
COMPUTE TN=0
COMPUTE FP=0
COMPUTE FN=0
DO IF (BWCT2 LE 10 AND TACT2 LE 10)
COMPUTE TP = 1
END IF
DO IF (BWCT2 GT 10 AND TACT2 LE 10)
COMPUTE FP = 1
END IF
DO IF (BWCT2 GT 10 AND TACT2 GT 10)
COMPUTE TN = 1
END IF
DO IF (BWCT2 LE 10 AND TACT2 GT 10)
COMPUTE FN = 1
END IF
SORT CASES BY WKSM
```

Programmes 43-78:

```
AGGREGATE OUTFILE = *
   / BREAK = WKSM / SUMNUM SUMTP SUMFP SUMTN SUMFN = SUM (NUM TP FP TN
                                                           FN )
COMMENT *** CALCULATE SENSITIVITY AND SPECIFICITY
COMPUTE AB = SUMTP + SUMFN
DO IF (SUMTP = 0 AND SUMFN = 0)
COMPUTE AB = -1
END IF
MISSING VALUES AB (-1)
COMPUTE SENS = SUMTP / AB
COMPUTE CD = SUMTN + SUMFP
DO IF (SUMTN = 0 AND SUMFP = 0)
COMPUTE CD = -1
END IF
MISSING VALUES CD (-1)
COMPUTE SPEC = SUMTN / CD
VARIABLE LABELS SENS 'SENSITIVITY OF TEST'
                SPEC 'SPECIFICITY OF TEST'
COMMENT *** CALCULATE PREDICTED VALUE OF POSITIVE RESULT AND
COMMENT *** PREDICTED VALUE OF NEGATIVE RESULT.
COMPUTE AB = SUMTP + SUMFP
DO IF (SUMTP = 0 AND SUMFP = 0)
COMPUTE AB = -1
END IF
MISSING VALUES AB (-1)
COMPUTE PVPR = SUMTP / AB
COMPUTE CD = SUMTN + SUMFN
DO IF (SUMTN = 0 AND SUMFN = 0)
COMPUTE CD = -1
END IF
MISSING VALUES CD (-1)
COMPUTE PVNR = SUMTN / CD
VARIABLE LABELS PVPR 'PRED. VAL OF + RESULT'
                PVNR 'PRED. VAL OF - RESULT'
COMPUTE PERCTP = (SUMTP/SUMNUM) * 100
COMPUTE PERCFP = (SUMFP/SUMNUM) * 100
COMPUTE PERCTN = (SUMTN/SUMNUM) * 100
COMPUTE PERCFN = (SUMFN/SUMNUM) * 100
LIST VARIABLES  WKSM SUMNUM SUMTP PERCTP SUMFP PERCFP SUMTN
        PERCTN SUMFN PERCFN SENS SPEC PVPR PVNR
FINISH
```

Programmes 43-78: (contd.)

Furthermore, for AA, AAFL, FL, ACFL and AC measurements, the rate of 'false-negative' (i.e. the percentage of an abnormal birthweight fetuses who are incorrectly detected by the test as having a normal birthweight) and 'false-positive' (i.e. the percentage of a normal birthweight fetuses who are incorrectly detected by the test as having an abnormal birthweight) was calculated and compared in a subgroup of women (group 2) between 28 and 36 weeks of gestation by a single examination within one week of delivery.

To compare the overall performance of AA, AAFL, FL, ACFL and AC measurements, two statistical procedures were applied on the bases of two assumptions: (1) The 'Law of Total Probability' was applied on the first assumption that 'false-negative' and 'false-positive' results are equally bad. (2) A variation of the first procedure was used to investigate the minimal average cost on the basis of a second assumption, namely that, in clinical terms, the cost of a 'false-negative' result is much higher than of a 'false-positive result. The cost of the 'false-negative' result was assumed to be more than 10 times that of the 'false-positive'.

