THE MEASUREMENT OF SKINFOLD THICKNESS IN NEWBORN INFANTS.

by

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TABLES AND ABBREVIATIONS

ABBREVIATIONS

SFT = Skinfold Thickness.
SF = Skinfold.
BW = Birth Weight.
LFD = Light-For-Dates.
C/R = Crown-Rump.
C/H = Crown-Heel.

ABBREVIATIONS (cont'd)

$$R_F = \frac{\text{Distance Substance Travels From Origin.}}{\text{Distance Solvent Front Travels From Origin.}}$$

ILLUSTRATIONS

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SUMMARY

This thesis concerns the Caliper Measurement of Skinfold Thickness in newborn infants. The technique has been used in adults for about eighty years and provides values which have been shown to be closely related to body fat as calculated from volumetric analysis, densitometry and roentgenogram measurements. Nomograms and regression equations allowing the direct calculation of total body fat from skinfold thickness measurements have subsequently been developed. Durnin in the University of Glasgow has extended the use of the technique to adolescents and Tanner has pioneered its use in children aged 1 month to 4 years. Its application however has been extremely limited in newborn infants. The reasons for this are probably two-fold: the first is the suspected unreliability of the technique, many potential sources of error existing, the second is lack of knowledge as to the exact clinical significance of the values.

The work presented here seeks to improve this position and is described in three sections. Section I consists of an examination of the technique as applied to neonates. Section II examines the values in normal, premature and light-for-dates infants and Section III describes the gross chemistry of skinfold tissue in autopsied infants.

The Technique - Section I

Three different calipers were examined with regard to ease of manipulation, size of scale, accuracy etc. The instrument preferred and used throughout was the Harpenden caliper. Different sites for measurement were considered and particular ones selected for reasons of accessibility and low error content.

Measurements were attempted in different order and with the infant in different positions. A standard technique was developed.

The error attached to the technique was calculated from duplicate measurements in the same infants after a period of one hour. The magnitude of the error was defined as 15% at 95% confidence limits. The sources of this sizeable error were examined as originating from the instrument, from the operator or from the tissue. The accuracy of the Harpenden caliper had been reported as adequate in the MRC study in 1951 and the error recorded there was of the same order as found here. The particular instrument used was of course calibrated first. The subjective aspect of the technique was examined for error content by comparing the standard error detailed above with that obtained when marked skinfolds were measured after one hour. No appreciable difference in error was demonstrated. The subjective aspect of the technique was further examined by experiments with an instrumented Harpenden caliper attached to an XY plotter. Operator readings were compared with those on the plotter. The readings of two operators were also compared with plotter values. Little difference in values was evident. Thus, none of these experiments pinpointed the exact location of the error which must by exclusion be levelled at tissue behaviour. The first experiment with the instrumented caliper portrayed the response of the tissue to caliper compression as a curve which was bi-phasic in character. Further examination of compression curves was undertaken later to detect any changes in tissue behaviour in different babies.

Comparison of compression curves in these infants did not show a link between skinfold thickness values and the rate of compression as defined by millimetres per second decrease in tissue thickness. If the time of reading is constant, as should be the case if successful standardization has been achieved, this suggests that alterations in the quantity of some tissue constituent may exist. The suggestion is made that this tissue constituent is in fact fluid and literature support for this view is presented.

The Values - Section II

Skinfold thickness values were recorded in a statistically selected normal group of infants, in a group of premature infants and in a group of light-for-dates infants. In the normal group of infants, strong correlations were obtained between skinfold thickness values and the infant's birth weight and crown heel length, but not with its gestational age. A highly significant difference also emerged between male and female values, male values being smaller. In the premature infants,the same relationships with birth weight and birth length emerged but in this group significant correlations appeared between skinfold thickness values and gestation,a trend to increasing values with advancing pregnancy being apparent. There were insufficient numbers to consider the sexes separately. In the "dysmature infants", all skinfold thickness values fell below the mean values recorded in the normal group. The relationships with the other growth indices and the differences between male and female values were absent. Findings in the few corresponding reports in the literature are compared.

The Chemistry - Section III.

This section describes the chemical analysis of autopsied skinfold tissue. Specimens consisted of the portion of tissue enclosed by the caliper blades at the standard site and were dissected by the writer personally. The percentages by weight of total water in fat-free specimens and of total fat in the dehydrated specimens were estimated. The fat extracts were subjected to thin layer chromatography. Changes with gestation and differences in male and female values at term were sought as explanations for the changes and differences found in the corresponding caliper values. A trend to decreasing water values with increasing gestation was evident and female infants had significantly less water than male infants at term. No such obvious trend was seen in fat values and no significant sex difference occurred. Thin layer chromatographs showed that triglyceride was by far the largest constituent of all fat extracts and that similar lipid patterns occurred from 30 - 40 weeks. No sex differences were apparent. No exact replica of this approach where skin and subcutaneous tissue are treated as a single organ has been found in the literature.

CONCLUSIONS

It is thus concluded from the evidence collected here;

A. That measurement of skinfold thickness in the newborn by the technique described is reliable and that the "error" in fact reflects a change in tissue behaviour and probably its water content.

B. That skinfold thickness values are closely related to the infant's birth weight and crown heel length, that they increase with gestation, and that female values are significantly greater than male values at term.

C. That the percentage of water in skinfold tissue declines with increasing maturity whether denoted by birth weight, crown heel length or gestational age; That female water values at term are significantly lower than male ones; and that no such trend or difference exists in percentage fat nor in lipid patterns as visualized in thin layer chromatographs.

Of particular interest in these findings is the recurring link between skinfold thickness and tissue water - in explaining the error; in the opposite but matching trends with gestation; and in the opposite but matching sex differences at term. The possibility must be raised that skinfold thickness values reflect tissue water in an inverse way .

In any case, this simple technique can be reliably used in newborn infants, is closely linked to other growth indices and may provide readily accessible information on the infants state of hydration.

INTRODUCTION

Clinical examination of the newborn infant provides doctors with a viewpoint reminiscent of that of the Roman God, Janus, whose two heads gazed, one backwards over the old road, one forwards over the new, at each portal. The moment of birth could be regarded similarly as a gateway in time at which it is convenient to assess the intra-uterine phase of the child's development in retrospect and at which the extra-uterine phase in prospect can be roughly mapped out. Initially, this assessment was based on the single criterion of birth weight. If the birth weight was low, i.e. less than 5 lbs 8 ozs or (2500g) the child was premature; if more than 5 lbs 8 ozs the child was mature (147). Birth weight was used also as an important prognostic feature, extremes being recognized as undesirable. A value of less than 4 lbs (1800g) implied increased susceptibility to infection, because of the malnutrition present (123), and long term risks of physical, intellectual and emotional handicaps (94), (38), (69). If the birth weight was very high on the other hand as for example in the infants of diabetic mothers, the late stillbirth and neonatal death rate was of the order of 25% - M.R.C. trial 1955 (91).

This protocol has proved to be an over-simplification. Babies could not thus easily and satisfactorily be divided into two categories. In addition it was realized that to rely so heavily on a single factor such as weight to decide conceptual age, functional maturity and long term prospects was inadequate. At best birth weight could be only a rough indication of the child's gestation and state of health.

The change in attitude probably stems from two main sources. The first of these is the progressive increase in the number of factors known to affect ultimate foetal size. Some of these influences have long been recognized of course. The effect of gross maternal size for example was shown in the classical study on Shire and Shetland horses by Walton and Hammond in 1938 (155) and of maternal under-nutrition in 1947 by both Smith (131) and Antonov (5) working on wartime populations in the Netherlands and Leningrad respectively. In 1947, Benda (11) showed an association between congenital abnormality (specifically mongolism) and low birth weight and in 1953 McKeown and Record (96) pointed out that birth weight in animals was related to litter size rather than placental weight. Within the last decade or so additional factors have been implicated. A study of very low birth weight babies in 1963, showed that they were most likely to be born to mothers whose obstetric histories indicated primary reproductive failure encompassing placental abnormalities, previous infertility and advanced age (162). Maternal cigarette smoking has been reported as resulting in infants weighing about 250g less than infants of non-smokers (22), (68), and other factors recently implicated included height above sea level, the antigenic structure of the y chromosome and the DNA formation time (83), (104), (36). All these observations indicated that birth weight was sensitive to so many influences that its use for " spot diagnosis " was impossible.

The second source of doubt was the realization that a large number of babies did not fit into either of the two categories low birth weight premature, or high birth weight mature. Clifford in 1954 (30) studying a group of infants defined as postmature, described stages of intra-uterine malnutrition resulting in some infants being underweight. (It is interesting to note that the Scottish Obstetrician Ballantyne had described a similar group as early as 1902 (9)). Sjostedt (128), in 1958 in a study of 968 babies, reported that not all of the infants showing malnutrition as described by Clifford, were postmature or even at term but that many in fact were born within 294 days and some could even be considered premature by dates. To define this group, he introduced the term " Dysmaturity " and suggested that it was due to placental insufficiency. In the British Perinatal Mortality Survey in 1963, Butler and Bonham (23) reported that one third of babies weighing less than 2500g at birth, were born at more than 39 weeks gestation, a finding exactly corresponding with that of Douglas (37) 13 years earlier who had contended that only 71 per cent of infants weighing less than 2500g were premature babies by gestation.

The demonstration of this group of infants who were underweight although frequently at term, dictated that birth weight and gestational age could not automatically be regarded as equivalent and culminated in the proposal by W.H.O. in 1961 (157) that the terms "prematurity" and "immaturity" be replaced by "low birth weight". More recently, a report by a joint working party of the second European Congress of Perinatal Medicine London 1970 (138) suggested avoidance of all words incorporating maturity and proposed that infants be classified as:-

i pre-term
ii term
iii post-term

In view of the confusion and controversy regarding terminology, standard textbooks are however understandably remaining loyal to the older terms " prematurity " and " dysmaturity " as representing recognizable clinical conditions-Hutchison 1971 (74).

Definitions aside, the breakdown of the simple equation:

Birth Weight = Maturity = Prognosis

posed three questions.

1. In view of the demonstrated lability of birth weight, what is the optimum weight for gestation?
2. What does constitute maturity if not birth weight?
3. What criteria will differentiate dysmature infants from premature and thus allow us to formulate prognosis?

Much recent research effort has been directed at these three questions.

1. As far as Optimum weight for gestation is concerned, efforts to provide standards had been made previously (77), (97), but these have been intensified in the last few years. Lubchenko in 1963 (86) produced the first percentile chart and her tenth centile values have been widely used to identify light-for-dates infants. Gruenwald in 1966 (64) preferred to use a birth weight of two or more standard deviations below the mean as definitive. Since then, weight for

gestation charts have multiplied (101), (164), (149). They have become increasingly sophisticated - " smoothed, corrected and extrapolated " to allow for racial and geographical differences (54), (137), (7), foetal sex and pregnancy number (146), maternal height and weight (142) and sibling weights (144) until they have become almost meaningless and useless for practical purposes. Indeed a recent letter in the " Lancet " referred to the " new statistical birth weight game ". Even if we confine our attention to two of the methods mentioned above - Lubchenko and Gruenwald, it will be seen that there is a great disparity between them. Using Lubchenko's method,the number of infants coming into the growth-retarded category (i.e. < tenth centile) is three times greater than when standard deviations are used. In fact,two standard deviations or more below the mean corresponds to approximately the third centile. In addition, the influence of socio-economic factors on the differences apparent in standards from different countries is immeasurable. The growth chart produced by Gairdner and Pearson in 1971 (57) allowing weight, length and head circumference to be charted together and incorporating a logarithmic time scale is undoubtedly of help in clinical practice. It is suspected however that more than 10% of Glasgow children fall below its 10th centile values as derived from Cambridge children. "It may be wrong to fit the curve of one group to that of another " (89). In Silverman's view expressed in 1963 (127) - Birth weight has served and continues to serve a useful practical purpose but its limitations become more obvious with time.

2. Defining maturity is even more difficult. Mitchell and Farr (88) have suggested that the word is used with two different meanings. In one context it means the stage of development at which the foetus is best adapted for the ordeal of birth : in the other it refers to the state of functional efficiency of the newly born infant. Since the latter represents a process relating to changing physiological needs, no single point on the spectrum can be considered as representing " maturity ". The nearest one can presently get to measuring maturity is to assess the gestational age and many attempts to improve the accuracy of this have been made. No assessment would be needed of course, if reliable menstrual data were available. Given the sizeable number of mothers presenting with no clear idea of their dates however, other means of assessing gestation have been mooted. Innumerable signs and measurements have been suggested as criteria of maturity. Among antenatal methods presently in vogue are the radiological estimation of ossification centres (119), (28) measurement of biparietal diameters by ultrasonography (24) and the cytological and biochemical investigation of amniotic fluid (73), (84), (99). Postnatally the emphasis has been on the neurological examination of the infant (4), (41), (80), (109), (115), (145) although some authors suggest that crown heel and crown rump lengths are as reliable indices of maturity as any other (46). Farr and co-workers in 1968 (48) tried to grade the state of development of certain physical characteristics such as nipple and areola, ear cartilage, skin

opacity and oedema: Dubowitz (40) suggested the measurement of nerve conduction velocity. Latterly (1969) immunoglobulin levels (106) and the degree of myelination of the optic nerve (21) have been proposed as criteria of gestation but the success of all these methods is limited. Earlier radiological studies such as those of Hartley in 1957 (70) and Berridge and Eton in 1958 (12) emphasized the variability in the time of appearance of specific ossific centres; especially in small babies and Scott and Usher in 1964 (122) claimed that skeletal development is more affected than other tissues in the growth-retarded foetus. Examinations of amniotic fluid such as estimation of Lecithin/Sphingomyelin ratios (100) arouse aptimism but illustrate functional maturity rather than chronological age. Subjective error and interpretation raise problems with neurological examinations and the weighting of scoring systems such as those of Dubowitz (41) and Farr (48) is always debatable. In any case, the reliability of calculating foetal age in terms of a specific week of pregnancy is uncertain, Tanner (140) stating that the true post-fertilization age is never known with accuracy and Casaer and Akiyama (25) claiming that accuracy as far as the post-menstrual age of the infant is concerned cannot be better than two or three weeks because of normal biological variations in ovulation/delivery time. Doubt as to the exact age of particular infants must remain.

3. The differentiation of dysmaturity and prematurity is frequently difficult. Its importance is related to both immediate and subsequent prognosis. The clinical features of dysmaturity, described in a series of studies (156), (150), (160), (116), (154), (148)

suggested that the prognosis in terms of survival alone was better if birth weight was appropriate for gestation. McDonald (95) commenting on Gruenwald's tables from the Perinatal Mortality Survey says " children weighing from 1501 to 2000g had a higher mortality when their gestational age was thirty-six weeks or more than when it was thirty to thirty-five weeks and in children weighing from 1001 to 1500g, mortality was greater between thirty-four to thirty-seven weeks than at shorter gestational ages ". In this particular hospital a retrospective study of 1116 infants weighing 800 to 2600g divided into appropriate for dates/premature or small-for-dates/dysmature using the Lubchenko tenth percentile and excluding lethal congenital abnormality showed a mortality rate of 13.5 per cent in the premature group and 2.2 per cent in the dysmature group (98). Although the prognosis for infants weighing 1500g or less overall seems to have improved (112), Drillien (39) notes that fewer light-for-dates infants were normal at two to three years than were infants of appropriate weight for gestation and Fitzhardinge et al (51) report specific learning difficulties among a group of LFD term infants. The dubiety about prognosis must remain due to the inability to determine accurately the gestational age of the infant.

Despite intensive work, these questions - What is meant by " light "? What are the " dates "? and What happens to the LFD infant? are still not satisfactorily answered.

The problems remain. Recognition of the LFD infant in the first place must be impeded by doubt as to the optimum weight and exact age of any individual. The original assumption that babies fitted into one of two categories premature or mature depending on a labile birth weight has been replaced by the idea that they fit into one of three categories premature, mature or dysmature depending on a labile birth weight and an often inexact gestational age.

The aetiological factors responsible for intra-uterine malnutrition are as varied as those involved in growth retardation in older children (117), and the physical patterns produced are equally numerous. The heterogeneity of lightweight babies has been emphasized by Ounsted (103) and Saugstad (120) has suggested recently that even the growth defect in Phenylketonuric infants was of antenatal onset, since their birth weights were significantly lower than those of their sibs. The main danger to dysmature infants appears to occur antenatally (154), the stillbirth rate in dysmature foetuses approaching eight times the neonatal mortality rate (89b). The difficulties inherent in elucidating intra-uterine growth processes have been described by Dunn and Butler (42) and the infrequency of any routine examination except birth weight in neonates partly held responsible.

In default of exactitude of lightness and dates, growth retardation at birth can only be recognized and its variants explained within the context of normal growth and additional criteria for evaluating growth and sub-optimal growth are essential.

This attempt at historical perspective partly explains to the writer's mind current interest in foetal growth, developmental paediatrics and gerontology so evident in the journals and of course these three presumably constitute a biological continuum where growth and enlargement merge into ageing and shrinkage. Are these processes essentially the same? One early author has described senescence as " development viewed from the other end of life ". There are certainly some interesting similarities between the immature and the ageing. Lack of subcutaneous fat, characterizes the immature infant as also the aged, although no quantitation in the infant yet exists (90). Hypothermia, linked to the fat content of brown adipose tissue (1) is a problem in the immature infant and in the old. It is perhaps worthwhile noting here that of a series of parameters, skin compressibility, thought to be dependent on subcutaneous fat had the most significant correlation with age (20), and with annual mortality rate (71). In any case, the kinetics of normal growth are becoming less and less a purely academic problem. It is interesting to reflect that normal growth permits simultaneously, decrease in size and activity of one organ with increase in size and activity of another and that some organs have fulfilled their life expectancy before the individual is even born. Atrophy of the foetal zone of the adrenal, of the thymus and of haemopoietic tissue in liver, spleen and long bones are examples of a diminishing system within an overall expanding one. It has been suggested that the rate at which organs grow and enlarge is not steady - that spurts of growth are succeeded by resting phases in a " stop-go " way, these periods of rapid growth being called " critical phases ". More specifically Brook (16) suggests that the total complement of fat cells should be formed by the end of the first year of life, the process starting in the late weeks of pregnancy. Interestingly enough, important developmental changes occur in the nervous system about the same time and Winick (163) and Davison and Dobbing (32) have argued that there may be an important connection between these two phenomena. Organs are said to be most vulnerable to deprivation during these " critical phases " and any retardation occuring then may not be completely reversible. Some fascinating American work on beetle larvae recently, (10) showed that growth could not only be delayed by starvation but could actually be reversed and that although the beetle eventually achieves mature size its fat body showed polyploidy or signs of age consistent with its true progress in time. The constantly recurring fat/age theme is interesting. Is it possible that the dysmature infant has actually lost weight before birth ?