To deal with these situations Infants with birthweights less than the 10th centile were refered to as abnormal (A), and those equal and more than the 10th centile were refered to as normal (N). Ten per cent of all infants were (A), so the probability of a randomly selected infant being abnormal is p(A) = 0.10. Similarly, p(N) = 0.90. Using these notations for the outcome of a predictive procedure, the error probabilities are:

probability (false-negative) = P (PN|A)
probability (false-positive) = P (PA|N)

To deal with assumption (1), the overall probability of error (mistake), i.e the probability that an infant chosen at random from the population will be wrongly classified by any of the measurements (AA, AAFL, FL, ACFL & AC) was calculated by using the following equation:

$$P \text{ (mistake)} = [\ P(PN|A) \ \times \ P(A) \ ] + [\ P(PA|N) \ \times \ P(N) \ ]$$

On the basis of assumption (2), that 'false-negative' results are more serious than 'false-positive' results, costs were assigned to each outcome,

i.e. C_1 = Cost of 'false-negative'

C_2 = Cost of 'false-positive'

To compare the performance of the different measurements the cost of a 'false-negative' was assumed to be more than 10 times than that of 'false-positive. e.g. 11 times

So $C1 = 11 \times C2$

   $C2 = 1/11 \ C1$

   $C2 = 0.09 \ C1$

The average cost for each measurement was calculated by applying the formula of the 'Minimal Average Cost' procedure.

$$[\ C1 \times P(PN|A) \times P(A) \ ] + [\ C2 \times P(PA|N) \times P(N) \ ]$$
$$= [\ C1 \times P(PN|A) \times P(A) \ ] + [\ 1/11 \ C1 \times [\ P(PA|N) \times P(N) \ ]$$
$$= C1 \ [\ [\ P(PN|A) \times P(A) \ ] + 1/11 \ [\ P(PA|N) \times P(N) \ ] \ ]$$

4.2.2 Intrauterine growth retardation and perinatal mortality and fetal malformation

Applying programme (79) on the computerised ultrasound and perinatal data bases, a total of 1838 women were selected in this part of the study and divided in to two groups, The study group (group 1) comprised 919 consecutive women who delivered growth retarded infants. The results in these pregnancies were compared with a control group of 919 women (group 2), delivered immediately subsequent to each study woman, whose infants were not growth retarded.

```
FILE HANDLE R /NAME=":GOUV01.LIB7.GROUPA"
FILE HANDLE A/NAME=":GOUV01.LIB7.GROUPB"
ADD FILES FILE = R/FILE= A
SELECT IF NOFETUSD EQ 1
RECODE BWCT2 (LO THUR 10=1)(11 THRU HI=2) INTO GROPA
CROSSTABS VARIABLES = GRPA (1,2) PNRW (0,1)
                    /TABLES = GRPA BY PNRW
STATISTICS 1
```

Programme 79: SPSS[x] programmes to calculate chi-square test for cases (group 1) and controls (group 2)(as defined on pp 86 & 87) with regard to perinatal mortality.

```
SELECT IF NOFETUSD EQ 1
RECODE BWCT2 (LO THRU 5=1)(6 THRU 10=2)(11 THRU HI=3) INTO
GRPB
CROSSTABS VARIABLES = GRPB (1,2) PNRW (0,1)
                  /TABLES = GRPB BY PNRW
STATISTICS 1
```

Programme 80: SPSS[x] programmes to calculate chi-square test for the study groups (group 3 & group 4) with regard to perinatal mortality.

```
SELECT IF NOFETUSD EQ 1
RECEDE BWCT2 (LO THRU 10=1)(11 THRU HI=2) INTO GRPA
RECODE FADEL@A (1 THRU HI=1)(ELSE=COPY)
CROSSTABS VARIABLES = GRPA (1,2) FADEL@A (0,1)
                  /TABLES = GRPA BY FADEL@A
STATISTICS 1
```

Programme 81: Same as programme 79, with regard to congenital malformation.

Women with multiple pregnancies were excluded. Infants were defined as growth retarded when the birthweight was below the 10th centile according to the Scottish birth weight for gestation nomogram (Forbes & Smalls, 1982). The study group (group 1) was divided into two subgroups, those of birthweight less than the 5th centile (group I), and those between the 5th and 9th centiles (group II). The control group (group 2) was those of birthweight centiles between 10th and 100th. Perinatal deaths were defined as stillbirths and deaths occurring in live born within 28 days of birth.

The study and control groups were compared in term of incidence of perinatal deaths and congenital malformation.

Congenital malformed infants were classified as: (1) neural tube defect (NTD); (2) abdominal wall defect (AWD); (3) urinary tract defect (UTD); (4) skeletal defect (Skeletal D); (5) chromosome defect (Chromosome D); (6) Rhesus disease (Rh/Ab); (7) cardiac defect (Cardiac D); (8) other (Other D).

The chi-square test was performed to analyse for differences.

4.3 RESULTS

4.3.1 Evaluation of the various ultrasound measurements

Of the 2180 women in the study population group 1, 990 (45.4%) were primiparae and 1190 (54.5%) multiparae . The mean birthweight of the infants was 3.150 Kg. Three hundred and fifty (350) newborn infants weighed less than 10th centile (16% prevalence).

Table 9 displays the diagnostic efficiency of single and combined ultrasonic measurements performed between 28 and 36 weeks of gestation. From table 9A, it can be seen that of the single parameters abdominal measurements have the highest sensitivity, predictive value of positive test and predictive value of negative test with a comparable specificity to the other parameters. Sensitivity was equal for AA and AC measurements, but lower with BPD and FL and considerably lower with HA and HC. The result obtained by combining two parameters in various ways is shown in table 9A. The AAFL and ACFL measurements showed a higher sensitivity, (36%) and (34%) respectively. Overall, the sensitivity of the AAFL measurement was the highest, and the difference between the number of growth retarded fetuses detected by AAFL and FL was statistically significant. (Chi-square = 6.55; p<0.02). The specificity

was high and similar for all measurements single or combined. The predictive values of negative tests were also high and almost the same for all measurements.

Substantial improvement in the sensitivity and the predictive value of a positive test for all parameters was seen when the scan was performed one week before delivery (group 2), (Table 9B). The differences between the number of growth retarded fetuses detected correctly by AAFL and FL was statistically significant, (chi-square = 4.42; $p < 0.05$) and that between AA and FL was significant, (chi-square = 4.24; $p < 0.05$).

Table 9: Detection of IUGR by various methods

A. Ability to detect IUGR by single examination between 28
   and 36 weeks of gestation

Para-meter	No.	Sensi-tivity %	Speci-ficity %	Predictive value of a (+ve) test %	Predictive value of a (-ve) test %	At risk group %
BPD	1234	21	95	44	87	7.5
FL	1074	20	93	36	86	8.8
HA	1229	24	93	39	87	9.6
HC	1260	27	94	44	87	9.7
AA	2137	29	95	52	89	8.0
AC	2150	29	96	52	89	8.0
LV	1501	13	92	22	86	8.9
AAFL	1050	36	95	57	89	9.8
ACFL	1062	34	95	58	88	9.0

B. Ability to detect IUGR when scan performed between 28 and
   36 weeks by a single ultrasound examination within one week
   of delivery

Para-meter	No.	Sensi-tivity %	Speci-ficity %	Predictive value of a (+ve) test %	Predictive value of a (-ve) test %	At risk group %
BPD	79	56	87	56	87	22.8
FL	75	28	81	31	78	21.3
HA	81	45	85	53	81	23.5
HC	185	46	89	61	81	20.0
AA	173	81	85	59	94	28.3
AC	175	86	84	58	96	30.1
LV	125	38	74	28	82	28.8
AAFL	72	94	76	57	98	41.7
ACFL	74	89	71	50	95	43.2

A similar trend was seen when those women with scans that were performed at 35 weeks of gestation (group 3) were considered (Table 10). The sensitivity for AAFL, ACFL, AA and AC was the highest (47%), (42%), (39%) and (34%) respectively, whereas BPD, FL and LV gave the lowest (19%), (17%) and (14%) respectively, the differences were statistically significant for AAFL and LV. (Chi-square = 3.62; $p < 0.05$).

Specificity was similar for all parameters. The predictive value of a positive test was higher for AAFL, ACFL, AA and AC, 82%, 80%, 79% and 72% respectively, and lowest for FL and LV, (33) and (25) respectively. The difference was statistically significant between AAFL and LV, (chi-square = 2.84; $p < 0.05$). the values for HC and HA were in between.