The writer concludes that since the problems of prematurity and dysmaturity are related to growth, and since growth must be assessed in series, there is good reason to bring the routine examination of newborn babies into line with the assessment of " well baby " or infant welfare clinics. Birth weight would then be regarded as merely a " milestone " in classical developmental paediatric terms (61), i.e. not as an " all or none " test (75) but as an item of value only if interpreted with flexibility in time and in conjunction with other growth factors.

Further, having acknowledged the plasticity of Birth Weight, the need arises for other assessment techniques. Since a degree of malnutrition characterizes most " immature " infants, an additional growth factor which reflected the infant's nutritional status would be of value. Large scale screening programmes for infant malnutrition already in existence include the simple expedient of caliper measurement of skinfold thickness among their indices (78), (65), (126). If skinfold thickness measurements in neonates are directly proportional to total body fat as they are said to be in adults (79), (43) efforts in this direction would be additionally attractive since the importance of fat in the neonate and in ageing in general seems to be profound. Although standards for skinfold thickness measurements in older British children have been published, (141), (67) no such standards exist for the newborn. It would seem worthwhile to pursue these standards as a measurement of the infant's nutrition.

Unfortunately, measurement of the thickness of a skinfold is not ideal in that the relative proportions of its constituents are unknown. The usefulness of skinfold thickness values will be severely limited unless this can be remedied. This study examines the technique of SFT measurement in neonates, attempts to determine normal ranges of measurements, and relates these findings to the chemical composition of autopsy skinfolds.

The work fell chronologically into three sections in which it is described.

1. The technique
2. The values
3. The chemistry

SECTION 1 - THE TECHNIQUE

Chapter One

INFORMATION FROM THE LITERATURE

Measurement of skinfold thickness by caliper as an indication of an individual's " fatness " is not new. Keys and Brozek (79) wrote a comprehensive review in 1953 describing its use by Richer as early as 1890 (113). Interest in the method is not surprising when one considers its advantages. It is simple and inexpensive, the instrument is easily portable and most important of all it is not prejudicial to the patient's health nor his comfort. It has been shown to provide information which correlates statistically with roentgenogram measurements of skin and subcutaneous tissue (59) with body density and consequently total body fat (19). This has led to the development of equations and nomograms for predicting fat content from SF thickness (43), (52), (129) the most widely used being the regression equation formulated in 1967 by Durnin and Rahaman (43) of Glasgow University. This enables one to estimate total body fat from the sum of four skinfold thickness measurements. There seems to be no doubt that skinfold thickness measurement in adults provides a good measure of the individual's state of nutrition.

In children it has been used in the MRC growth trial (143) using standards published in 1962 by Tanner (141). It has been used widely in field studies of child malnutrition (78), (65), (126) mostly as recommended in the 1966 monograph by Jelliffe (76) and conversely it has been used as a measure of childhood obesity (111), (124). Finally in 1971 Brook (17) provided a modification of

Durnin and Rahamans regression equation for use in pre-pubertal children.

Few studies of SFT measurements however, have been reported in neonates, and this possibly reflects the difficulties and sources of error inherent in the method and the fact that some of these difficulties are at their most acute in neonates. The main difficulties, described fully in the article by Keys and Brozek (79), arise from the physiological variations of skinfold components. The hydration of the subject; the varying amount of fat in adipose tissue; possible changes in the quantitative relationship between subcutaneous and internal fat; differences in skin thickness - all these constitute problems which are maximal in the neonate - "Never in the later life of man do such climactic changes occur in so short a time" - Clement Smith (132). Other difficulties occur in the locating of identical sites in different subjects; the positioning of the child and the lifting of the skinfold, the application of the blades in a standard way, and the reading of the instrument. The last is particularly troublesome in newborn infants because the compressibility of the skinfold results in a steadily decreasing value with consequent difficulty in obtaining a stable reading. The reciprocal relationship between tissue compressibility and ageing described in 1960 by Brozek and Kinzey (20), implies maximum compressibility in neonates. The Committee of Nutrition of the American Academy of Pediatrics has summarized this:- "Uncontrolled variables such as skin compressibility and the normal flux in subcutaneous thickness characteristic of growing subjects may reduce the significance of measurements in early life " (3).

Such studies as have been reported in newborn infants indicate general agreement that SFT increases with birth weight. They manifest conflicting views as to the relationships between SFT and the sex and between SFT and the gestational age of the baby.

Vincent and Hugon (152) in 1962 included the measurement of SFT at Subscapular and Triceps sites in a battery of techniques used to assess the maturity of African babies. Parizkova (107) in 1963 reported SFT values at ten sites in Czech babies. Gampel (58) in 1965 and Farr (47) in 1966 both working in the United Kingdom published a series of SFT measurements at Subscapular and Triceps sites in the former and at Subscapular, Triceps, Lateral Thoracic, Umbilical and Thigh sites in the latter. Wagner et al (153) in 1967 in the United States recorded values at Triceps, Quadriceps, Lateral Thoracic and Umbilical sites and Usher and McLean (149) in 1969 the values at an Umbilical site in Canadian infants born between 25 and 44 weeks of gestation. It can be seen that the populations studied in the various reports are dissimilar and that there were also considerable differences in the calipers and techniques involved.

Vincent and Hugon (152) and Gampel (58) used the Harpenden caliper recommended in the MRC trial of 1955 (45), Farr (47) compared the Harpenden with a caliper described by Verel and Kesterven in 1960 (151) and preferred a corrected version of the latter, Parizkova (107) used Bests caliper (13), Wagner et al (153) used Langes caliper and Usher and McLean (149) used an unnamed caliper requiring the application of light pressure.

The technique described by Tanner and Whitehouse (141) in 1962 has now become widely used but a different method of application was used by Wagner et al (153).

As previously stated, all authors agree that SFT values increase with increasing Birth Weights. Vincent and Hugon (152), Parizkova (107) and Farr (47) describe significantly greater SFT values in female infants. Gampel (58) and Wagner et al (153) however did not find sex differences to be significant. Usher and McLean (149) did not discriminate between the sexes for reasons of insufficient numbers. Both Gampel (58) and Usher and McLean (149) report increasing SFT values with length of gestation, but Farr (47) attributed this to the relationship with birth weight and reported in fact a tendency for SFT values to fall with increasing maturity.

In general therefore, limited efforts have been made to standardize the technique in the newborn. For this reason, and because the occasional report casting doubt on the reliability of the technique in adults still appears (15), it was thought wise to do some exploratory work on methodology before looking at actual measurements.

Chapter Two

MATERIALS & METHODS

Choice of Caliper

The M.R.C. trial described by Edwards et al (45) considered the characteristics essential in a skinfold caliper and concluded that these criteria were satisfied by the Harpenden caliper (Fig. 1). One of the authors was mentioned however as preferring lower pressures for use in small children. Certainly there were difficulties in obtaining stable readings in some new infants because of the skinfold deformation. The contribution made to this deformation by the pressure load of the Harpenden was difficult to estimate. Initially, an attempt was made to reduce this pressure by halving the spring load. This however made it difficult to maintain compression and introduced the danger of the blades slipping off and injuring the skin. Another difficulty was that the size of the instrument made it awkward to use inside incubators.

Two other calipers were examined:- the Lange caliper (Fig. 2) used by Wagner, Wagner and Mathis (153) had a scale recording whole millimetres - not a small enough gradation for babies' measurements. The second caliper (Fig. 3) described as particularly suitable for use in children was found to have a scale measuring 0.25 cms. and not 0.25 mms. as reported by Verel and Kesterven (151). With the latter instrument there was also the problem of parallax and with the fact that pressure had to be maintained while the reading was taken. It was decided that despite

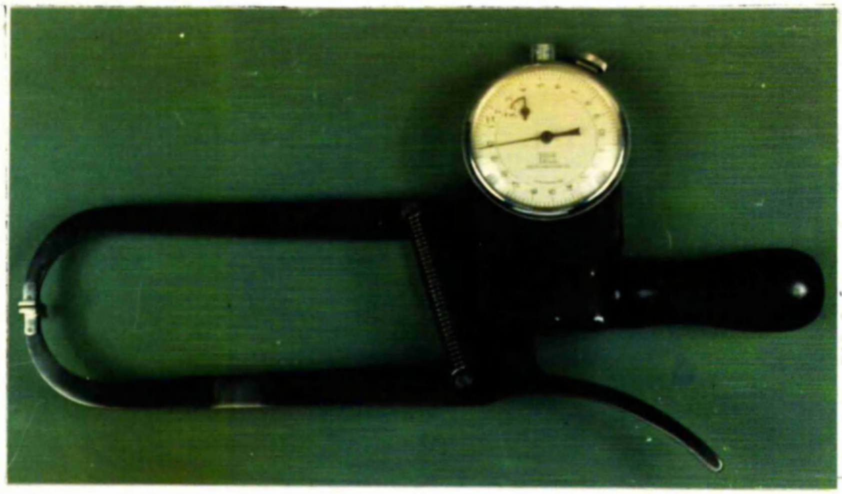


Fig. I The Harpenden Caliper

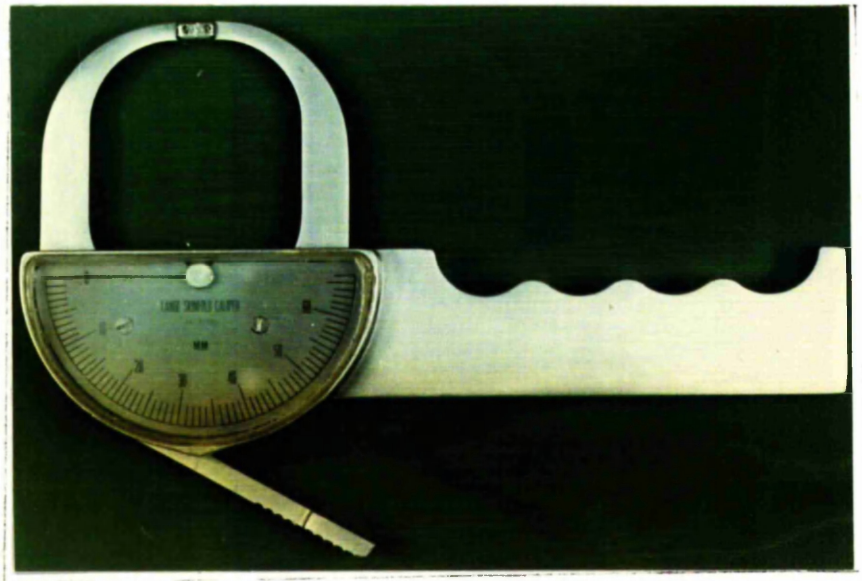


Fig. 2 The Lange Caliper

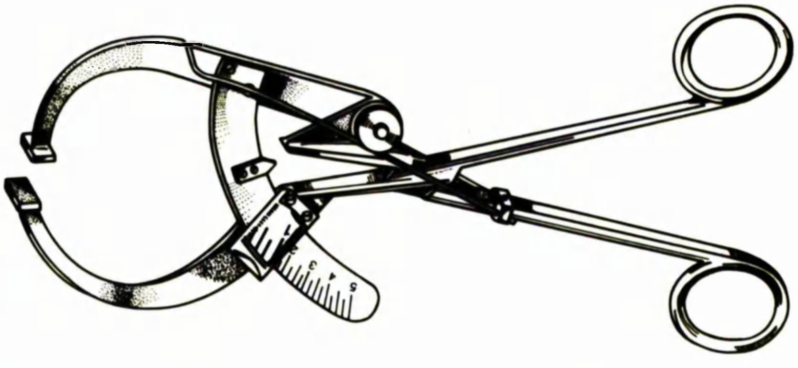


Fig. 3 Verel and Kesterven Caliper

its possible disadvantages of size and pressure load the Harpenden caliper was the only instrument available which would give reasonably uniform measurements.

Choice of Technique

The method described by Tanner and Whitehouse (141) of lifting a skinfold between left finger and thumb and applying the caliper blades in the middle of the fold was preferred to that used by Wagner, Wagner and Mathis (153) who open the caliper to 15 mm., lay the blades against the skin and release them allowing them to pinch up the fold. Although an inter-observer trial gave good correlation coefficients when this technique was used, the infant was so distressed that subsequent measurements were difficult and thus liable to error.

Choice of Sites

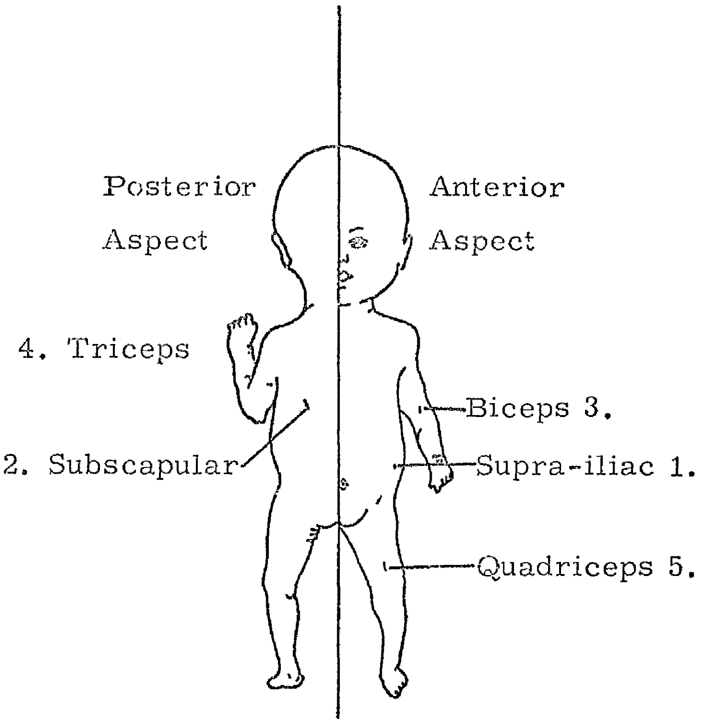
The choice of sites was made by adhering to the basic principles described by Edwards (44) namely, ease of location because of proximity to bony landmarks, alignment with natural body contours, and with sufficient tissue for correct application of the blades. The last mentioned requirement dictates certain sites and precludes others in small neonates. The caliper blades of recommended area 6 x 15 mm. need a reasonably deep fold for correct application. It was difficult to obtain sufficiently deep folds at the more anterior sites such as the anterior axillary, the umbilical and the lateral thoracic sites as used by Wagner, Wagner and Mathis (153). Subscapular and Triceps sites are used so uniformly-Vincent and Hugon (152), Gampel (58), Tanner and Whitehouse (141) and

Hammond (67) as to be almost mandatory. Because of the possible sex difference, the Supra-iliac site reported by Parikova as the site where this difference was significant (107) was used. Additional limb sites were also included because limb fat studies showed sex differences in Tanner's work on adolescents (139). More specifically, the five sites used throughout the study were Supra-iliac, Subscapular, Biceps, Triceps and Quadriceps and these are shown in Fig. 4 together with their exact anatomical position. The left side traditional in anthropometry was used throughout.

Choice of Posture

Two requirements decided the positioning of the baby during the actual measuring, firstly - easy access to the operator and secondly - the most relaxed position for infant and nurse. The actual postures adopted were as follows:

The infant was placed in its crib in the right lateral position with its left arm abducted 90°. Measurements were taken at the Supra-iliac and Subscapular sites. The left arm was then drawn towards the edge of the crib, held in a position midway between abduction and adduction and the Triceps measurement taken. Finally, the child was placed supine in its crib and the remaining Biceps and Quadriceps measurements taken. These positions were of course chosen arbitrarily and it may be that they are not the most suitable. Professor Tanner in a personal communication expressed doubts as to the position of the arm for the Triceps measurement, his practice being to have the arm suspended. This however would entail removing small infants from incubators which is not always



1) Supra-iliac	- Along mid-axillary line blades applied immediately superior to iliac crest.
2) Subscapular	- Along a line running from the inferior angle of the scapula. Blades applied 1 cm. medial to the inferior angle.
3) Biceps	- Along a line running parallel to the longitudinal axis of the arm on the anterior surface. Blades applied 1 cm. superior to the skin crease at the elbow joint.
4) Triceps	- Along a line running parallel to the longitudinal axis of the arm on its posterior surface. Blades applied midway between Olecranon and Acromion processes.
5) Quadriceps	- Along a line running parallel to the longitudinal axis of the leg on the anterior surface. Blades applied immediately superior to the uppermost skin crease of the knee joint.

Fig. 4 - Sites for measurements of SFT in neonates.

possible.

Choice of Subjects

The selection of infants will be described in more detail later but only singleton Caucasian children were used for SFT measurements.

In conclusion, measurements of SFT at five sites - Supra-iliac, Subscapular, Biceps, Triceps and Quadriceps using a Harpenden caliper as recommended in the M.R.C. trial (45) and the technique described by Tanner and Whitehouse (141) was adopted as standard procedure throughout the succeeding work.

Chapter Three

SIX EXPERIMENTS TO ASSESS THE RELIABILITY OF THE TECHNIQUE TOGETHER WITH THEIR RESULTS

When this initial exploratory work was completed, six experiments were planned to assess the reliability of the method. These are now described together with their results.

Experiment 1 The Operator - Site Variance

The within-operator, within-site variance was established by comparing duplicate skinfold measurements on thirty-one subjects with an interval of one hour between observations. The distribution of differences between replicates was examined sequentially and sufficient cases studied until the variance of the differences tended towards a constant value, thus ensuring a measure of the differences themselves rather than sampling error. The results of the investigation into duplicate SFTs taken one hour apart is shown in Table 1 . It can be seen that in all cases there is a substantial standard deviation. The site exhibiting minimal difference between replicates is the Supra-iliac followed by Triceps and Quadriceps. The poorest replication was obtained with the Sub-scapular site.

Experiment 2 The Within - Operator Variance

A further group of twenty babies had the standard skinfolds marked with a skin pencil and duplicate readings taken, again at an interval of an hour.

Table 1 - Within operator - within site variance for neonatal skinfolds (paired observations at one hour interval)

	Mean S. F. T. (mm)	Differences in S. F. T.		$\frac{95\% \text{ Limits}}{\text{Mean}}$ (%)
		STD. DEV (mm)	95% Confidence Limits (mm)	
Biceps	4.7	0.53	± 1.04	22
Triceps	5.5	0.53	± 1.04	19
Quadriceps	8.2	0.62	± 1.22	15
Supra-iliac	4.6	0.36	± 0.71	15
Subscapular	5.6	0.70	± 1.37	24

Table 2 - Within operator variance - paired observations on marked sites at one hour interval

	Mean S. F. T. (mm)	Differences in S. F. T.		$\frac{95\% \text{ Limits}}{\text{Mean}}$ (%)
		STD. DEV (mm)	95% Confidence Limits (mm)	
Biceps	5.7	0.45	± 0.88	15
Triceps	5.6	0.52	± 1.02	18
Quadriceps	9.8	0.65	± 1.27	13
Supra-iliac	5.4	0.35	± 0.69	13
Subscapular	7.0	0.55	± 1.08	15

The differences in variance between this experiment and the last should give some estimate of the error involved in the application and reading of the caliper as opposed to that of site selection. The within-operator variance obtained by taking replicate measurements at marked sites is seen in Table 2 . It can be seen that the standard deviation of the difference between replicates is not very different from those shown in the last experiment (Table 1) and that the ninety-five per cent limits of each distribution are of the same order of magnitude. Once again the Supra-iliac measurement seems to be most consistent followed by Quadriceps and Triceps.

Experiment 3 The Mechanics of Skinfold Compression

A standard Harpenden caliper was modified as shown in Fig. 5 . A linear displacement transducer was attached across the arms of the instrument in such a way that its electrical output was directly proportional to the displacement of the "pads" of the caliper. An Ether Ltd. L 11 resistance displacement transducer was used in a purpose-built bridge-circuit whose output was fed directly to a Bryan's 4200 high-speed X-Y plotter. The instrument was calibrated statically with standard slip gauges. With this system it is possible to record dynamically the displacement/time characteristics of skinfold compression and to compare subjective readings by the operator with objective readings from the plotter. A typical output from the instrumented Harpenden caliper is shown diagramatically in Fig. 6 . The displacement time response takes place in three well defined

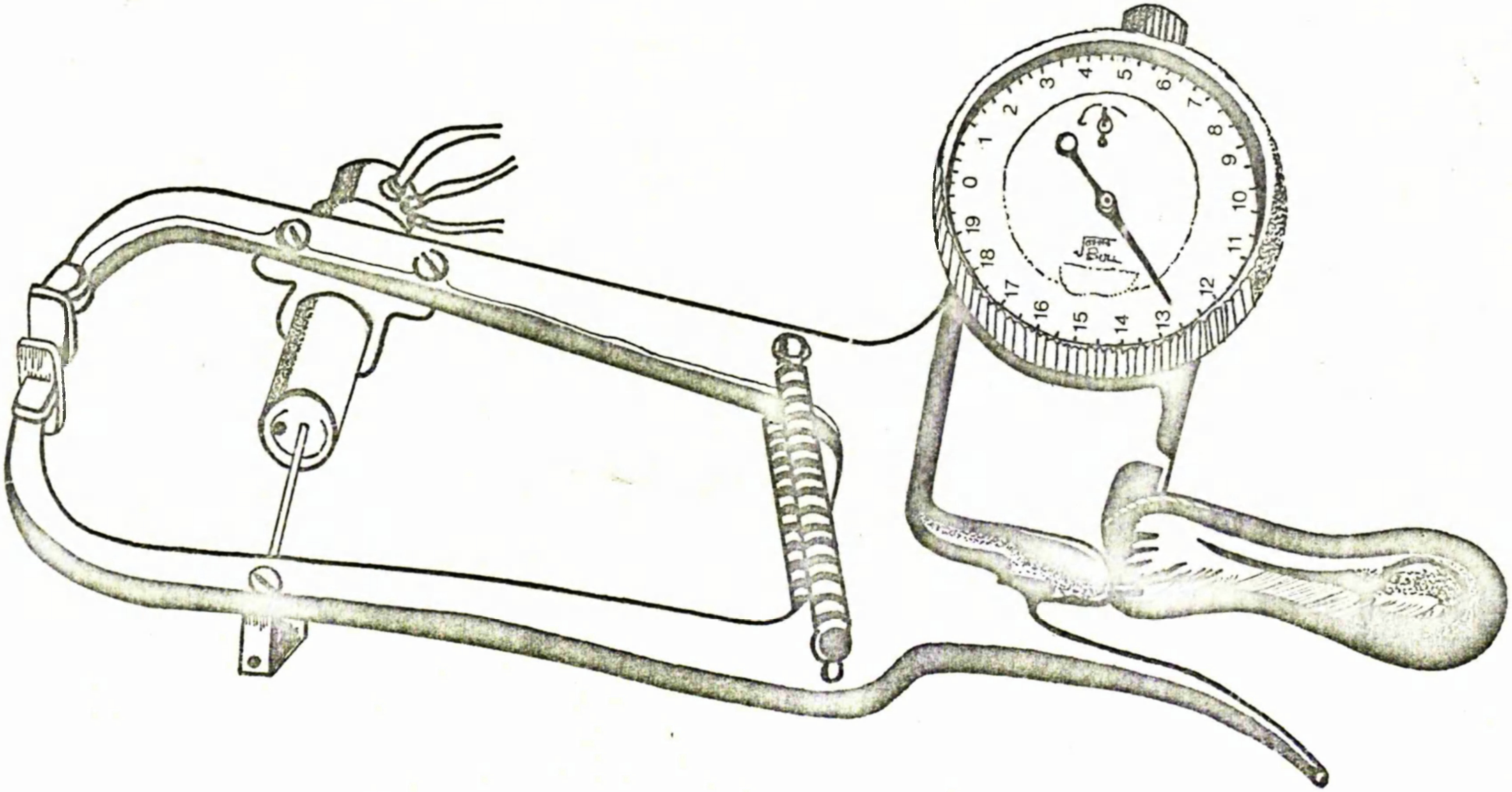


Fig. 5 - The Instrumented Harpenden Caliper

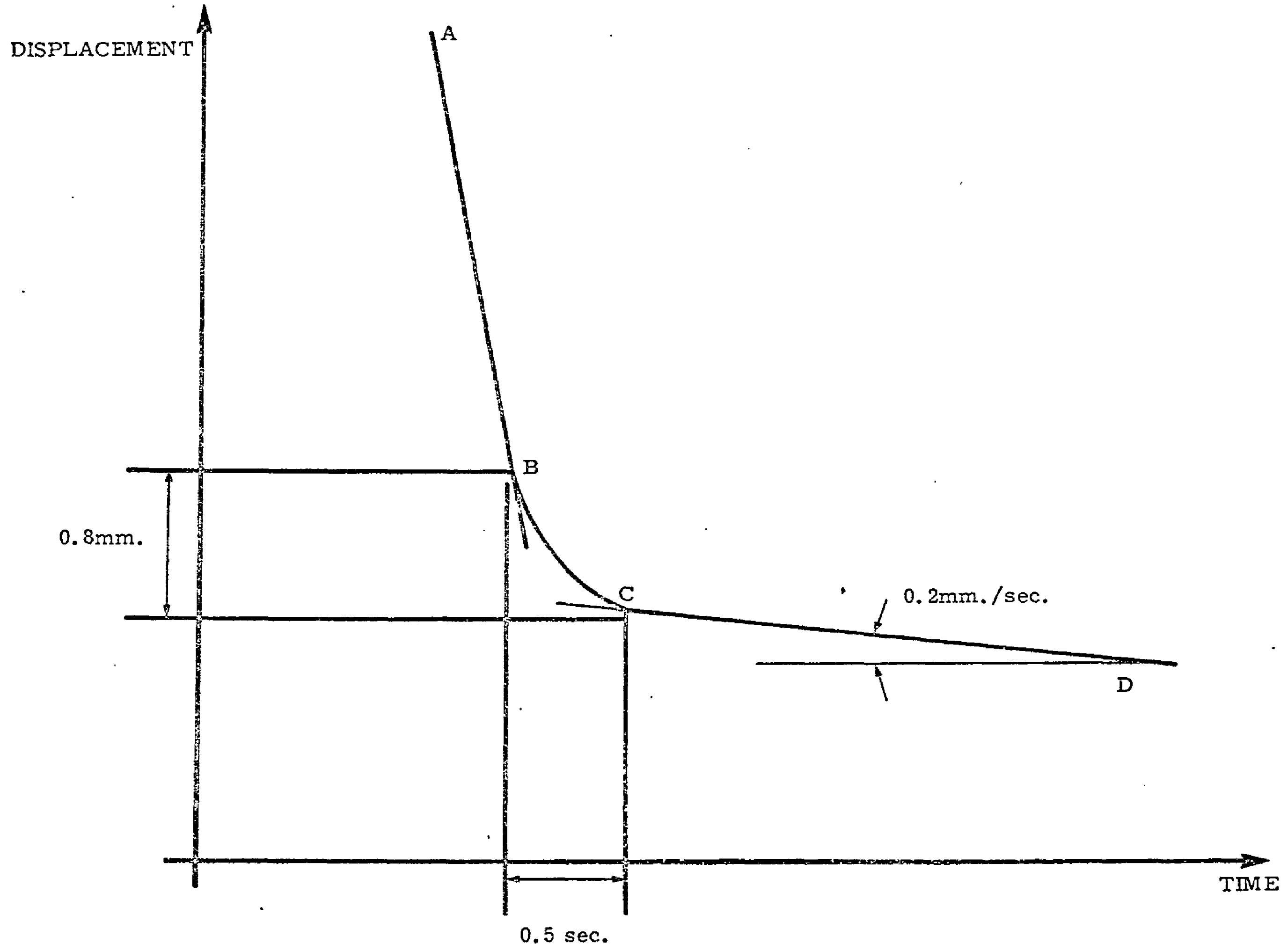


Fig. 6 - Typical output from an instrumented Harpenden Caliper.

stages. Initially, at point A, the instrument has been opened to enable the operator to place it on the skinfold. As the instrument is closed onto the skinfold, the slope of the line A-B is under the control of the operator. At point B, the "pads" of the caliper first touch the skin and resistance to further closure of the instrument is encountered. Over the period B-C, which typically may last up to 0.5 seconds, the rate of change of deformation with time reduces continually until at point C, the final phase is entered. This last is a continuous deformation of about 0.2mm. per second which may last for several seconds but represents the minimum rate of change of deformation from the moment of application to the skinfold up to the end of a period of several seconds. The point C, represents that point at which the rapidly changing deformation has reduced to the steady fall. An example of an actual trace is reproduced in Fig.7. On subsequent calibration of the displacement-time record, it was found that the skinfold measurement cited by the operator was closely related in magnitude (and also in time) to the part of the displacement curve where the slow displacement phase commenced, i.e. point C.

Experiment 4 Comparison of the values from the time/displacement record with the readings by two operators

The help of a second person was obtained for the purposes of comparing the differences between SFT readings from the displacement/time record and those obtained by two individual operators. Table 3 shows the mean, standard deviation and

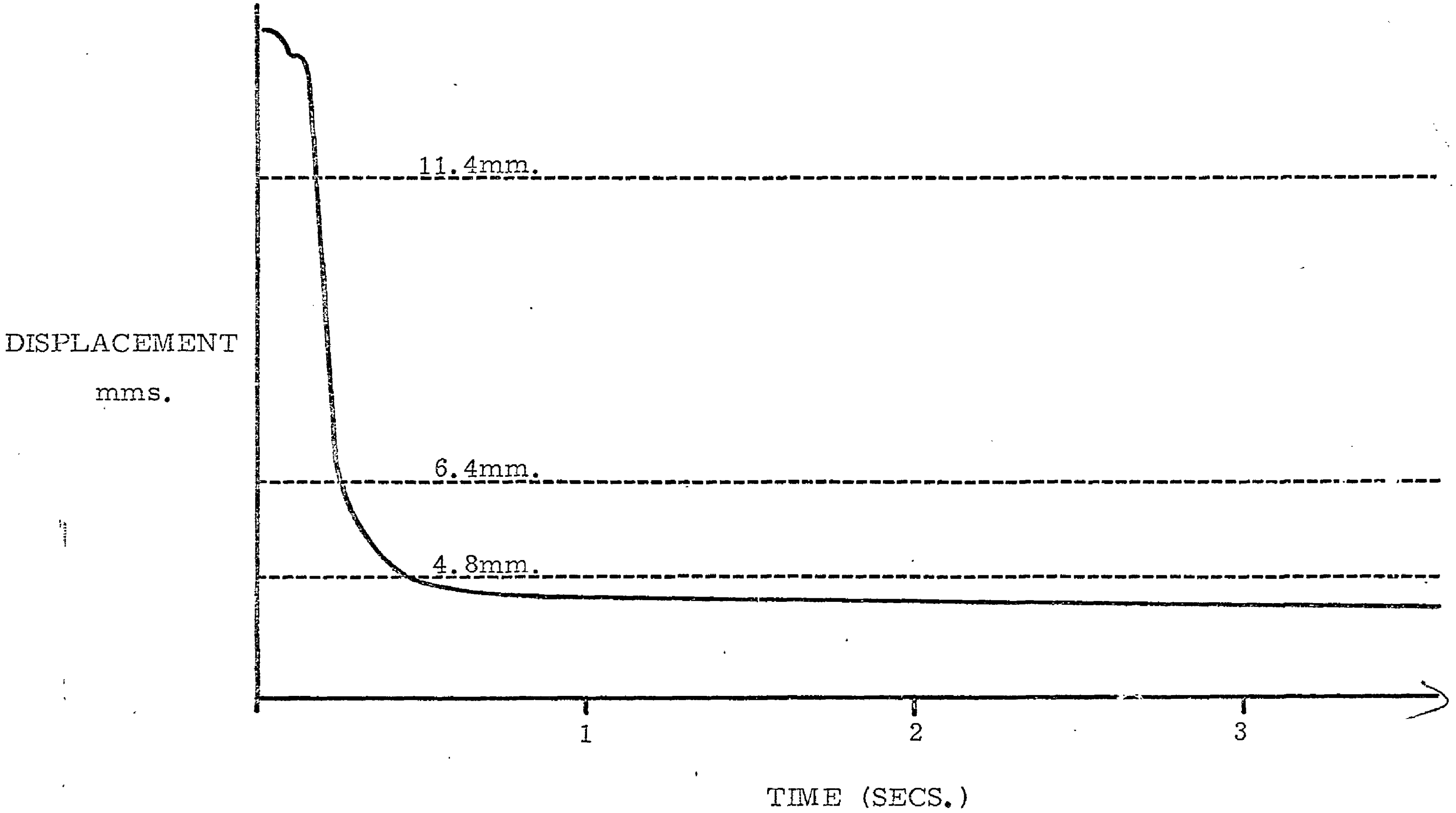


Fig. 7 - Reproduction of an actual response of a Skinfold to Caliper Compression.

Table 3 - Mean of instrumented caliper measurement minus the operator's recorded measurement for two operators (SFT's in mm.).

	Operator 1 (6 Cases)			Operator 2 (3 Cases)
	Mean Difference	S. D.	S. E.	Mean Difference
Biceps	-0. 05	0. 24	0. 109	0. 17
Triceps	-0. 04	0. 13	0. 059	0. 18
Quadriceps	0. 00	0. 18	0. 080	-0. 17
Supra-iliac	0. 12	0. 12	0. 054	0. 08
Subscapular	0. 01	0. 12	0. 052	0. 12

Table 4 - Average error (computed on the modulus of caliper measurement minus recorded measurement) for the combined results of the two operators (SFT's in mm.).

	Average Error	S. D.	S. E.
Biceps	0. 22	0. 16	0. 055
Triceps	0. 18	0. 10	0. 037
Quadriceps	0. 14	0. 11	0. 040
Supra-iliac	0. 15	0. 10	0. 034
Subscapular	0. 13	0. 09	0. 031

and standard error of the differences in the six cases examined by the first operator and the mean difference in measurements on the three cases examined by the second operator. These mean values do not differ significantly from zero, and therefore no difference between the "subjective" readings from the dial and the "objective" readings from the plotter could be demonstrated.

As an estimate of the magnitude of the differences between the subjective and objective readings, means of moduli of the differences from the nine cases of both operators were calculated. As can be seen from Table 4 average errors are generally less than naught point two millimetres.

Experiment 5 A pilot study on eighty-seven normal neonates

SFT measurements in eighty-seven apparently normal neonates were examined. It was intended

a) to demonstrate any differences existing between male and female children and

b) to demonstrate any relationship between SFT and the infants weight and length.

Babies from a series of eighty-seven deliveries whose B.W. exceeded two point six kilograms (Lubchenkos 10th centile) and who were admitted to unit nurseries in the normal way were studied on their second day of life. Standard SFT measurements were taken at the five sites and note was made in addition of their B.W., gestation, sex, birth rank and crown/heel length.

The crown/heel lengths were measured on a purpose-built whole body meter produced specially by the Bio-Engineering department of Strathclyde University.

a) Sex differences

The distributions of parity and gestation at delivery were examined in the forty-eight male and thirty-nine female infants and proved to be similar (Table 5). Comparisons were therefore assumed to be valid. Table 6 shows the comparisons between males and females in terms of length, birth weight, SFT measurements. Also shown are the total limb, total trunk and overall sum of all five measurements. Both the Supra-iliac and the Quadriceps measurements show significant differences between the sexes and these differences also appear in total measurements involving either site. Differences in the variances of data of the two groups occur in the Biceps and Subscapular measurements, with the males having a larger variance than the females.

In an attempt to equalise variances, logarithmic transforms of all the measurements were calculated. The results of the transformations are shown in Table 7 . The coefficients of variation (standard deviation as a percentage of the mean) are all substantially reduced in comparison with the original data, which suggests a much tighter distribution of data, but the differences in variances remain. The significance levels of the differences between means are similar to those shown in Table 6 with Supra-iliac SFT again appearing as the most

Table 5 - Distribution of birth rank and gestation at delivery by sex in sample of "normal" neonates

(48 Males + 39 Females)

	Male (48)		Female (39)	
	No.	%	No.	%
Primigravidae	17	35	14	37
Multiparae	31	65	25	63
Gestation				
36 -37 wks.	5	10.4	4	10.5
38 wks.	7	14.6	4	10.3
39 wks.	13	27.1	9	23.0
40 wks.	13	27.1	12	30.8
41 wks.	7	14.6	7	17.9
42+ wks.	3	6.2	3	7.7
Total	48	100	39	100

Table 6 - Differences in mean value of length, birth weight, and various skinfold measurements of male and female neonates (48 Males + 39 Females)

	Male				Female				Difference
	Mean	S.D.	S.E.	C.V	Mean	S.D.	S.E.	C.V	Significance Level
Length (cm)	50.40	1.90	0.273	4	50.11	2.00	0.321	4	N.S.
Birth Weight (kg)	3.54	0.51	0.070	13	3.41	0.42	0.070	12	N.S.
Limb									
Biceps (mm)	4.03	0.91	0.131	22	4.26	0.61	0.099	14	N.S.*
Triceps (mm)	4.62	0.94	0.139	20	4.95	0.76	0.123	15	N.S.
Quadriceps (mm)	5.91	1.32	0.193	22	6.50	1.29	0.209	20	$P<0.05$
Trunk									
Supra-iliac (mm)	3.82	0.74	0.108	19	4.23	0.63	0.103	15	$P<0.01$
Subscapular (mm)	4.67	1.09	0.159	23	4.96	0.80	0.130	16	N.S.*
Total Limb (mm)	14.56	2.89	0.422	20	15.69	2.30	0.074	15	N.S.
Total Trunk (mm)	8.49	1.72	0.252	20	9.19	1.34	0.220	15	$P<0.05$
Sum Total (5 sites)	23.05	4.48	0.654	19	24.88	3.48	0.564	14	$P<0.05$

* Significant difference in variance

Table 7 - Differences in skinfold measurements of male and female neonates using logarithmically transformed values

	Male				Female				Difference
Skinfold Site	Mean	S.D.	S.E.	C.V	Mean	S.D.	S.E.	C.V	Significance Level
<u>Limb</u>									
Biceps	1.37	0.208	0.030	15	1.44	0.152	0.025	11	N.S.*
Triceps	1.51	0.199	0.029	13	1.58	0.172	0.029	11	N.S.
Quadriceps	1.76	0.224	0.033	13	1.85	0.209	0.034	11	N.S.
<u>Trunk</u>									
Supra-iliac	1.33	0.188	0.027	14	1.44	0.150	0.024	10	P<0.005
Subscapular	1.53	0.225	0.033	15	1.59	0.168	0.027	11	N.S.*
Total Limb	2.66	0.205	0.030	8	2.74	0.153	0.025	6	P<0.05*
Total Trunk	2.13	0.205	0.030	10	2.21	0.146	0.024	7	P<0.05*
Sum Total (5 sites)	3.12	0.198	0.029	6	3.21	0.154	0.025	5	P<0.05

* Significant difference in variance

sensitive measurement.

b) Relationships between SFT, Birth Weight and Length

Table 8 shows the correlation coefficients of birth weight, and length with the various SFTs. There are strong correlations of all the measurements with birth weight. Length does not correlate well with the exception of Quadriceps SFT in the males.