The predictive value for a negative test was greater than 81% for all ultrasound variables.

The four parameters AA, AC, AAFL and ACFL, were compared in those patients (group 4, 5, 6 & 7) whose scans were performed at 34 weeks of gestation, within two weeks, within one week and within two days of delivery respectively (Table 11A, B, C & D). In this comparison, AAFL and ACFL showed equally good results. Also, it was

apparent that the sensitivity and the predictive values of positive test for all the measurements rose steadily with the rise in the percentage of 'at risk' group, for example the sensitivity for AAFL rose from 44% to 100% when the percentage of 'at risk' group rose from 10.9% to 66%.

Table 10: Efficiency of various measurements in predicting
          IUGR at 35 weeks of gestation

Para-meter	No.	Sensi-tivity %	Speci-ficity %	Predictive Value of a (+ve) Test %	Predictive Value of a (-ve) Test %
BPD	127	19	97	63	82
FL	101	17	93	33	84
HA	122	25	93	50	81
HC	124	26	92	47	82
AA	246	39	98	79	90
AC	249	34	98	72	89
LV	183	14	92	25	85
AALF	99	47	97	82	89
ACFL	102	42	98	80	88

Table 11:   Detection of IUGR by AA, AC, AAFL & ACFL
            measurements

A. Ability to detect IUGR by single ultrasound examination
   at 34 weeks of gestation

Para-meter	No.	Sensi-tivity %	Speci-ficity %	Predictive value of a (+ve) test %	Predictive value of a (-ve) test %	At risk group %
AA	272	36	97	62	91	8.5
AC	276	35	95	54	90	8.7
AAFL	129	44	97	82	89	10.9
ACFL	130	42	95	62	91	10.0

B. Ability to detect IUGR when scan performed at 34 weeks
   of gestation by a single ultrasound examination within
   two weeks of delivery

AA	41	73	87	67	90	29.3
AC	41	91	87	71	96	34.1
AAFL	18	86	82	75	90	44.4
ACFL	18	100	73	70	100	55.6

C. Ability to detect IUGR when scan performed at 34 weeks
   of gestation by a single ultrasound examination within
   one week of delivery

AA	27	88	84	70	94	37.0
AC	27	100	74	62	100	48.1
AAFL	13	100	71	75	100	61.5
ACFL	13	100	57	67	100	69.2

D. Ability to detect IUGR when scan performed at 34 weeks
   of gestation by a single ultrasound examination within
   two days of delivery

AA	14	100	70	57	100	59.0
AC	14	100	60	50	100	57.1
AAFL	5	100	67	67	100	66.0
ACFL	5	100	33	50	100	80.0

Table 12: Comparison of AA, AAFL, FL, ACFL & AC in detection of IUGR between 28 and 36 week of gestation by a single examination within one week of delivery

Parameter	Detection of growth retarded fetuses %	False-negative %	False-positive %
AA	81	19.0	8.5
AAFL	94	5.5	24.0
FL	28	72.0	19.0
ACFL	89	11.0	29.0
AC	86	14.0	16.0

Table 12 gives the results for AA, AAFL, FL, ACFL & AC measurements between 28 and 36 weeks of gestation. The FL measurements were inefficient since they identified only 28% of growth retarded fetuses. In contrast, the combination of AC or AA with FL correctly identified 86% and 81% of cases respectively.

Though the 'false-negative' rate obtained with FL was 72%

and that with AA was 19%, the product of these two measurements AAFL gave a 'false-negative' rate of only 5.5% (Table 12). Also the product ACFL gave a 'false-negative' rate of 11% which is less than FL and AC which were 72% and 14% respectively. Overall, AAFL was the most efficient combined parameter (Table 12).