Experiment 6 SFT measurements in six clinically dysmature infants

A small series of clinically dysmature neonates was examined to establish the relationships of their skinfold thicknesses to distribution of the norm. These babies were at term, of birth weight less than 2.6kgs., and exhibited the typical scrawny, wrinkled, mature appearance characteristic of dysmaturity. Data from the eighty-seven infants studied in experiment 5 was used to calculate the "normal" distribution of values for each measurement in males and females separately. These normal values were used to classify the dysmature infants as shown in Table 9. The table shows the relation of the dysmature cases to the "normal" distribution, i.e. those below the first percentile those between the second and fifth percentile etc. All cases were considered by sex.

Table 8 - Correlation coefficients of birth weight and length against skinfold measurements

Skinfold Sites	Birth Weight		Length	
	Male	Female	Male	Female
<u>Limb</u>				
Biceps	0.53	0.42	0.40	0.19
Triceps	0.52	0.47	0.31	0.27
Quadriceps	0.70	0.51	0.52	0.24
<u>Trunk</u>				
Supra-iliac	0.47	0.48	0.26	0.21
Subscapular	0.63	0.35	0.36	0.13
Total Limb	0.65	0.55	0.46	0.27
Total Trunk	0.60	0.43	0.33	0.17
Limb and Trunk	0.65	0.53	0.43	0.25

Significance of results

$\geqslant 0.30$ - sig. at 5% level
$\geqslant 0.37$ - sig. at 1% level
$\geqslant 0.46$ - sig. at 0.1% level

The position of each case on the distribution depends on SFT site but Quadriceps, Supra-iliac, total limb, and sum of five sites all show discrimination.

Table 9 - Number of Dysmatures within various percentile ranges of the "normal" distribution

	Percentiles of "Normal" Distribution			
	<1%	<5%	<10%	>10%
Biceps	4	1	1	0
Triceps	2	1	3	0
Quadriceps	4	2	0	0
Supra-iliac	5	0	0	1
Subscapular	4	1	1	0
Total Limb	5	1	0	0
Total Trunk	4	0	1	1
Limb and Trunk	4	2	0	0

Chapter Four

DISCUSSION OF EXPERIMENTAL RESULTS

Any attempt to develop the use of a spring tension caliper into a simple clinical tool for assessing body fat must take into account the many potential sources of error and ensure that they are adequately controlled.

The sources of error once again are:

1. Errors inherent in the instrument
2. Errors in site selection
3. Variation in handling of skinfold and application of caliper
4. Tissue variability
5. Errors in reading the gauge

1. Errors inherent in the instrument:

The accuracy of the Harpenden caliper itself has been detailed in the M.R.C. trial (45). At jaw openings of about 7 mm., the standard deviation of differences between duplicates for a single observer is of the order of 0.3 - 0.6 mm.

2. Errors in site selection:

It is readily demonstrable in adults that slight variation in selection of the site has a considerable effect on the measurements obtained. In the neonate, it appears that this is not a difficulty. The investigations using duplicate measurements on marked and unmarked sites, (Tables 1 and 2) show that the error involved (15% to 24% at the 95% confidence limits) is not substantially reduced by marking the site. It is also worthwhile noting that the sites with the smallest error were Supra-iliac and Quadriceps.

3. Variation in handling of skinfold and application of caliper:

These variations can be overcome only by rigorous specification of technique. This may limit widespread use of the method by different people in screening programmes. The investigation with the instrumented caliper however (Expt. 4) demonstrated quite clearly that two operators could achieve acceptable consistency in applying the caliper and obtaining reasonable displacement/time profiles.

4. Tissue variability:

Recent studies of the mechanisms of human skin (50), (62), (136) have shown that it exhibits a marked response to tension and compression whether applied uni or multi-axially. It follows that attempts to measure skin and subcutaneous tissue thickness by means of applying a standard compression to a fixed area of skinfold must produce a value dependent upon the time of application of the load. The information presented in Table 3 which shows the difference between the operator's estimate of the SFT and that measured from the trace, illustrates that the time dependent characteristic is of minimal significance and that reading the caliper immediately after the rapid compression phase is perfectly adequate for our purpose. After this initial phase, the compression is of the order of only 0.2 mm. per second (Fig. 6).

5. Errors in reading the gauge:

Great difficulty was encountered in obtaining a stable reading in many infants - steadily and sometimes rapidly decreasing values being apparent. Tanner and Whitehouse (141) described this difficulty as occurring in some older children, and suggested the remedy of reading immediately after the application of the spring's pressure instead of waiting for the needle to settle. This remedy is subsequently adopted as standard in this study. The remedy just described does however place the time of reading on that part of the time/deformation curve left of point C (see Fig. 6), where a decrease in value of the order of 0.8 mm. occurs within 0.5 seconds. Despite this, the results of Expt. 3 showed a close relationship between operator readings and point C in both time and magnitude and those of Expt. 4 demonstrated no marked difference between two operators - vindicating the subjective aspect of the technique. The bi-phasic character of the deformation curve (Fig. 6) raises the interesting question of whether this is due to a period of fluid displacement followed by one of fat displacement and whether a more detailed investigation of the response under controlled rates of loading might make it possible to separate viscous response due to oedema from that due to compression of adipose tissue.

In the series of investigations just described, the sources of error have been examined and it appears that most is associated with tissue compressibility and the reading of the caliper. The difficulties encountered in reading the caliper may in fact be due almost entirely to the tissue compressibility. Errors from other sources are small enough to be ignored provided adequate care is taken in examination technique.

The results of the pilot study in infants (Expt. 5 and 6) can only be regarded as suggestive in view of the way in which the infants were selected. The comparisons between the sexes were shown in Table 6 . Length and birth weight were not significantly different. SFT measurements as Supra-iliac and Quadriceps sites did show a difference at the 1% and 5% levels respectively. The combined measurements were also significantly different between the sexes (at 5% level) but this was due to the influence of the Supra-iliac and Quadriceps measurements and did not improve on the difference of single measurements.

Since it has already been demonstrated (45) that the error associated with SFT measurements is logarithmically distributed, one would expect those measurements which have a smaller magnitude to have a smaller error. To overcome this problem and to improve the distributions of the measurements, logarithmic values of the data were calculated. These log transforms improved the distributions as shown by the reduced coefficients of variation which show the magnitude of the standard deviation as compared with that of the mean (compare Tables 6 and 7).

It was also thought that the transforms would equalise the variances attached to the Biceps and Subscapular measurements but this was not the case. The reason for this is not clear and is difficult to investigate in this trial on the limited data available.

The only difference in SFT between the sexes in the transformed data is in the Supra-iliac measurement, the significance of which has been increased (0.5% level). The difference in Quadriceps measurements is now not significant at 5% level but it is significant at 10% level and can still be considered important.

The group of dysmature infants examined in Expt. 6 is obviously too small to allow firm conclusions to be drawn but it is interesting to note that they all fall into the lower end of the "normal" distributions of each measurement particularly in the Supra-iliac and Quadriceps measurements (Table 9). For comparison the points at which the LFD neonates fall on the distribution of birth weight for the "normal" group is repeated below:

	Percentile of Normal Distribution		
Birth Weight	1%	5%	10%
Number of Cases	5	1	0

To conclude, experiments 1, 2, 3 and 4 suggest that error is mainly associated with reading of values and hence tissue compressibility. It may be that one must regard caliper estimation of SFT mainly as a measure of tissue compressibility and this might be worth pursuing at a later date. The reasonable approximation of subjective readings to instrumental readings enhances the usefulness of the simple tool. Finally, although the error is undeniably large, the fact that significant differences can be demonstrated between the sexes and also between low and high birth weight infants within the context of a preliminary trial is sufficiently encouraging to make further examination of values worthwhile.

SECTION 2 - THE VALUES

Chapter Five

SELECTION OF INFANTS

This section of the work is devoted to the examination of SFT values in Normal, Premature and LFD infants. A preliminary study of time/displacement curves in a small series of normal babies is included.

These experiments were undertaken for the following reasons:

A. It was first of all necessary to verify the relationships between SFT and Birth Weight and between SFT values in males and females respectively, suggested by the pilot study. It was also intended to determine whether any relationship existed between skinfold thickness values and gestation. B. Examination of values in Premature and Light for Dates infants and their comparison with those in the Normal infants should indicate whether the same relationships exist in these infants and, if so, at what gestation they appear. C. Since the question has been raised as to whether skinfold thickness values may be purely a measure of tissue compressibility and since the compression can be shown graphically by means of the instrumented caliper it would be interesting to see if and how the shape of the time/displacement curve alters with the SFT value.

Selection of the normal group

This was straightforward. It was decided to examine the babies of all mothers who attended the Antenatal Clinic of the Royal Maternity

Hospital for their first visit of that pregnancy in September, 1971. It was also decided to omit a) infants of any mothers subsequently found to be Rhesus negative because of the child's predisposition to Hydrops. b) non-caucasian infants and c) infants of multiple pregnancies. Three hundred and thirty-nine first attenders were interviewed and two hundred and thirty-one infants made up the final sample. The difference is accounted for by the omissions mentioned above and by reason of abortion, stillbirth, etc. The exact numerical disposition of the group is given in Table 10. Percentages for the hospital where available are shown alongside.

Selection of Premature and LFD Infants

Isolation of the premature and LFD infants for seperate study was more complicated. Three problems were apparent. It was first of all necessary to identify within the normal group of two hundred and thirty-one infants any who fell into these categories. To do this accurate recording of E.D.D. (expected date of delivery) was obviously essential. Certain precautions aimed at standardizing the collection of this information were therefore employed. These roughly followed the lines of the Aberdeen obstetric survey as described by Thomson, Billewicz and Hytten (146). This involved the writer personally interviewing each patient at her first antenatal visit and questioning her as to the exact date of her last menstrual period and how certain of that date she was. A facsimile of the proforma filled in at that time is shown in Fig. 8 . No account was taken of menstrual irregularity or of any oral contraceptive taken. Although these are known to influence the cycle in an important way,

Table 10 - Numerical disposition of 339 first attendances at G. R. Mat. H. A-N Clinic in September 1971. Together with the hospital incidence for 1969.

Designation	Number	%	Hospital % Incidence
Rh negative	53	15.73	15
Non-Caucasian	9	2.66	-
Plural pregnancy	3	0.88	1.2
Abortions	7	2.07	0.3
Stillbirths	4	1.08	1.55
Delivered elsewhere	9	2.66	1.30
Babies missed	23	6.78	-
Babies examined	231	68.14	-
Total	339	100	-

Name: Hospital Number:

1. First day of last menstrual period ?
2. Is patient sure of dates ? Yes / No
3. If answer to 2 is no, within 2/52

   what limits of doubt exist ? more than 2/52

Category 1, 2 or 3.

Fig. 8 - Facsimile of Proforma on Menstrual Dates.

it was felt that the material would be beyond the scope of the project. The women were graded as to their certainty about the date:

Category 1. Certain of exact date.
Category 2. Certain within 2/52.
Category 3. No certainty.

It was thought that the infants of mothers in category 3 could not except in gross terms be designated LFD or premature and would have to be omitted.

A second problem existed in the recognition of the LFD infant in that no standards of weight for gestation exist for Glasgow. Although Lubchenkos 10th percentile is widely used, the writer preferred to use the standards produced for Aberdeen babies (146) for the following reasons. Although Aberdeen mothers are described as taller, healthier and probably different racially, from Glasgow women, the mothers in Lubchenko's work were mostly from different groups immigrant to the Colorado area and the Indian mothers indigenous to the area were excluded. It is difficult to see how this population approximates more closely to Glasgow women than Aberdeen women do. Secondly Colorado is high above sea level and this is now known to affect birth weight. Thirdly, the Aberdeen data was corrected for parity and infant sex, both factors known to be important in deciding birth weight.

The third problem was a question of numbers. From hospital figures it was suspected that the premature infants would number in the region of 40 and the light-for-dates would number about 35.

It was decided to supplement the statistically premature and LFD infants within the normal population sample by additional infants clinically diagnosed as premature by the duty paediatric registrar and statistically diagnosed as "LFD" by the writer using the delivery room records. These babies were examined as they became available in the several months elapsing between the antenatal interview and the subsequent deliveries.

Selection of Cases for Time/Displacement Curves

The difficulties involved in collection of this data were different again. The Bryans XY plotter kindly loaned by Strathclyde University is an expensive piece of equipment and much in demand. Since the machine is rather heavy and comes with assorted minor pieces of equipment such as power sources etc. it is not easily transportable. In addition, choice of scale, calibration etc. involve specialized and constant attention while the machine is in use. The coinciding of baby, writer, engineer and machines poses obvious difficulties. It was decided to collect time/displacement curves on all 2, 3 and 4 day old infants in the three unit nurseries of the hospital on one particular day. Twenty-one babies in fact were examined. The values obtained in these selected groups are detailed in the next three chapters.

Chapter Six

NORMAL POPULATION SAMPLE

Two hundred and thirty-one infants had SFT values estimated in the standard way. The data was analysed a) to confirm the differences between male and female children apparent in the pilot study and b) to demonstrate the relationship between SFT and weight, birth length and gestation.

a) Differences between male and female infants

The distributions of gestation at delivery, social class and maternal age were examined in the 118 male and 113 female infants and proved to be similar (Table 11). Comparisons of SFT values between subjects of different sex were therefore assumed to be valid. It is interesting here to note the disparity between males and females as far as peak delivery times are concerned, the males being mostly delivered at 39 and 40 weeks; the females at 40 and 41 weeks. Table 12 shows the comparisons between males and females in terms of length, birth weight and SFT measurements. Both the Supra-iliac and the Quadriceps measurements again show significant differences between the sexes, female values being higher. Significant differences are also appearing in birth weight and length, female values being lower.

This normal sample thus confirms the findings of the pilot study. Supra-iliac and Quadriceps sites again emerge as the best sites for discriminating between the sexes. Logarithmic transforms of the measurements were calculated but provided no

Table 11 - Distribution of gestation at delivery, maternal age and social class by sex in normal population sample

(118 males, 113 females)

	Male		Female	
	No.	%	No.	%
Gestation at delivery				
0 - 34	2	2	3	3
35	3	3	0	0
36	2	2	0	0
37	6	5	3	3
38	11	9	10	9
39	29	25	15	13
40	32	27	33	28
41	22	18	29	25
42	2	2	12	11
43	4	3	4	4
44+	4	3	4	4
Total	117	100	113	100
Maternal Age				
0 - 15	1	1	0	0
20	16	14	14	13
25	41	34	51	46
30	26	21	23	21
35	20	16	18	16
40	13	10	4	4
40+	1	1	2	1
Total	118	100	112	100
Social Class				
1	10	8	10	9
2	16	14	11	10
3	59	49	49	42
4	15	13	23	20
5	18	15	20	18
Total	118	100	113	100

Table 12 - Comparison between Males and Females in terms of Length, Birth Weight and SFT values in Normal Population Sample (118 males, 113 females)

	Male			Female			
	Mean	S.D.	S.E.	Mean	S.D.	S.E.	Significance Level
Length cm.	50.48	2.47	0.229	49.27	2.23	0.211	$P < 0.001$
Birth Weight kg.	3.41	0.57	0.052	3.26	0.48	0.046	$P < 0.05$
<u>Limb</u>							
Biceps mm.	4.89	0.86	0.079	4.99	0.96	0.091	N.S.
Triceps mm.	5.30	1.04	0.096	5.43	1.08	0.102	N.S.
Quadriceps mm.	7.93	1.70	0.157	8.51	1.85	0.175	$P < 0.05$
<u>Trunk</u>							
Supra-iliac mm.	5.23	1.00	0.092	5.70	1.15	0.108	$P < 0.005$
Subscapular mm.	6.15	1.40	0.129	6.31	1.34	0.129	N.S.

$P < 0.01$ = highly significant

$P < 0.05$ = significant

additional information and are thus not presented.

b) The relationship of SFT values to Birth Weight, Birth Length and Gestation

Correlation coefficients of birth weight, birth length, gestation and SFT values are shown in Table 13. All SFT values correlate well with birth weight. Quadriceps appears to be the site providing the most significant relationship. Correlations are also obvious between SFT values and length. No relationship seems to exist between SFT values and gestation.

This study of SFT values in a normal population sample thus confirms the findings of the pilot study namely, a significant difference seems to exist between males and females at the chosen Supra-iliac site and the measurements have a significant relationship with the infants birth weight and birth length. This particular experiment emphasises also the differences between male and female infants at term with regard to birth weight and length already demonstrated in for example the Birthday Trust Study (23).

Table 13 - Correlation Coefficients of Birth Weight, Length and Gestation with SFT Measurements in Normal Population Sample (118 males, 113 females)

Skinfold Sites	Birth Weight		Length C/H		Length C/R		Gestation	
	Male	Female	Male	Female	Male	Female	Male	Female
<u>Limb</u>								
Biceps	0.50	0.53	0.34	0.32	0.47	0.44	-0.04	0.10
Triceps	0.53	0.60	0.36	0.37	0.44	0.48	0.06	0.16
Quadriceps	0.72	0.72	0.50	0.40	0.59	0.58	0.12	0.17
<u>Trunk</u>								
Supra-iliac	0.60	0.57	0.47	0.30	0.49	0.42	0.11	0.086
Subscapular	0.65	0.57	0.54	0.29	0.56	0.40	-0.31	0.12
Birth Weight			0.89	0.73	0.87	0.82	0.21	0.24
Length C/H							0.26+	0.09
Length C/R							0.25+	0.15

>0.3 = significant

>0.4 = highly significant

Chapter Seven

THE PREMATURE INFANTS

The problems of identifying the premature infants have been mentioned in Chapter Five and the Aberdeen method (146) of tightening selection by categorizing the mothers certainty about her dates put into practice.

Of the 231 infants available for examination, 19 (14 male and 5 female) had birth dates earlier than 37/52 gestation and belonged to mothers with categories 1 and 2 certainty. This is 8.2% compared with the hospital incidence in 1971 of 12.4% premature live births for all mothers. Details of these infants are given in Appendices 1 and 2. It can be seen that several of the cases are incongruous presumably reflecting mothers who were sure but wrong. The crown/heel, crown/rump lengths and position on the birth weight centile chart (146) are given and may be useful as an indication of whether the gestation noted is appropriate. The preponderance of males is interesting and reminiscent of their earlier gestation peak in the normal infants.

Details of the supplementary group of infants, 10 males and 14 females are given in Appendices 1 and 2. As previously stated, the assessment of the infant as premature by the duty paediatric registrar was used as the qualification for admission to this group.

The total number of premature infants ultimately examined was 43, 24 male and 19 female.

Differences between male and female infants

The distributions of the infants gestation were plotted graphically Figs. 9,10,11,12, and it was immediately obvious that no comparison of the sexes could be undertaken. Although the difference in numbers had been anticipated to some extent, it should have been appreciated earlier that numbers in the region of perhaps 30 males and 30 females at each week of gestation would be necessary for comparison. The question as to sex differential at earlier gestation remains unanswered. The graphs Figs. 9,10,11, 12, do suggest however a trend to increasing values of SFT with gestation, at least at later gestations.

Relationship between SFT, Birth Weight, Birth Length and Gestation

Correlation coefficients were determined and the results are presented in Table 14. Males and females are considered together to boost the numbers. The correlations between skinfold thickness values and birth weight and length seem to have improved and a significant correlation with gestation has appeared. This is probably due to wider ranges of gestation.

It seems obvious now that less emphasis on the definition of prematurity and more emphasis on large numbers to accommodate statistical inaccuracies would have been more fruitful. Nevertheless, the highly significant correlations between SFT and birth weight, birth length, and gestation suggest that further work along the same lines might provide useful information.

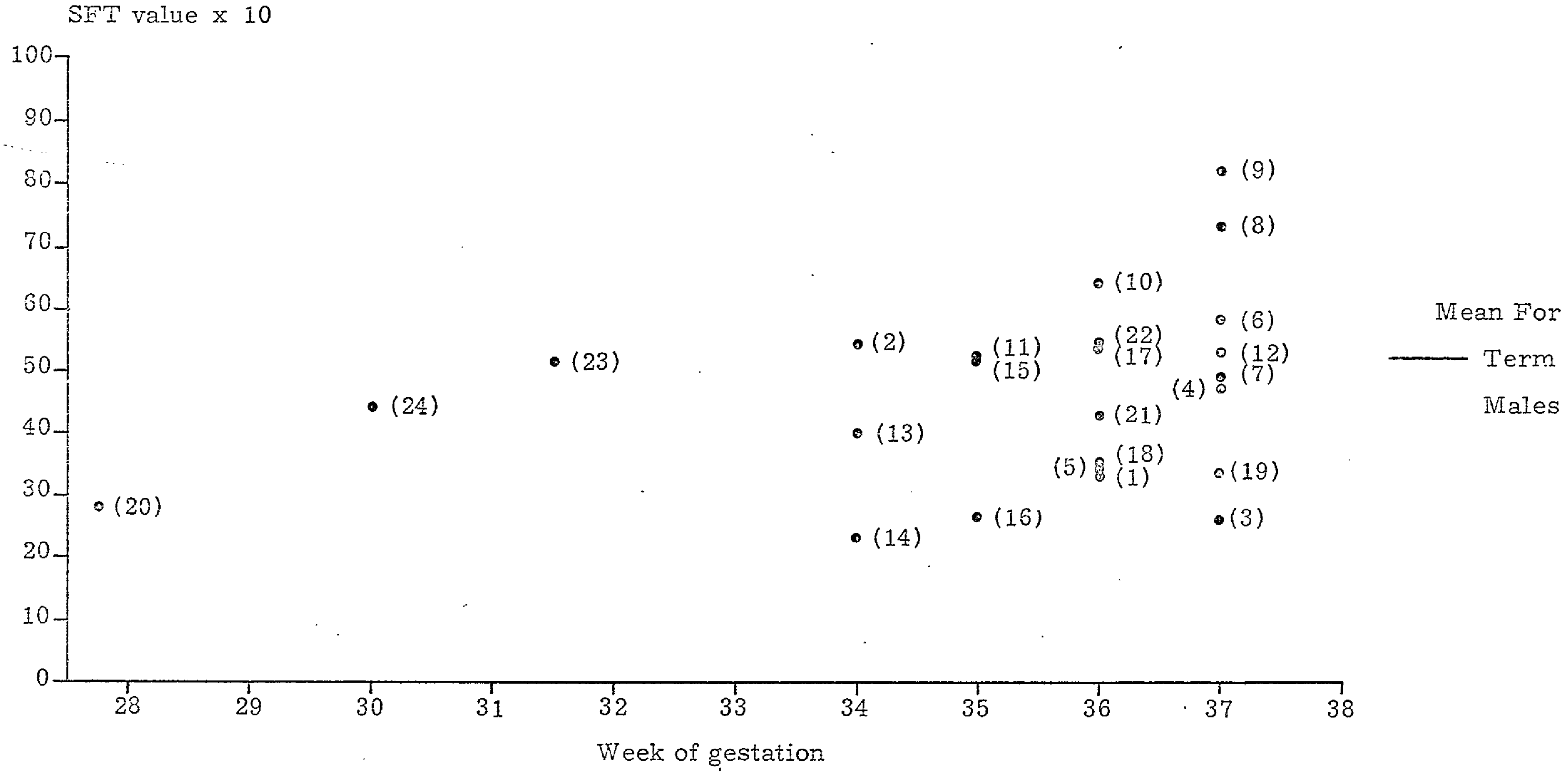


Fig. 9 - SFT measurements at Supra-iliac site against week of gestation in 24 premature male infants.

14 From normal sample + 10 Clinically selected

Appendix numbers ( )

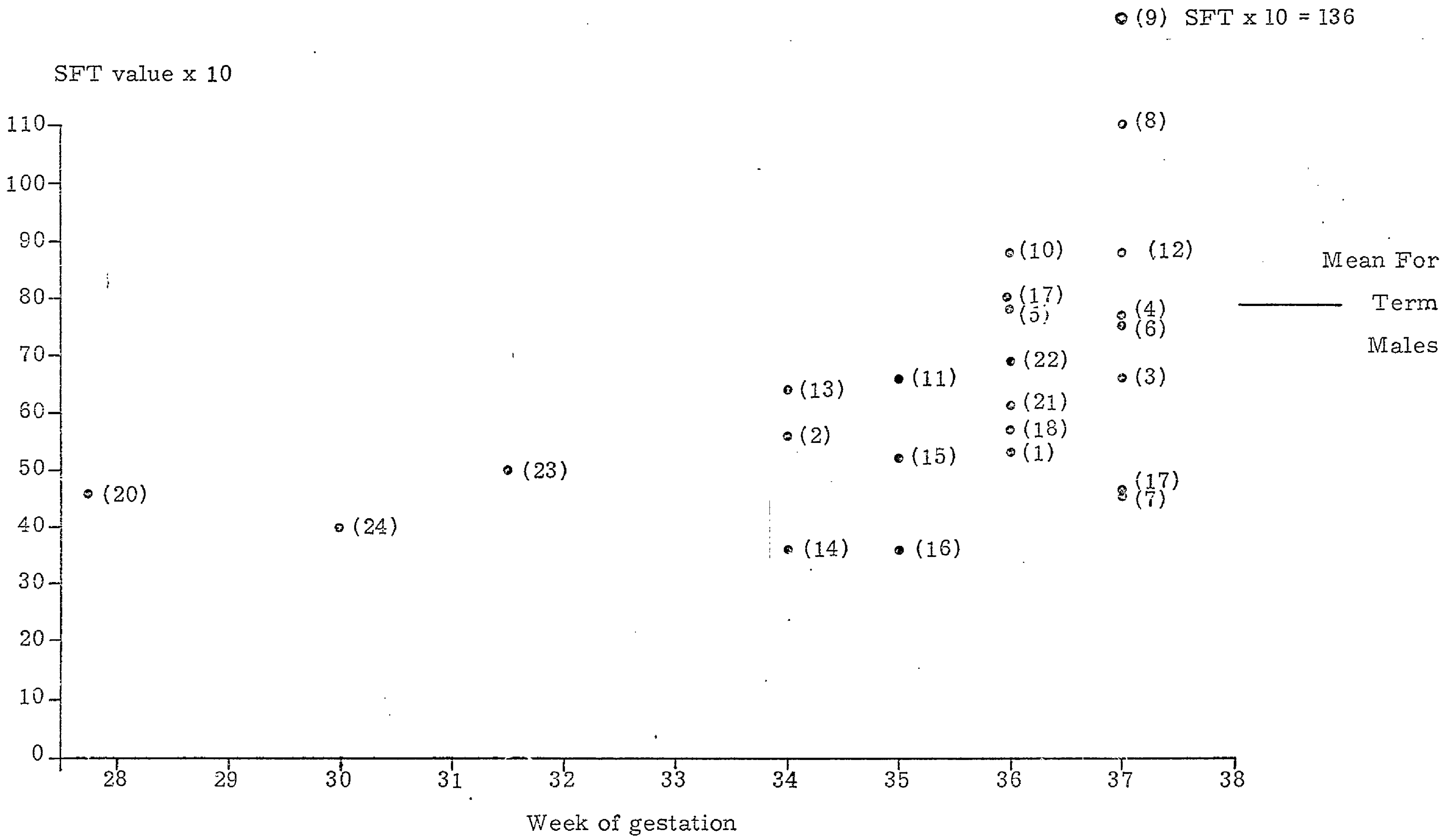


Fig. 10 - SFT measurements at Quadriceps site against week of gestation in 24 premature male infants.

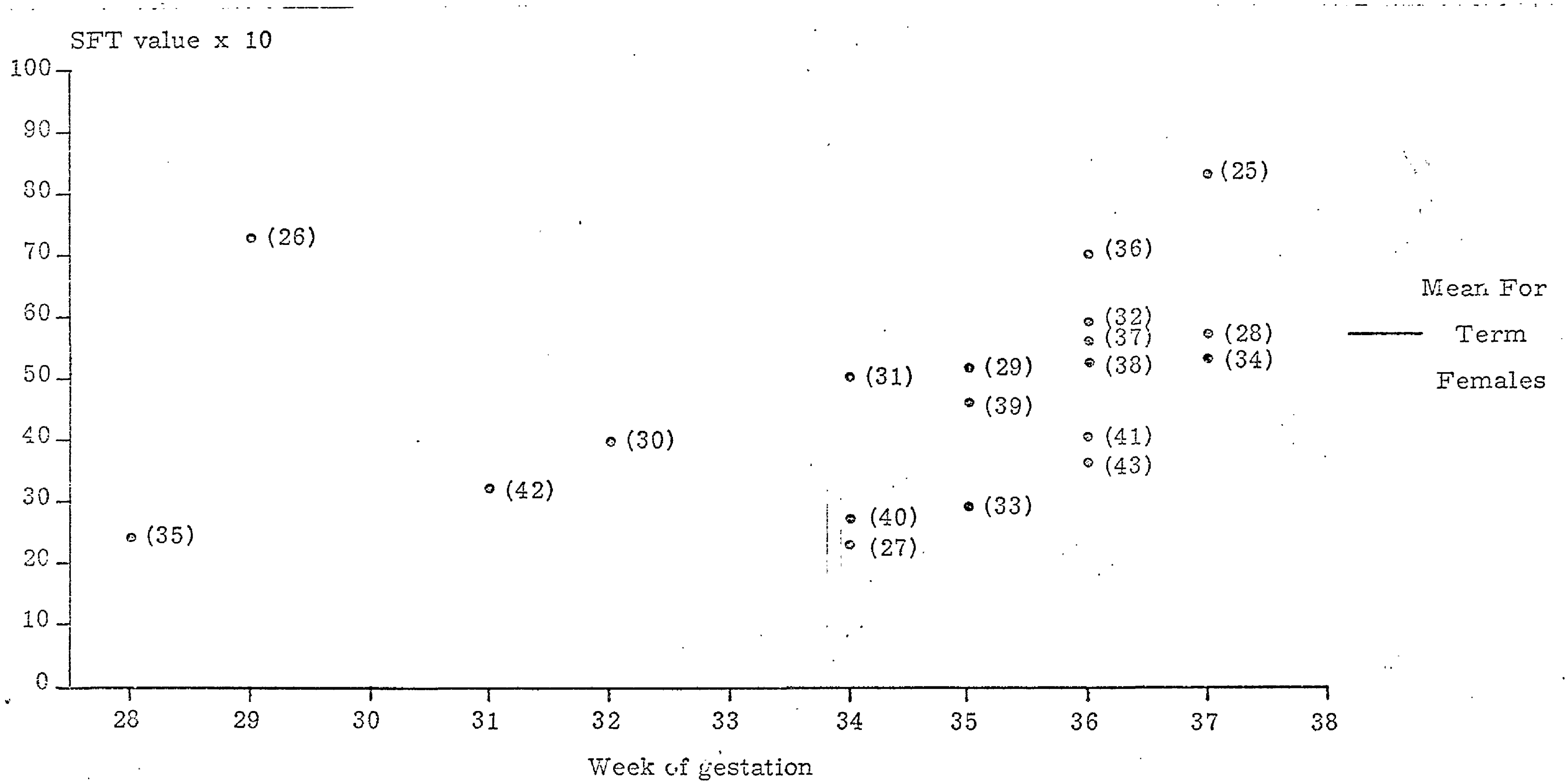


Fig. 11 - SFT measurements at Supra-iliac site against week of gestation in 19 premature female infants.

5 From normal sample + 14 Clinically selected

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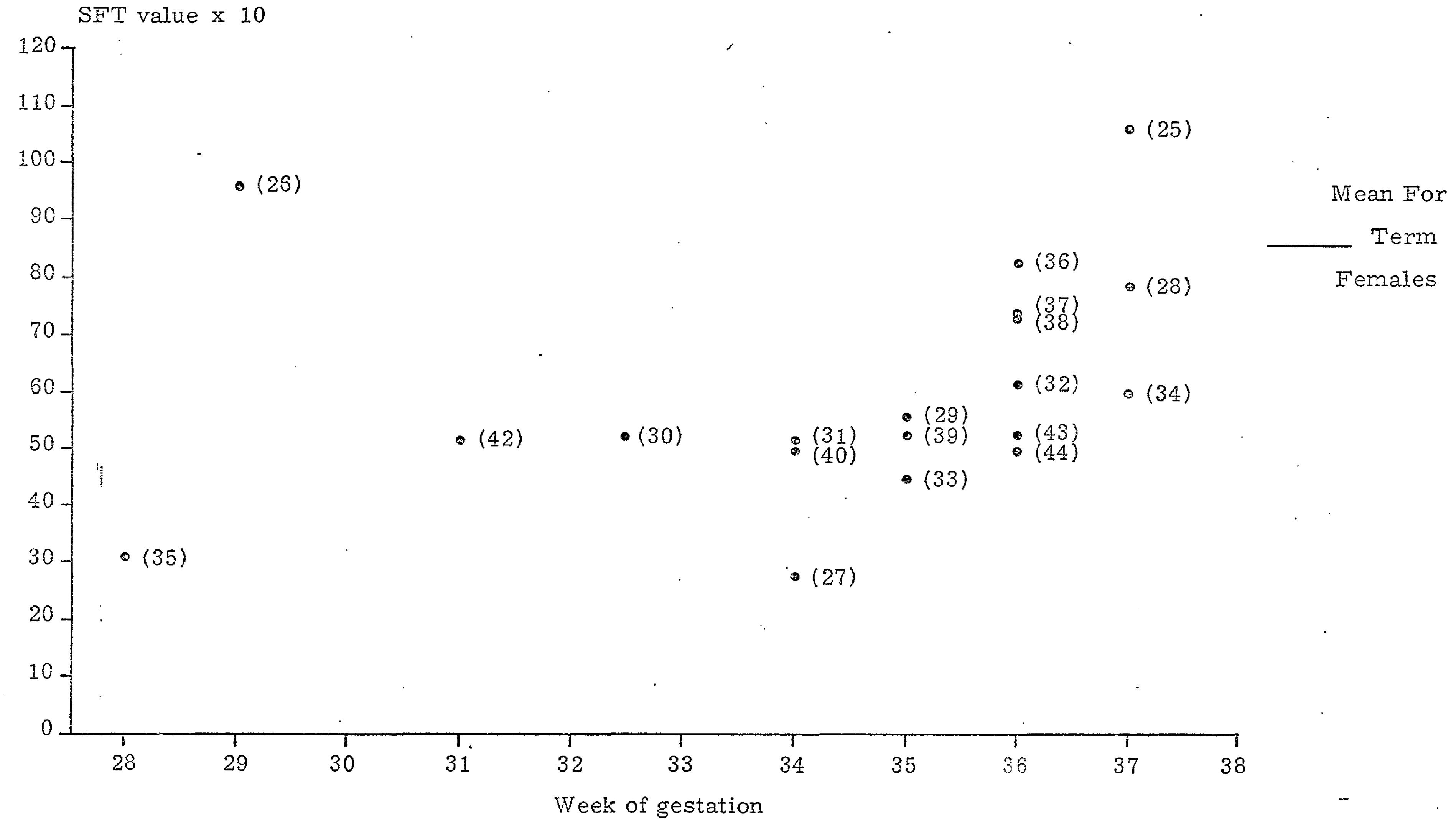


Fig. 12 - SFT measurements at Quadriceps site against week of gestation in 19 premature female infants.

Table 14 - Correlations between Skinfold Thickness and Birth Weight, Birth Length and Gestation in 43 Premature Infants

Skinfold Thickness	Birth Weight	Birth Length C/H	Gestation
Supra-iliac	0.65	0.55	0.44
Quadriceps	0.83	0.67	0.52
Birth Weight		0.95	0.77
Birth Length			0.84

All correlation coefficients are significantly different from zero at the 1% level.