To compare the overall performance of AA, AAFL, FL, ACFL and AC measurements, the 'Law of Total Probability' was applied on the basis of the first assumption that 'false-negative' and 'false-positive' results are equally bad (page 85). The formula of the 'Minimal Average Cost' procedure (page 86) was applied on the second assumption that the cost of a 'false-negative' result was more than 10 times higher than that of a 'false-positive' result, e.g. 11 times. One example of these applications as used on the figures related to AA measurements in table 12 (page 95) generated the following results:-

```
                0.915
0.90 N
                0.085 PA*
        0.190 PN*
0.10 A
        0.810 PA
```
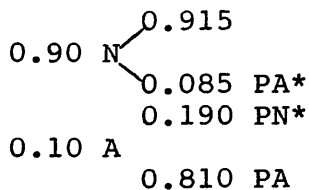
* mistakes

Assumption (1)
If C1 = C2

$$P(mistake) = [P(PN|A) \times P(A)] + [P(PA|N) \times P(N)]$$
$$= [0.190 \times 0.10] + [0.085 \times 0.90]$$
$$= 0.0190 + 0.0765$$
$$= 0.0955$$

Assumption (2)

```
If Cl = 11 x C2
[Cl x P(PN|A) x P(A)] + [C2 x P(PA|N) x P(N)]
So average cost = Cl [0.0190 + 0.0765/11]
                = Cl [0.0190 + 0.00695]
                = Cl x 0.026
```

Table 13 shows the probability of mistake for AA, AAFL, FL, ACFL & AC measurements. On the basis of assumption that ,in clinical term, the 'false-negative' and 'false-positive' results are equally bad, the AA was the best measurement since it gives clearly the lowest probability of mistake (0.0955). While on the assumption that, in clinical terms, the cost of 'false-negative' result is much higher than the 'false-positive' result and on the assumption that the cost of the 'false-negative' is more than 11 times the average cost of AAFL measurement was 0.025 x Cl (Table 14).

Table 13: Summary of the probabilities of mistake for
AA, AAFL, FL, ACFL & AC parameters

Parameters	P(mistake)
AA	0.0955
AAFL	0.2215
FL	0.2430
ACFL	0.2720
AC	0.1580

Table 14: Summary of the average cost for AA, AAFL, FL,
ACFL & AC parameters

Parameters	Average cost
AA	0.026 X C1
AAFL	0.025 X C1
FL	0.087 X C1
ACFL	0.034 X C1
AC	0.027 X C1

4.3.2 Intrauterine growth retardation and perinatal mortality and fetal malformation

Perinatal mortality

Table 15 shows that the perinatal mortality rate associated with fetal growth retardation in the study group was 3.9% compared with 0.3% in the control group. The difference was statistically significant (chi-square = 26.82; p = 0.0000)

Within the study group, the perinatal mortality rate for infants of birthweight less than the 5th centile (group 1) was 6.4% while that for those whose birthweight between 5th and 9th centile (group II) was 1.7%, and the difference was statistically significant (chi-square test = 12.39; p = 0.0004), (Table 16).

Table 15: Two-way table of alive versus dead fetuses for
         study group (group 1) versus control group
         (group 2)

Group	Birthweight centile	Alive	Dead	Total
Study (group 1)	0 - 9	883 (96.1%)	36 (3.9%)	919 (50%)
Control (group 2)	10 -100	916 (99.7%)	3 (0.3%)	919 (50%)
Total		1799	39	1838

Chi-square = 26.82
       DF = 1
        p = 0.0000 (significant)

NB - Twenty-one congenitally malformed fetuses are
      included in the study and control groups.

Table 16: Two-way table of alive versus dead fetuses for
         study group (group I) versus study group
         (group II)

Group	Birthweight centile	Alive	Dead	Total
Study (group I)	0 - 4	410 (93.6%)	28 (6.4%)	438 (47.7%)
Study (group II	5 - 9	473 (98.3%)	8 (1.7%)	481 (52.3%)
Total		883	36	919

Chi-square = 12.39
       DF = 1
        p = 0.0004 (significant)

Fetal malformation

There was a significant difference between the incidence of fetal malformation in the study and the control group (chi-square = 12.33; p = 0.0002) (Table 17).

Table 18 shows the distribution in fetal malformation categories for study and control group. It was obvious that the numbers of cases of different types of fetal malformation were higher in the study group.