Chapter Eight

THE LIGHT FOR DATES INFANTS

The infants who were light for dates at term were picked out from the normal population sample using Aberdeen standards of weight for gestation (146). Corrections for pregnancy number and infant sex were applied. Term was defined as more than 37 completed weeks. The number of infants in this category born to mothers of category 1 and 2 certainty was 22 (10 female, 12 male). Details of these infants are given in Appendices 3 and 4 . The supplementary group was as previously stated, selected by the writer from the delivery room record in the months between the antenatal interviews and the deliveries of the normal infants. It numbered 47 (22 female and 25 male). Some of these infants were admitted to the Paediatric Unit for various reasons including low birth weight, but the basis of selection was essentially numerical. Details of these infants are given in Appendices 3 and 4 . The total sample analysed numbered 69 (32 female, 37 male). Distributions of these infants with regard to gestation, pregnancy number and maternal age are given in Table 15. It can be seen that they prove comparable. It is again interesting to note the differing gestational peaks between male and female and the high incidence of primigravida. The hospital incidence of primigravid births in 1969 was 34.7%.

Table 15 - Distribution of Gestation at delivery, Pregnancy Number and Maternal Age by sex in the Light For Dates infants

(37 Male, 32 Female)

	Male		Female	
	No.	%	No.	%
Gestation (Weeks)				
37	7	19	2	6
38	5	14	5	16
39	11	30	4	12.5
40	4	11	9	28
41	6	16	7	22
42	2	5	4	12.5
42+	2	5	1	3
	37	100	32	100
Pregnancy Number				
1	18	48	14	44
2	7	19	8	25
3	5	14	2	6
4	1	3	1	3
5	2	5	2	6
5+	4	11	5	16
	37	100	32	100
Maternal Age (Years)				
0-15	1	3	-	-
15-20	11	30	8	25
20-25	14	39	9	28
25-30	5	14	6	19
30-35	4	11	7	22
35-40	1	3	2	6
40+	-	-	-	-
	36	100	32	100

Analysis

No significant differences were apparent between males and females except in terms of birth weight but this difference is probably inbuilt as a result of the selection process. None of the relationships shown to exist in the normal sample were evident in this group. The comparison of values in the light for dates infants with those in the normal infants is presented in Figs. 13 and 14 . These show that SFT values at the Supra-iliac and Quadriceps sites are conforming to the birth weight pattern and occupying levels at and below the mean.

It is probably invalid here to compare the sexes because of the discrimination in the selection and to expect correlation coefficients within the relatively narrow range of values. The writer personally however finds it rather surprising that to all appearances, the relationships between the various criteria of growth and the differences between the sexes have so completely disappeared.

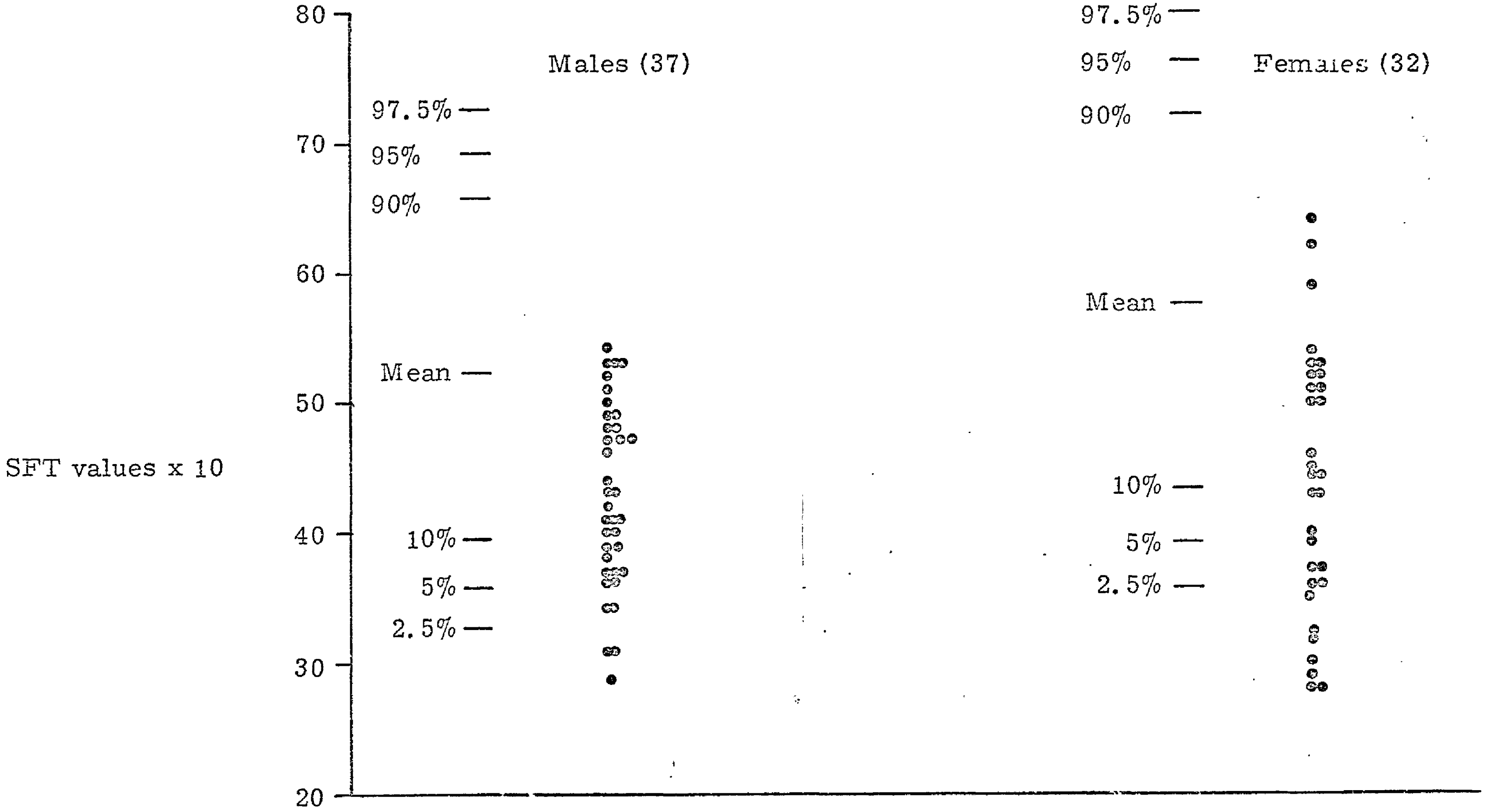


Fig. 13 - Distribution of SFT values at the Supra-iliac site in LFD infants against Centiles derived from "Normal" infants

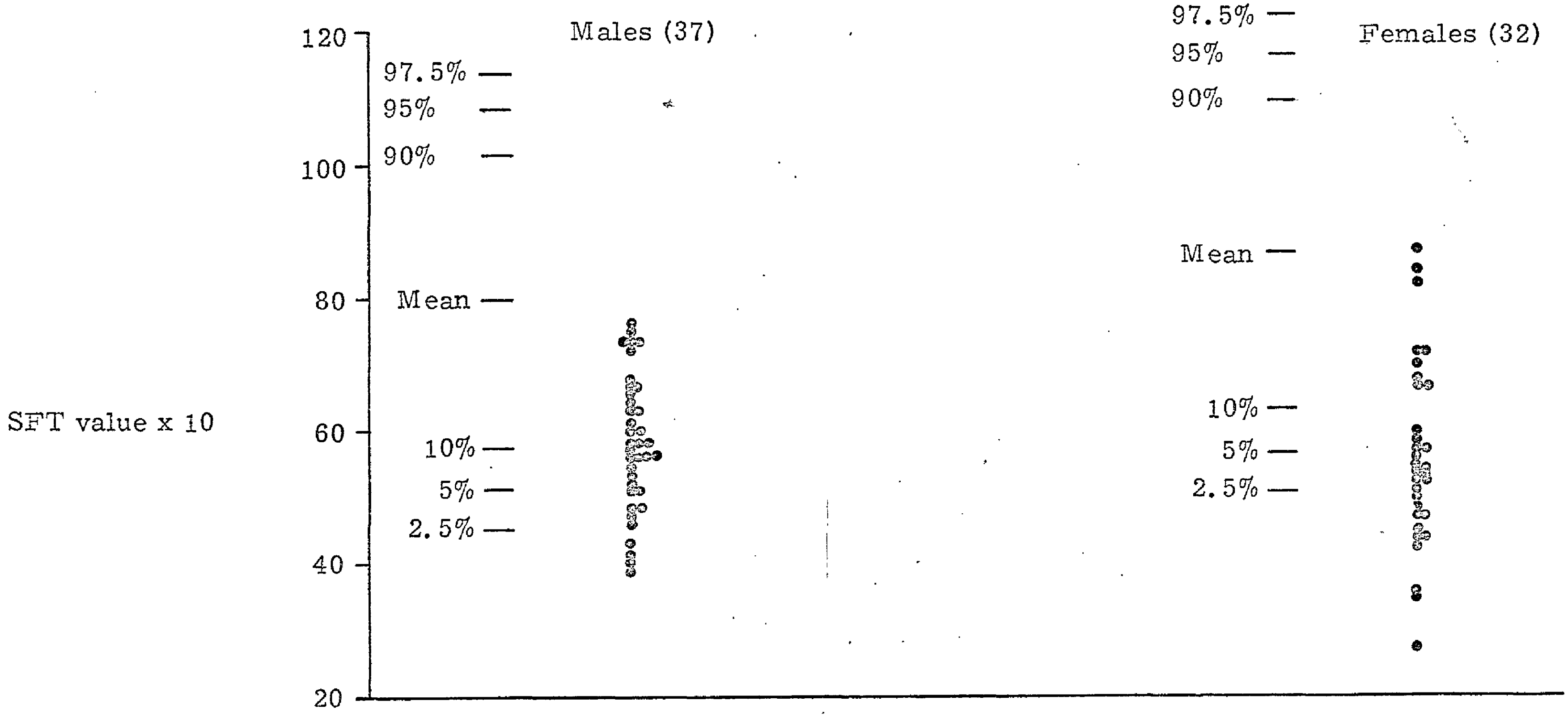


Fig. 14 - Distribution of SFT values at Quadriceps site in LFD infants against Centiles derived from "Normal" infants

Chapter Nine

THE TIME/DISPLACEMENT CURVES

This particular section of the work was designed to see how the shapes of the time/displacement curves altered with different S.F.T. values and to find out how S.F.T. values were related to compressibility as defined by millimetres per second decrease in tissue thickness. It was also hoped to demonstrate any sex difference existing in the curve components. Using the instrumented caliper and the Bryans XY plotter as previously described, graphical illustrations of skinfold distortion were obtained at the Supra-iliac site in twenty-one apparently normal infants. Eleven females and ten males comprised this sample - being the total number of 2, 3 and 4 day old infants present in the obstetric nurseries on one particular day. This was minus three whose mothers refused permission. Details are given in Appendix 5 The difficulties in collecting these graphs have been mentioned already in the chapter on selection, and the consequent smallness of sample means unfortunately that findings must be regarded with some suspicion as to their statistical significance especially since the mean birth weight in the females is atypically greater than that in the males.

Curve Components

On naked-eye examination no gross differences in the shapes of the various curves were obvious. Mathematical descriptions of the curves were then obtained and subjected to analysis.

These descriptions are now given in detail using the key diagram Fig. 15. Point hf was identified corresponding to point C on the original diagrammatic representation (Fig. 6). The value hf should be similar to the SFT value as previously shown (Expt. 4). t_1 was then measured, being the time taken for the tissue to be deformed by one third of a millimetre (h_1) to the hf value. S_1 was calculated as the rate of compression in mm/sec. of h_1 mm in t_1 seconds.

A further one third of a millimetre loss in thickness (h_2) was measured and the time for this deformation t_2 estimated. S_2 was then calculated as the rate of compression in mm/sec. of h_2 mm in t_2 seconds. A point was then identified on the curve corresponding to point B on the original diagram (Fig. 6). This is the point at which a change in the direction of the slope becomes apparent. h_3 was then measured, this being the loss of tissue thickness between point B and point C (hf). t_3 was the time taken for h_3 deformation to occur and S_3 was calculated as the rate of compression in mm/sec. of h_3 mm in t_3 seconds. hf + h_3 should thus represent total uncompressed tissue thickness.

Point A was identified at a point on the curve after manual control was released and before point B. Since this part was in fact a straight line, the rate of deformation, at any one point, should be the same as at any other. S_A was calculated as the rate of compression in mm/sec. for a chosen distance h_4 in t_4 seconds at point A.

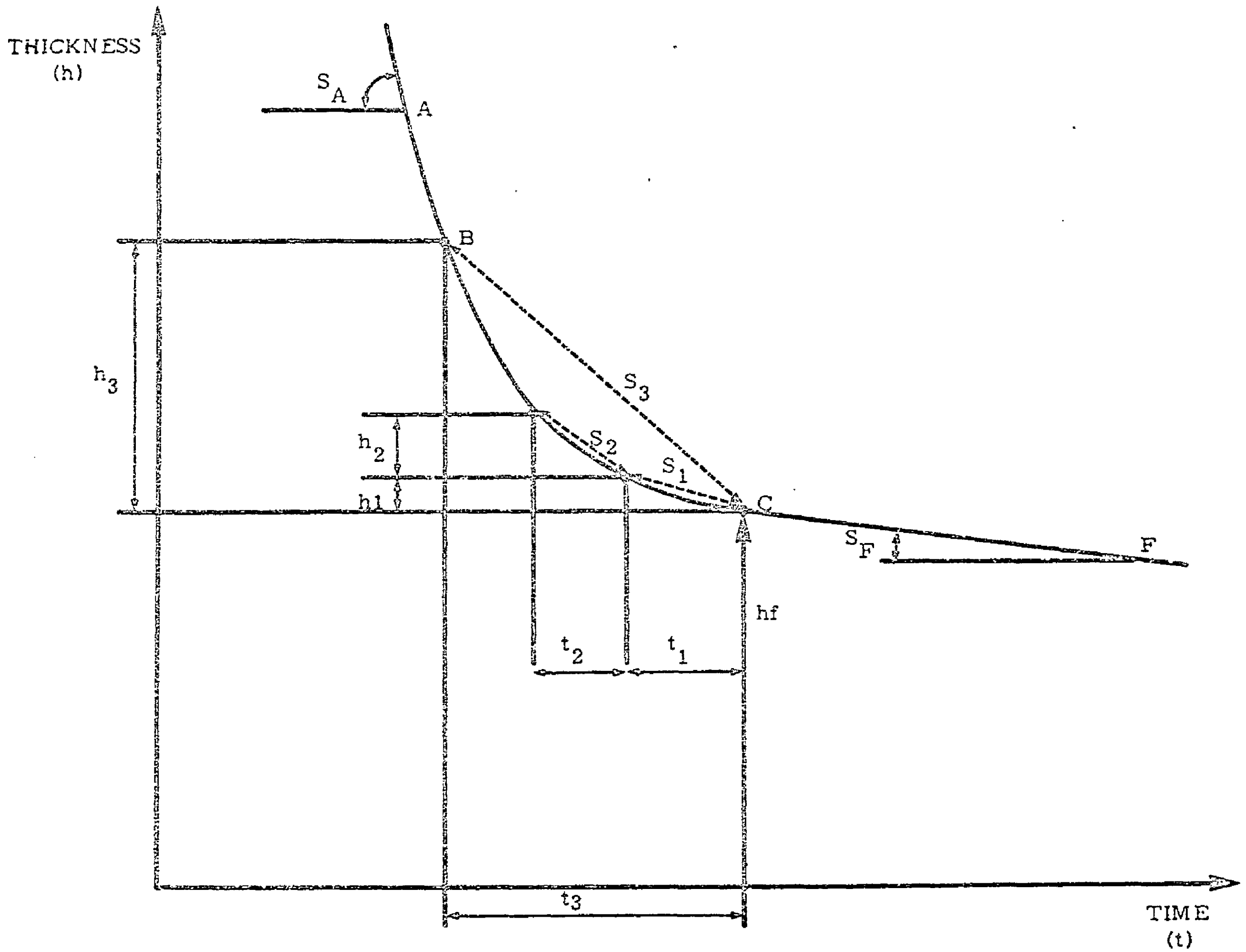


Fig. 15 - Description of Curve Components

A final point F was identified, again at a point on the straight line part of the curve and in the slower compression phase. S_F was calculated as the rate of compression in mm/sec. for a chosen distance h_o in t_o seconds at point F.

Several other formulae were developed, based on the premise that if a correction could be applied for quantity of tissue, some measure of the properties of the material could be obtained. This would technically speaking be a measure of " strain " which is a measure of the properties of material independent of the quantity.

$\frac{h_3}{hf + h_3}$, $\frac{S_F}{hf + h_3}$, $\frac{S_1}{hf + h_3}$, $\frac{S_2}{hf + h_3}$, $\frac{S_3}{hf + h_3}$, were the formulae used.

ANALYSIS

Differences between the sexes

No significant differences were discovered between the sexes. comparison of such small numbers however is probably invalid and details are not included.

Relationships between SFT, Birth Weight and Curve Components

Table 16 shows the correlation coefficients of birth weight and SFT as recorded in the standard way against the curve components just described. It can be seen that excellent correlations exist, as one would expect from Expt. 4 , between SFT and hf (compressed tissue thickness). Good correlations also appear between SFT and $hf + h_3$ (total tissue thickness) and between SFT and S_1, S_2 and $\frac{S_3}{hf + h_3}$. A slight correlation is appearing between SFT and t_1.

Regression of hf against SFT is presented in Fig. 16. One point

Table 16 - Correlation Coefficients between SFT, Birth Weight and Curve Components (21 infants)

	Birth Weight		S. F. T.	
	Corr. Coeff.	t value	Corr. Coeff.	t value
B.W.			0.30	1.39
hf	0.30	1.38	0.94	11.83
t_1	0.13		0.46	2.29
t_2	-0.03		0.33	1.52
t_3	-0.01		0.08	
S_1	-0.14		-0.25	
S_2	0.12		-0.31	
S_3	-0.04		-0.13	
h_3	0.08		0.15	
S_A	-0.37	1.75	-0.12	
S_F	-0.24		-0.16	
$hf + h_3$	0.34	1.56	0.73	4.66
$\frac{h_3}{hf + h_3}$	-0.03		-0.21	
$\frac{S_F}{hf + h_3}$	-0.29		-0.29	
$\frac{S_1}{hf + h_3}$	-0.23		-0.60	3.27
$\frac{S_2}{hf + h_3}$	0.02		-0.48	2.40
$\frac{S_3}{hf + h_3}$	-0.16		-0.40	1.90

Significance	19 degrees of freedom	
Level	$t > 2.09$	$p < 0.05$ significant
	$t > 2.86$	$p < 0.01$ highly significant
	$t > 3.88$	$p < 0.001$

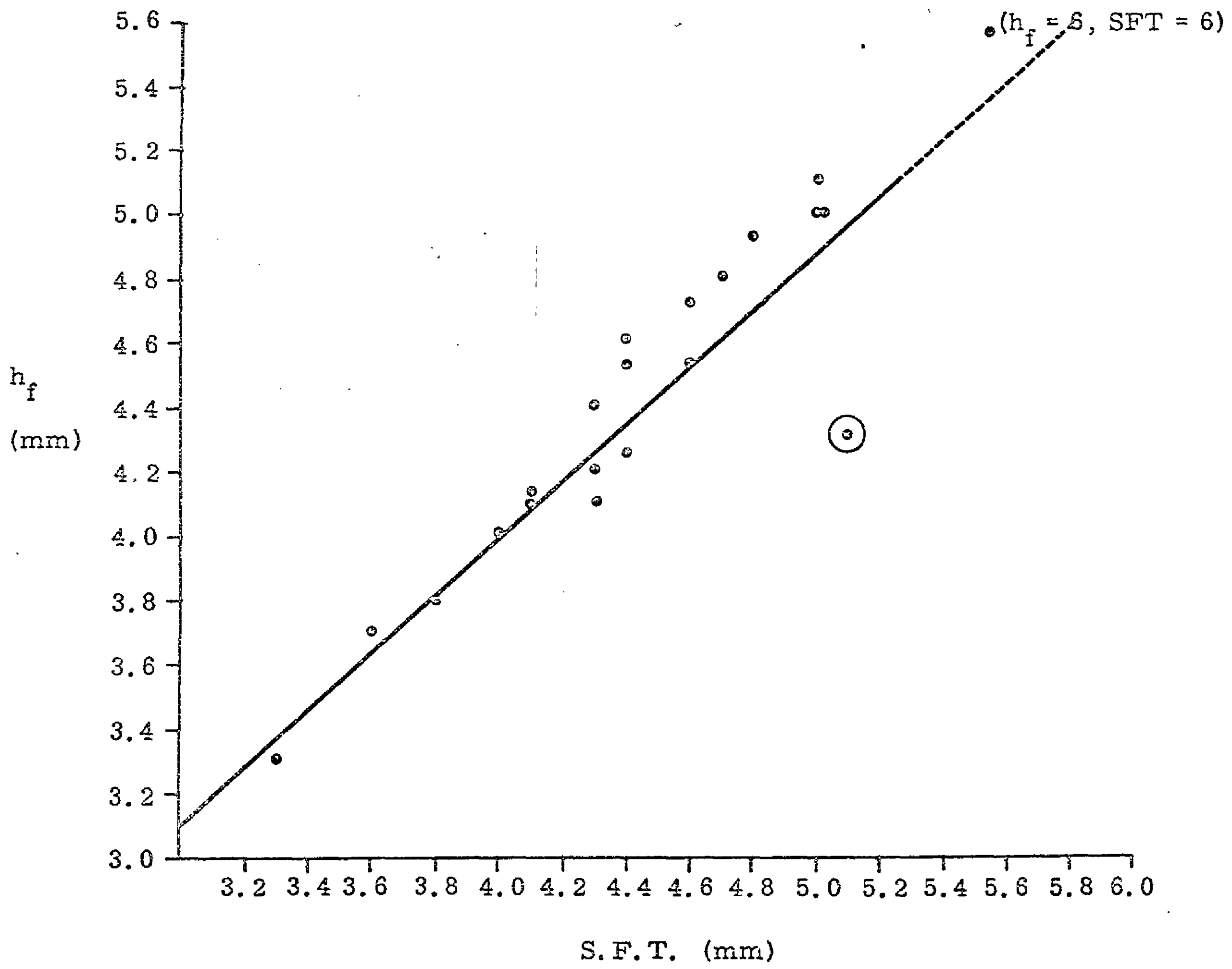


Fig. 16 Regression of h_f against S. F. T. $(y = 0.92 x + 0.35)$

(ringed) seems to be way out, and a re-fit minus this point was calculated. This is presented in Fig. 17 . It can be seen that the deviation from the line of regression is less than 5%. The error appears to be "all or none". The correlations between SFT and S_1, S_2 and $\frac{S_3}{hf + h_3}$ are probably accounted for by the constant highly related hf. These results seem to suggest that SFT is indeed a measure of compressed thickness and not of rate of compression, despite a slight correlation with t_1. The correlation with $hf + h_3$ may however also be due to the presence of hf. Some caution must remain however since the sample is small and the SFT values may differ in two day old and four day old infants. Also, points on the curve were chosen arbitrarily and no accurate record exists of where the operator ceased to control the vertical phase of the curve. A further cautionary note is raised by the fact that the mean birth weight is higher in the females than in the males and that there is no correlation between birth weight and SFT contrary to the findings in the normal group. It is noticeable that strong relationships are appearing exclusively around point C. It may be that an improved sample and a caliper incorporating a pressure-operated time switch such as that used by Robertson et al (114) would demonstrate stronger correlations to the left of the system.

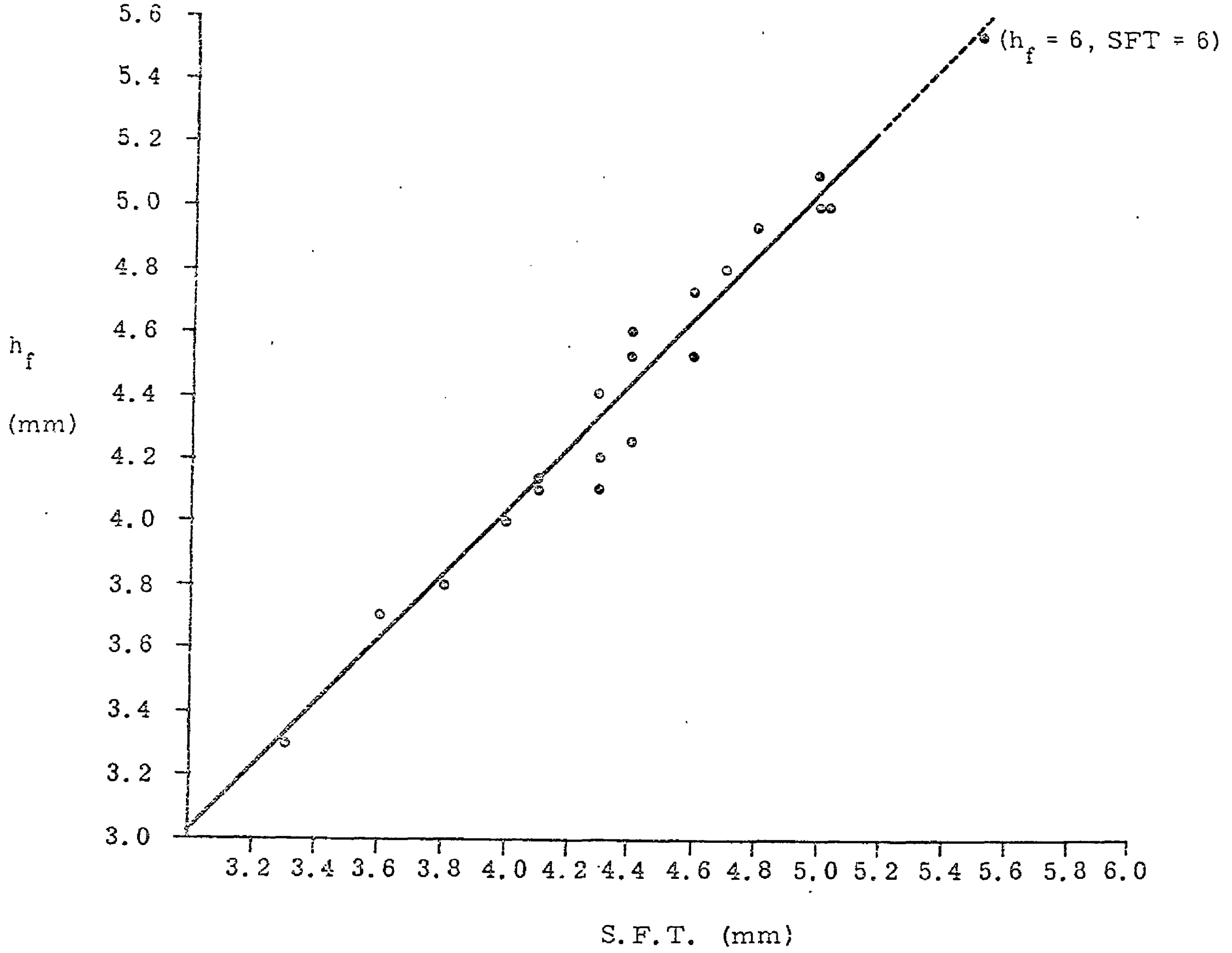


Fig. 17 Regression of h_f against S.F.T. (amended) ($y = 1.009\,x - 0.001$)

Chapter Ten

DISCUSSION OF EXPERIMENTAL RESULTS

The section of work just concluded was devoted to answering the following questions:

1. Did the relationships between SFT and birth weight and between SFT and sex, demonstrable in the pilot study, hold in a properly selected normal population sample and was there in addition any link between SFT and gestation?
2. Secondly, how did the values in premature and LFD infants compare with those of the normal infants and did the same relationships exist in these groups?
3. Thirdly, are the values obtained in the measurement of SFT more representative of compressibility, as defined by mms loss of thickness in seconds of time, than of tissue quantity and is a sex difference apparent in compressibility?

The findings in the normal infants, as reported in Chapter Six, confirm those of the pilot study. SFT values particularly at the Supra-iliac and Quadriceps sites correlate with the infant's birth weight and crown rump lengths to a highly significant degree (Table 13). There appears to be little correlation of SFT with gestation within the comparatively narrow range of gestation in excess of 38 completed weeks. Comparing the sexes within this same sample, (Table 12) there is a significant difference between males and females with regard to Quadriceps SFT values and a highly significant difference with regard to Supra-iliac SFT values.

The female infant has higher SFT values than the male. There is quite an interesting if predictable difference in birth weight and length, male infants having significantly higher birth weights and highly significantly greater lengths.

In the premature infants (Chapter Seven) SFT values proved to have even stronger correlations with birth weight and birth length than the normal infants (Table 14). At the Quadriceps site these correlations were 0.83 with birth weight and 0.67 with crown heel length as opposed to 0.72 and 0.50 respectively in the normals. At the Supra-iliac site, the correlations were 0.65 with birth weight and 0.55 with crown heel length in the prematures as opposed to 0.60 with birth weight and 0.47 with crown heel length in the normals. In addition, highly significant correlations with gestation have become apparent although this may be the result of the greater range of gestation considered. The relevant figures are 0.52 in the prematures against 0.12 in the normals at the Quadriceps site and 0.44 in the prematures against 0.11 in the normals at the Supra-iliac site. All these correlation coefficients are significantly different from zero at the 1% level. The comparisons made here are between all 43 premature infants and the male normals only. There were not sufficient numbers overall to draw statistical conclusions as to how SFT values change with gestation or to consider the sexes separately. It does seem reasonable however to assume that SFT measurements provide an additional and reliable criterion of growth, linked to birth weight and birth length and perhaps through these to gestation.

The light-for-dates infants (Chapter Eight) have SFT values at or below the mean for normal infants (Figs. 13 and 14). This fits the birth weight pattern of these infants as one would expect. No significant relationships were found between SFT values and birth weight, birth length and gestation in this group and the figures are not presented. Comparisons between males and females in this group (figures not presented) showed that the sex differences in SFT values occuring in the normal and premature infants had disappeared in company with the other growth relationships. In fact as might be expected in babies with an abnormal growth picture, the inter-relationships between the various growth parameters in LFD infants are disturbed. It may well be that the absence of these correlations between SFT and birth weight, birth length and gestation and of the sex difference could be a method of determining doubtful cases of " dysmaturity ".

The information gained from the compression curves (Chapter Nine) obtained from all the normal 2, 3 and 4 day old babies in the hospital on a single day, is more limited than one would have hoped. Briefly this experiment has provided corroboration of the close relationship between observer-read values from the hand caliper and values read from the graph. Error seems to be mostly within 5%. An " all or none " basis for this error appears to exist. It does seem at the moment that SFT values are a measure of double the compressed tissue thickness. i.e. SFT = hf. There is however a significant relationship with t_1 i.e. the time taken for the loss of 1/3 mm of thickness to the hf = SFT value.

As already suggested, improving control of the first vertical phase of the curve with a time-switch dependent on a pressure level might improve correlations to the left of the system. No differences between the sexes were apparent although again the validity of comparison in this sample is in question.

It is probably justifiable from these experiments to proceed on several assumptions:-

Skinfold thickness is a reliable concomitant of birth weight and birth length in the infants growth.

The value appears to be equivalent to double the compressed tissue thickness.

In term infants, the female despite being lighter and shorter has consistently thicker SFT values.

The relationships present in normal infants are absent in light for dates infants.

It remains to be seen how chemical values in skinfold tissue relate to these findings.

SECTION 3 - THE CHEMISTRY

Chapter Eleven

INTRODUCTION

The technique is reproducible; standards can be obtained for term infants; but there remains the question of exactly what the values constitute. Since female infants apparently have greater values of skinfold thickness, do they have thicker skins or more subcutaneous fat? Doubt remains as to the existence of sex differences in compressibility. Have males more compressible tissue than females so that consistently lower values are obtained after the same time span? Is the tissue then more fluid in the male, more viscous in the female? Chemical analysis will, it is hoped, go some way to explaining the significance of caliper values of skinfolds, in term vis-a-vis pre-term infants and in male vis-a-vis female infants. This third section is consequently devoted to answering four questions:

1. What are the proportions of H_20 in the skinfolds of the various groups?
2. What are the proportions of fat in the skinfolds of the various groups?
3. Do gross qualitative differences in lipids exist in the skinfolds of the various groups?
4. Are the differences possibly existing in these values sufficient to explain the caliper differences which have been demonstrated?

Although comparison of biopsy values would have been preferred as offering the most direct answers to these questions, it was thought to be ethically unacceptable and it was decided that autopsy material would have to be used despite its disadvantages.

No exact replica of this approach , where skin and subcutaneous tissue are treated as a single organ from the point of view of their chemical composition, can be traced in the literature. Similar estimations of fat, water and lipid patterns have in general been presented under one of the following four headings.

a. Total Body Chemistry b. Compartmental Water Chemistry

c. Skin Chemistry d. Adipose Tissue Chemistry.

a. Total Body Chemistry

The classical autopsy studies of Widdowson, McCance and co-workers in the early fifties (158), (159), (135), (93) have shown that body water decreases with increased gestation. Values of total body water in the region of 82.5 per cent of body weight in premature infants of about 1.5kg weight and 68.8 per cent in term infants of about 3.5kg weight were recorded (159). These water values were accompanied by an increase of fat as a percentage of body weight from 3.5 per cent to 16 per cent over the same weight span. On these studies and that of Wilmer (in 1940) are based the general acceptance up to the present day that the total fat content of the foetus increases particularly during the last trimester of pregnancy. Wilmer (161) in fact recorded a 35-fold increase in subcutaneous fat. No differentiation on grounds of sex is available.

b. Compartmental Water Chemistry

These of course have been performed mainly by dilution techniques in older living children. The close agreement however between the values obtained by autopsy and those by in vivo measurements has been commented on by Friis-Hansen (56), Cassady (26) and Assali, Dehaven and Barrett (6). Again, confirmation of the decline in total body water and extracellular water with increasing age has been reported. Friis Hansen in 1956 (55) summarised the few studies in foetuses and recorded average values of 94 per cent total body water decreasing to 76 per cent over the time span of one to ten lunar months. The corresponding values for extracellular water were a decrease from 62 per cent to 43 per cent from the fifth to the tenth month. Clapp et al in 1962 (29) reported values of 82.5 per cent total body water in prematures and 77.4 per cent in term infants and Smull in 1958 (134) confirmed the range of values in premature infants as being 78 - 88 per cent. Only Smull (134) and Fink and Cheek in 1960 (49) consider the sexes separately and both record the absence of any sex difference. More recently Cassady (26) confirmed that the extracellular space represents a diminishing fraction of total body weight as foetal maturity advances using corrected bromide space estimates. In 1972 average figures collected from the literature were presented by Assali, Dehaven and Barrett (6). These figures were 87 per cent total body water and 62 per cent extracellular water in the 20 week foetus and 78 per cent total body water and 44 per cent extracellular water in the 40 week infant.

c. Skin Chemistry

Little in the way of information as to skin water has been recorded, reliance again being placed on early work such as that of Meyer in

1931 (87). He records the water content of skin as 80 per cent in the human foetus falling to 68.4 per cent in the newborn. He also records a pronounced decline of skin cholesterol with foetal skin having more than three times the content of adult skin. The only study recording any sex difference is that of Haldi (66) in albino rats. He showed that the female skin had a significantly lower water content than that of males. As far as skin fat is concerned, Rothman (118) states that the total fat content of human skin varies in a wide range and it is hardly possible to establish " normal " values. Various authors have reported values varying from 0.7 - 10 per cent but some values as high as 25 - 26 per cent have been recorded and Rothman is of the opinion that these have been heightened by the inclusion of subcutaneous fat in the specimens. Contradictory information comes from animal experiments. Kooyman (81) reported that the fat content of rat skin varied inversely with the size of the animal, the skin of larger rats showing lower and that of smaller rats having higher total values. He also reported higher fat values in female animals than in males. Whether this difference exists in humans is unknown. Smedley - MacLean and Hume (130) reported that the longer rats were starved, the higher was the lipid content of their skin and Gortner (63) made a study of fat in the foetal pig and showed that the percentage of total lipid remained constant for most of its embryonic life.

d. Adipose Tissue Chemistry

Most recent research work in adipose tissue has been on experimental animals and concerned with the complex system of lipid metabolism in the foetal liver. It is generally supposed in recent surveys of the field - e.g. by Dawes in 1968 (33) and by Myant in 1971 (92) that tissue storage of lipid increases in late post-natal life. The main experimental evidence used to support this is, as already stated, that of Widdowson, McCance and co-workers (158), (159), (135), (93) and of Wilmer (161). The constituents of human adipose tissue in general are in fact reported to be about 80 per cent lipid, and 15 per cent water, the proportions varying with site and nutritional state - Pawan (108).

As far as the quality of adipose tissue is concerned, the most notable recent advance was the recognition in 1965 (34) that in the foetus this tissue exists in two forms - brown adipose tissue thought to be mainly thermogenic, and white adipose tissue mainly a calorie reserve. Dawkins and Stevens in 1966 (35) examining brown and white forms from an autopsied newborn infant found however that triglyceride was the major lipid in both forms and that no consistent difference in the fatty acid composition of these triglycerides existed. Considering subcutaneous adipose tissue specifically, Baker (8) reported in 1969 that lipid accounted for 45 - 46 per cent of human newborn tissue from an abdominal site and that the percentage of water in this tissue declined with age. Again triglyceride seems to be the major constituent - " chiefly of stearic, palmitic and oleic acids with small amounts of the more unsaturated acids and various steroids including cholesterol, ergosterol and lipochromes " - Lobitz in 1954 (85). There is also some suggestion that the proportion of monounsaturated acids to saturated fatty acids in subcutaneous adipose tissue differs from one site to another depending on the ambient temperature - Brook in 1971 (18). Hirsch and co-workers in 1960 (72) report a difference between the 99 per cent triglycerides of human adult subcutaneous tissue and the dilution of this in premature tissue by 2. 2 per cent phospholipid and 1. 2 per cent total cholesterol. The higher quantity of cholesterol in premature subcutaneous adipose tissue is reminiscent of the higher cholesterol in human foetal skin recorded by Meyer (87) and referred to under skin chemistry earlier in this chapter. Hirsch (72) alone reports on the sexes separately and states the absence of any consistent difference.