Table 17: Two-way table of congenitally malformed versus normal fetuses for study group (group 1) versus control group (group 2)

Group	Birthweight centile	No fetal malformation	Fetal malformation	Total
Study (group 1)	0 - 9	900 (97.9%)	19 (2.0%)	919 (50%)
Control (group 2)	10 -100	917 (99.8%)	2 (0.2%)	919 (50%)
Total		1817	21	1838

Chi-square = 12.33
      DF = 1
       p = 0.0004 (significant)

Table 18: Distribution in fetal malformation categories for study group (group 1) and control group (group 2)

Fetal malformation	Study (group 1) n=919	Control (group 2) n=919
Neural Tube Defect	1	0
Abdominal Wall Defect	4	0
Urinary Tract Defect	1	0
Skeletal Defect	0	1
Chromosomal Defect	6	0
Rhesus	1	0
Cardiac Defect	1	0
Others	5	1
Total	19 (19/919=2.07%)	2 (2/919=0.22%)

4.4 Discussion

4.4.1 Evaluation of various ultrasound measurements

The development of accurate ultrasonographic method for
the antenatal detection of IUGR remains a major concern.
Several studies assessing the effectiveness of various
ultrasonic measurements have been published. Direct
comparison with these studies is difficult as demonstrated
by Deter and associates (1982). Studies vary in their
definition of IUGR, the criteria used in the postnatal
identification of IUGR infants, the cut-off point of the
ultrasound measurement values and the dating method
employed. Published normal birthweight distributions also
vary as they are dependent on genetic, environmental, and
social factors, as well as statistical handling.
Interstudy comparisons are also made difficult by the
lack of reporting results with all standard statistical
parameters, e.g. the predictive value of a positive test
may be given, but without the sensitivity. The sensitivity
and true positive rates are also affected by the nature of
the study population, whether it is a small group of
intensively studied patients at a high risk or a screening
test for a large patient population. In this study we
determined the sensitivity, specificity, and predictive
values of positive and negative tests, when groups of the

QMH obstetric population and subgroups of 'at risk' patients were considered.

In contrast to the previous studies which had the confounding factor of using only menstrual dating, in this study all patients had an estimation of gestational age made by ultrasound by 20 weeks gestation followed by a second examination at 28 to 36 weeks. This approach, in conformity with other investigators (Neilson et al, 1980; Neilson et al 1984) gave a unique opportunity to remove the effect of uncertain gestational age from the study.

This study showed that head measurements were generally less efficient than the trunk measurements, the poorest sensitivity values being for BPD (21%). This finding is consistent with previous investigations by Warsof and associates (1986) who reported detection rates of 25% for a single BPD determination. Although previous reports by Queenan and associates (1976), Sabbagha (1978), Neilson and associates (1980), Kurjak and associates (1980), gave detection rates ranging from (50-60%), still these results were disappointing. Similarly, in this study, HA and HC measurements were inefficient since their detection rates were only 24-27%. Because the fetal HC has a close relationship to brain weight (Epstein & Epstein, 1978) and is a more shape-independent measurement than the BPD

(Hadlock et al, 1983), it should, theoretically, set a better standard of head size which might explain why HC had a higher detection rate than HA and BPD. The common explanation of the lower detection rates of head measurements is that of brain-sparing effect in many cases of IUGR. In such cases, brain weight is relatively less diminished than liver weight where hepatic glycogen stores and Liver mass are severely reduced (Gruenwald, 1974; Evans et al, 1983).

Our results showed that AC and AA, when used singly, had high detection rates (86% and 81%, respectively) and the 'false-negative' rates were considerably lower (14% and 19%, respectively). This finding agrees with that of Neilson and associates (1980) who reported a detection rate for SGA fetuses of 83% with AC and (81%) with AA, and the 'false negative' rates were 17% and 19%, respectively.

Other investigators (Varma et al, 1979; Neilson et al, 1984) studied the efficiency of AA in an 'at risk group' and the sensitivity was 80% and 91% respectively. Our result was comparable to that at 81%.

The effect of IUGR on the sonographic growth profile of the neonate depends on the time of initial insult and the duration and degree of the insult (Villar & Belizan,

1982). Fetuses that are affected in the first trimester of pregnancy (chromosomal abnormality, infection) are symmetrically small throughout gestation with weight, length and head circumference below the 10th centiles. If the insult occurs late in the second trimester of pregnancy, the first organ to be affected is the fetal liver, while there is a relative sparing of the fetal head size and length (asymmetrical growth retardation)(Villar & Belizan, 1982). It is this period of time when the ultrasound findings are compatible with the decreased fetal AA and AC, therefore abnormal AA and AC.

In the present study, FL measurement was the least accurate of all variables. The sensitivity was 28% and the 'false-negative' rate was 72%. Similarly, Woo and associates (1985) could not detect any pattern of growth retardation in the FL. Though Gregory and associates (1982) found that symmetrical growth retardation could be identified by shortened FL, they believed that the ability to detect IUGR should be improved with a three-dimensional image of the fetus with the use of FL and AC.

In this study, the addition of the FL measurement to that of the AC or AA improved the detection rate and decreased the 'false-negative' rates. The 'false-negative' rate obtained with FL alone was 72% and that obtained with AA

alone was 19%, while the combination of FL and AA gave a 'false-negative' rate of only 5.5%. Similarly, the combination of FL and AC gave a 'false-negative' rate of 11% while that obtained with AC alone was 14%. The most likely explanations is that, the growth of the fetal abdomen is the first to be impaired in some cases of IUGR. Besides, in utero the AC or AA is known to be the factor most closely related to fetal weight (Warsof et al, 1977; Woo et al, 1984), whereas the fetal long bones (femur) are known to correlate with the length of the fetus (O'Brien & Queenan, 1981) and closely related to the fetal crown-heel length (Hadlock et al, 1984). Therefore, the combination between the FL and AC or AA may provide better assessment of fetal size.

Several investigators evaluated the usefulness of the relationship between the FL and BPD in utero and showed that a high detection rate for growth retarded fetuses by the FL/BPD ratio was possible (Waldimiroff et al, 1978; Varma et al, 1979; Wittman et al, 1979; Neilson et al, 1980; Hohler & Quetel, 1981; Woo et al, 1985). In this study, trunk measurements were added to that of FL because they had an added advantage of being more affected than head measurement by growth retardation. Moreover, BPD is subject to head shape variation (e.g. dolichocephaly, brachycephaly) in utero, both as a variant of normal

development and as a result of molding, or rarely, premature closure of sutures (Hadlock et al, 1981; Kasby & Poll, 1982; Wolfson et al, 1983) and fetal position (e.g. breech presentation, transverse lie), which could result in falsely high or low values when evaluating FL against BPD.

The AAFL and AA were equally good as they, respectively, picked out 94% and 81% of growth retarded fetuses of a population where the prevalence of the birthweight less than 10th centile was 16%. However a 24% of 'false-positive' rate for AAFL should not be ignored. In general, a procedure that gives a low 'false-negative' rate will give a high 'false-positive' rate and vice versa. Because 'false-negative' results are of greater significance than 'false-positive' results, i.e. the 'false-negative is more costly than the 'false-positive', AAFL had a better performance, since it gave the lowest average cost. Also it was a more useful index than the ACFL, which was associated with a slightly higher 'false-negative' and 'false-positive' rates.

In this study, the sensitivity of LV of less than 10th centile (i.e. ranging from 4.4-4.6 cm from 28 to 36 weeks of gestation) was suboptimal at 38%. This was slightly higher than the previous reports. Philipson and

associates (1983), Chamberlain and associates (1984) and Divon and associates (1986) showed that the sensitivity of LV of less or equal to 2 cm for identification of growth retarded fetus was 15.5%, 13% and 11% respectively. This difference may be accounted for, in part, by the difference in the criteria for normal and abnormal LV, for the cut-off value of less than 10th centile was used in this study which may have attributed to a slightly higher sensitivity.

The predictive accuracy of a test is determined in part by the interval between scan and delivery. The greater the time interval the more chance that a growth abnormality could develop after the scan or that catch-up growth would occur by appropriate therapeutic intervention. This is seen clearly in improved accuracy in table 11A, B, C & D. On the other hand, the clinical usefulness of the information in providing early warning of IUGR decreases as pregnancy advances. As obstetric events frequently cannot be predicted, it usually is difficult to control this time interval. Nevertheless, scanning at 34 weeks of gestation with high rates of sensitivity and specificity would compromise between the efficiency of the test and the clinical usefulness of the information provided.

4.4.2 Intrauterine growth retardation and perinatal mortality and morbidity

Intrauterine growth retardation is recognised as a cause of significant perinatal morbidity and mortality. The present study, in conformity with previous investigations (Scott & Usher, 1966; Low & Galbraith, 1974; Jones et al, 1977; McIlwaine et al, 1979; Dobson et al, 1981; Forbes et al, 1982) showed that fetal growth retardation had a significant positive association with perinatal mortality and congenital malformation. It also showed that fetuses of birthweight less than the 5th centile for gestational age were at greater risk of perinatal death than those whose birthweight was between the 5th and 9th centiles. This result is in agreement with that of Dobson and associates (1981).

Previous reports indicated a close association between intrauterine growth retardation and fetal malformation (Scott & Usher, 1966; Dobson et al, 1981). This association was confirmed in this study. Many factors contribute to the association between IUGR and perinatal morbidity and mortality. Perinatal asphyxia is the most serious clinical complication of infants with IUGR (Scott & Usher, 1966). These infants are prone to develop intrauterine asphyxia and are at increased risk in the

neonatal period from hypothermia (Burnard & Cross, 1958), hypoglycaemia (Lubchenco & Bard, 1971), hypocalcemia, polycythemia (Lugo & Cassady, 1971; Tsang et al, 1974). Furthermore, babies who survive the neonatal period, are susceptible to higher incidences of subsequent neurological and behavioral disturbances, such as cerebral palsy, convulsion, mental retardation, and educational subnormality (Fitzhardinge & Steven, 1972; Fancourt et al, 1976)

4.5 <u>Conclusions and Recommendations</u>

In obstetrics today, IUGR can be diagnosed in almost all cases by ultrasound. This study demonstrates that head measurements (BPD, HA, HC) are poor predictors of the growth retarded fetus due to the brain-sparing effect present in many cases of IUGR. The abdominal measurements (AA, AC) are more sensitive guide to IUGR because reduced liver size is an early feature of IUGR.

The sensitivity of LV measurement, within one week of delivery, of less than 10th centile (range: 4.4-4.6 cm from 28 to 36 weeks of gestation) was suboptimal. Consequently, LV measurement does not appear to be useful, on its own, in the detection of growth retarded fetus.

It is interesting that the combination of FL measurement with that of abdomen has markedly improved the diagnostic accuracy over that of single measurement of FL, AA and AC. This indicates again that the growth of the fetal abdomen is the first to be impaired. It also supports the hypothesis that a combination of length and cross-section provides a better assessment of fetal size.

In conclusion, the combination of AA with FL is the most predictive measurement of IUGR as it has the highest sensitivity, specificity and predictive value of positive and negative test rates, and the lowest 'false-negative' rate. Because 'false-negative' results are of greater significance than 'false-positive' results, the AAFL measurement is a more useful indicator than the AA as it gives the lowest average cost. Despite a 'false-positive' rate of 24%, the AAFL measurement is still potentially useful in the management of a high risk pregnancies. It may be used as part of a standard obstetric ultrasound examination for the assessment of fetal growth in the second and third trimesters. Furthermore, calculation of the product of AA and FL by a single examination in mid third trimester is practically quick and simple. Combined with accurate ultrasound dating of gestational age early in pregnancy, high sensitivity, and predictive value of negative test, it would be potentially suitable as a screening procedure for the detection of IUGR. Such procedure would accommodate itself well into the philosophy of antenatal care that risk is better assessed by investigation of the individual fetus than by epidemiological considerations (BMJ Editorial, 1978).

This study shows that fetal growth retardation has a significant positive association with the perinatal mortality and fetal malformation. In particular, infants of birthweight below the 5th centile are at a greater risk of perinatal mortality. To reduce the existing mortality and morbidity associated with the growth retarded fetus, an early antenatal diagnosis of impaired fetal growth is of paramount importance for appropriate timed delivery and intensive intrapartum and neonatal care.

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