To conclude, no values appear to exist for exact comparison with those to be estimated. However, there appears to be a general trend toward decrease of water and increase of fat in the later weeks of pregnancy, and some suggestion of a decline in cholesterol, in skin and subcutaneous adipose tissue. It remains to be seen whether values from skinfolds correspond with these trends.

Chapter Twelve

MATERIALS AND METHODS

Subjects

Chemical analysis of SF material was undertaken in 46 infants. These were all infants coming to autopsy at Glasgow Royal Maternity Hospital over the space of one year. The group included fresh stillbirths and neonatal deaths of infants aged less than seven days. Distributions of the groups with regard to type of death (i.e. stillbirth or neonatal deaths), birth weight, and gestation are given in Table 17. It can be seen that quite a large disparity exists between male and female with regard to type of death, the smaller stillbirth rate and consequently larger neonatal death rate in females probably accurately reflecting better female survival. The predictably lower birth weight for females is evident as is the progressive decline in total numbers with increasing gestation. The two groups, male and female, can thus be regarded as comparable. Fuller details of the infants involved are given in Appendices 6 and 7 .

Specimens

The actual specimens analyzed were dissected by the writer personally. The infant's body was placed as if for standard caliper measurements in the right lateral position with left arm abducted to 90°. The standard SF was pinched up immediately above the iliac crest in the mid-axillary line. The portion of skin between finger and thumb matched as nearly as possible that enclosed by the

Table 17 - Distribution of Autopsied Infants with regard to type of Death, Gestation and Birth Weight

	Male		Female	
	No.	%	No.	%
Type of death				
Stillbirth	10	34.5	3	17.6
Neonatal	19	65.5	14	82.4
Total:	29	100.0	17	100.0
Birth Weight				
<1kg.	-	-	1	5.9
1 - 2kgs.	15	51.6	10	58.7
2 - 3kgs.	8	27.6	3	17.7
>3kgs.	6	20.8	3	17.7
	29	100.0	17	100.0
Gestation (Wks.)				
28 - 32	12	41.4	6	35.3
33 - 37	9	31.0	6	35.3
38 - 42	8	27.6	5	29.4
	29	100.0	17	100.0

caliper blades in the standard SFT measurements and this portion was excised. Care was taken to remove and include all fat from the surface of the underlying muscle. The final specimen thus consisted of a section of skin and subcutaneous tissue occupying approximately 1sq. cm. skin surface and weighing between 0.5 and 1g. The 46 specimens obtained in this way were subjected to the 3 experiments now described.

Experiment 7 Estimation of Total Percentage of Water by Weight

1. A glass container with a metal-lined lid was weighed.
2. The section of skin and subcutaneous fat taken as described was placed in the container and the whole was re-weighed.
3. The container and specimen were placed immediately in an Edwards vacuum drying machine and left until of constant weight. This was generally in 24 - 48 hours.
4. The dried specimen, together with its container and lid were again weighed.
5. The weight of water driven off was estimated and its percentage of the total specimen weight calculated.

Experiment 8 Estimation of Total Percentage of Fat by Weight
(after Folch, Lees and Sloane-Stanley 1961) (53)

1. The weighed dehydrated specimen of Experiment 7 in the same weighed container was distintegrated in 5mls. of two parts to one, 2:1, volume for volume chloroform : methanol by using an Ultra-Turrax homogenizer for 60 seconds at voltage 100.
2. The resulting suspension was washed into a centrifuge tube together with the washings from the homogenizer using a

further 5mls. chloroform : methanol.

3. The extract was centrifuged at 3000 revs./min. for 5 mins.
4. The supernatant fluid containing the lipid was poured into a test-tube.
5. A further 5mls. chloroform : methanol was added to the deposit in the centrifuge tube which was again centrifuged at 3000 revs/min. for 5 mins.
6. The second supernatant fluid was added to the first in the test-tube and the non-lipid deposit discarded.
7. Three mls. of distilled water was added to the lipid solution in the tube which was then shaken well and centrifuged at 2000 revs/min. for 5 mins.
8. The upper phase was removed with a Pasteur pipette and discarded.
9. The lower chloroform phase containing the lipid was filtered through Whatman's No. 1 filter paper into a second weighed glass tube. Chloroform alone was used to wash through the previous test-tube and filter paper.
10. The extract was evaporated to dryness by blowing through Nitrogen in a fume cupboard.
11. The weighed test-tube together with the dry total lipid was re-weighed and the percentage fat content of the dehydrated specimen thus estimated.

This pure fat extract was promptly analyzed to minimise oxidative and other changes. Samples requiring storage were kept in solvent in sealed vials at 70° centigrade.

Experiment 9 To determine if any Gross Differences in Lipid Patterns exist in Various Groups.

1. The lipid extract obtained in the last experiment was re-dissolved in chloroform to produce a 50% solution.
2. This solution was transferred to silica gel glass fibre chromatogram sheets.
3. Chromatographs were developed ascending twice in di-ethyl ether/ glacial acetic acid / normal hexane / of volume 7 : 1 : 93.
4. The individual fractions were visualized by short exposure to Iodine vapour.
5. The chromatographs were immediately photographed so that a permanent record of the freshly obtained pattern was available.
6. Lipid markers were run in an identical manner and similarly photographed for purposes of identification of individual lipid fractions.

Chapter Thirteen

THE RESULTS OF THE CHEMICAL EXPERIMENTS

The purpose of the experiments described in Chapter Twelve was to determine the percentage of water, the percentage of fat and the existence or otherwise of different lipid patterns in the skinfold of a. premature vis-a-vis term infants and b. male infants vis-a-vis female ones.

Experiment 7 Estimation of Total Percentage of Water by Weight

The complete group of 46 infants was initially considered together for the purposes of examining the differences between pre-term and term infants. The values of percentage water in the fat-free specimens were depicted graphically as they related to the infants gestation (Fig. 18) to their birth weights (Fig. 19) and to their crown/heel lengths (Fig. 20). It can be seen from these illustrations that the water content of skinfold tissue decreases with increasing maturity whether denoted by increasing gestational age, increasing body weight or increasing skeletal growth. The data indicates that the water content of skinfold tissue in babies of 30 weeks is about 86 per cent fat-free tissue and in babies of 40 weeks is about 65 per cent. Separate plotting of male and female water values in fat-free tissue against gestation (Figs. 21 and 22) birth weight (Figs. 23 and 24) and crown/heel length (Figs. 25 and 26) illustrate the same overall patterns of decrease. There is perhaps a steeper decline in females from higher values than the male around 32 weeks to lower values than the male around 39 - 40 weeks. At term all female infants have lower skinfold water values

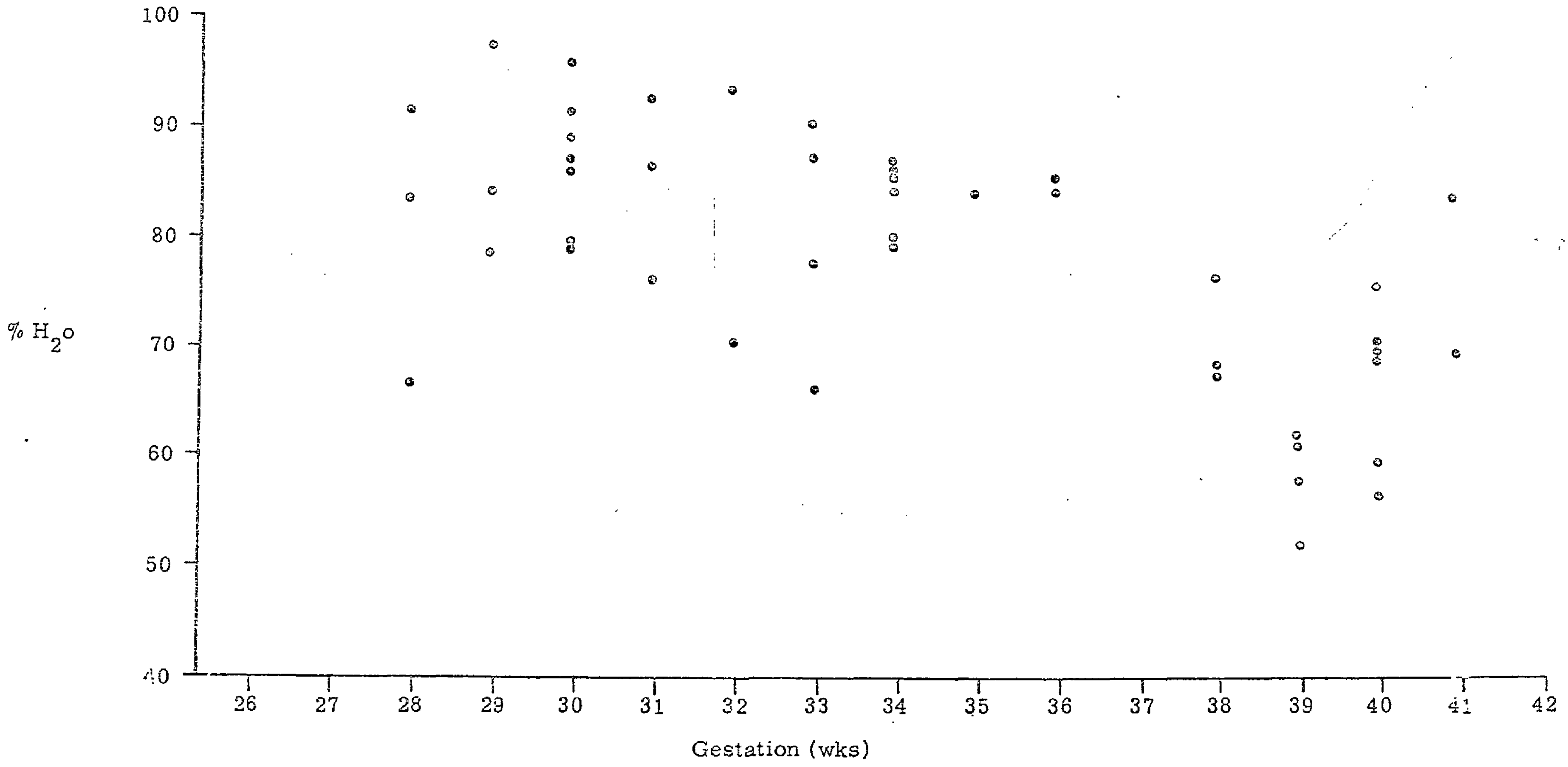


Fig. 18 - % H_2O in fat-free tissue against gestation (46 Cases)

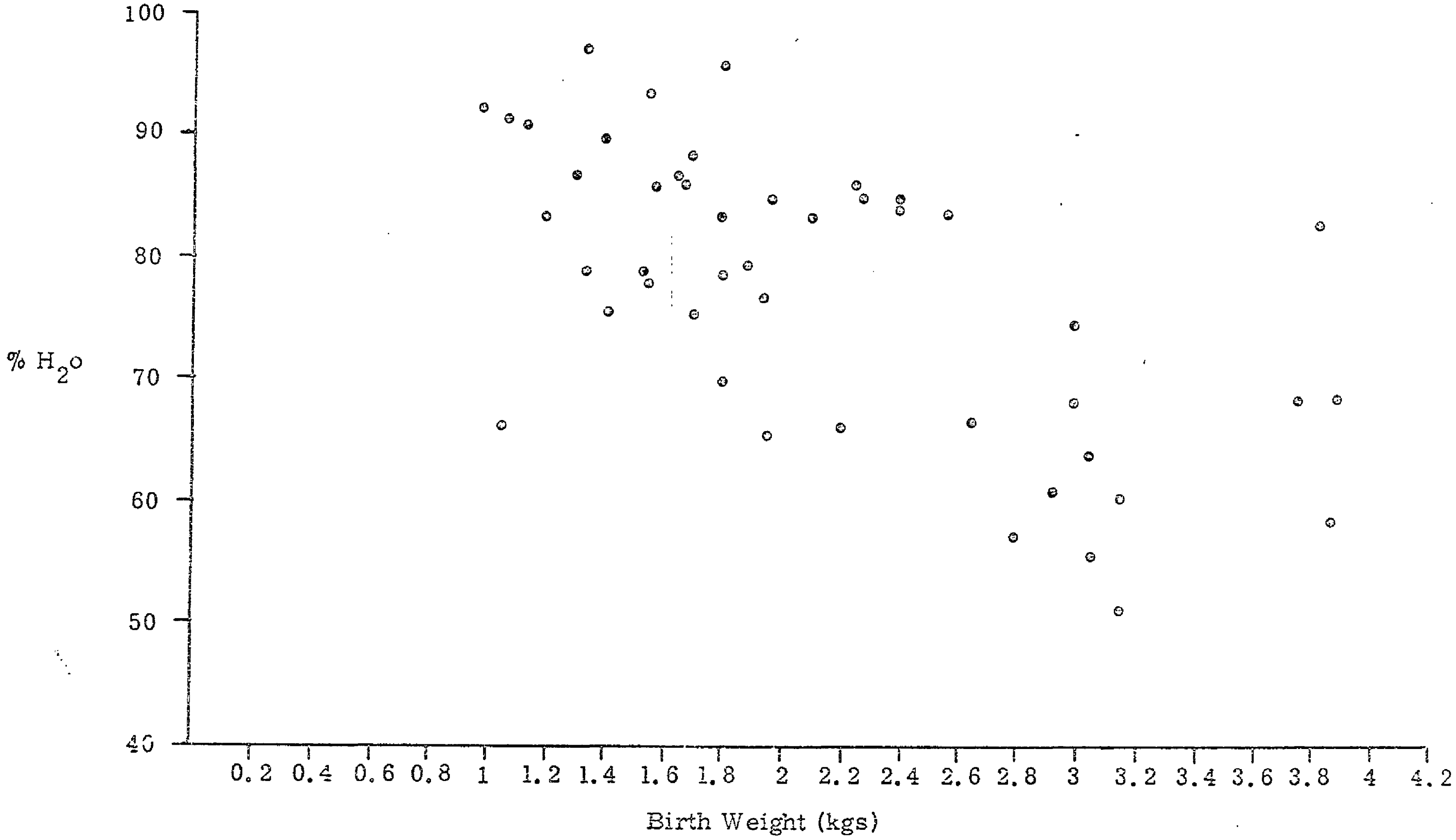


Fig. 19 - % H_2O in fat-free tissue against birth weight (46 Cases)

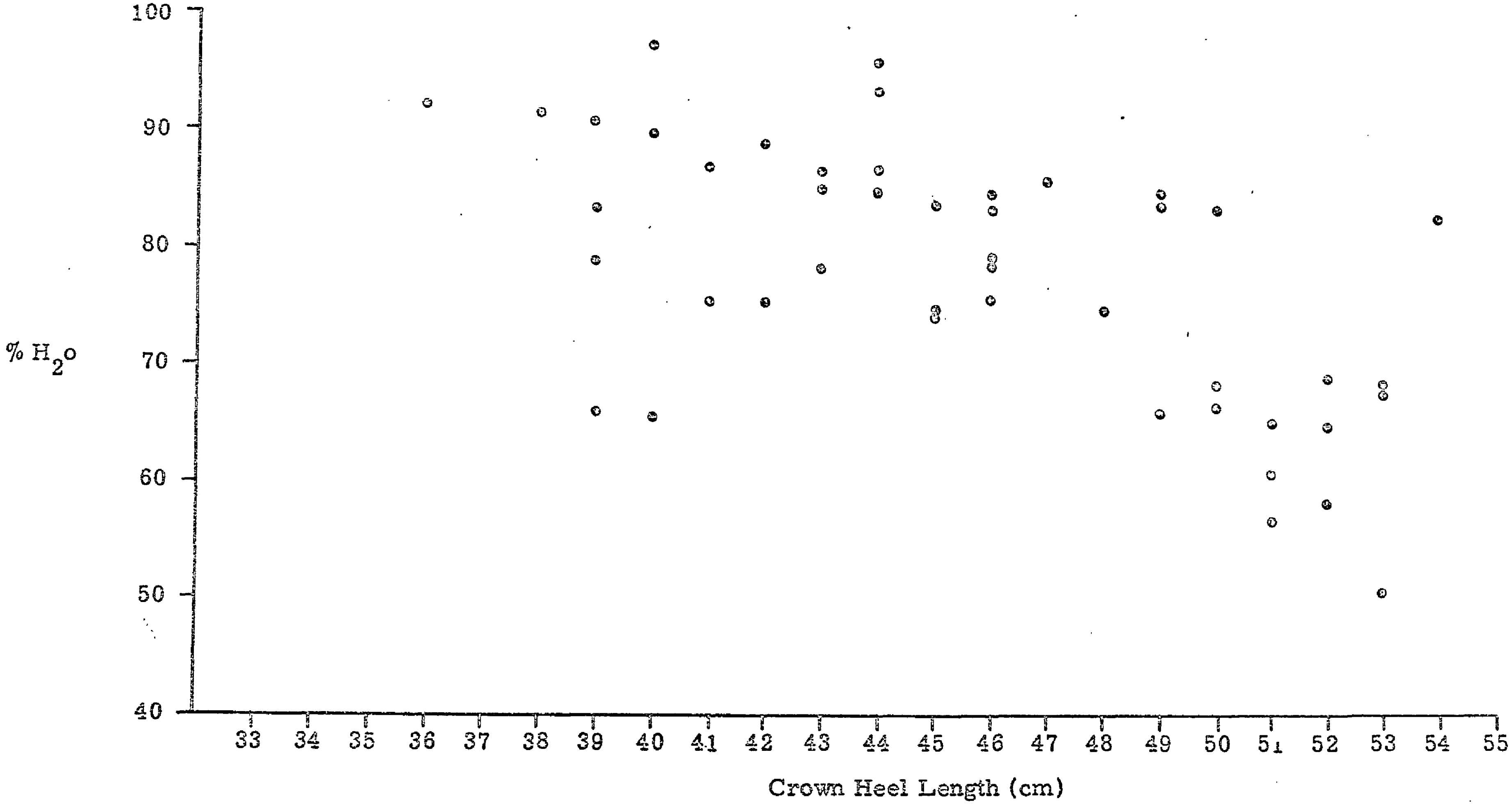


Fig. 20 - % H_2o in fat-free tissue against crown heel length (46 Cases)

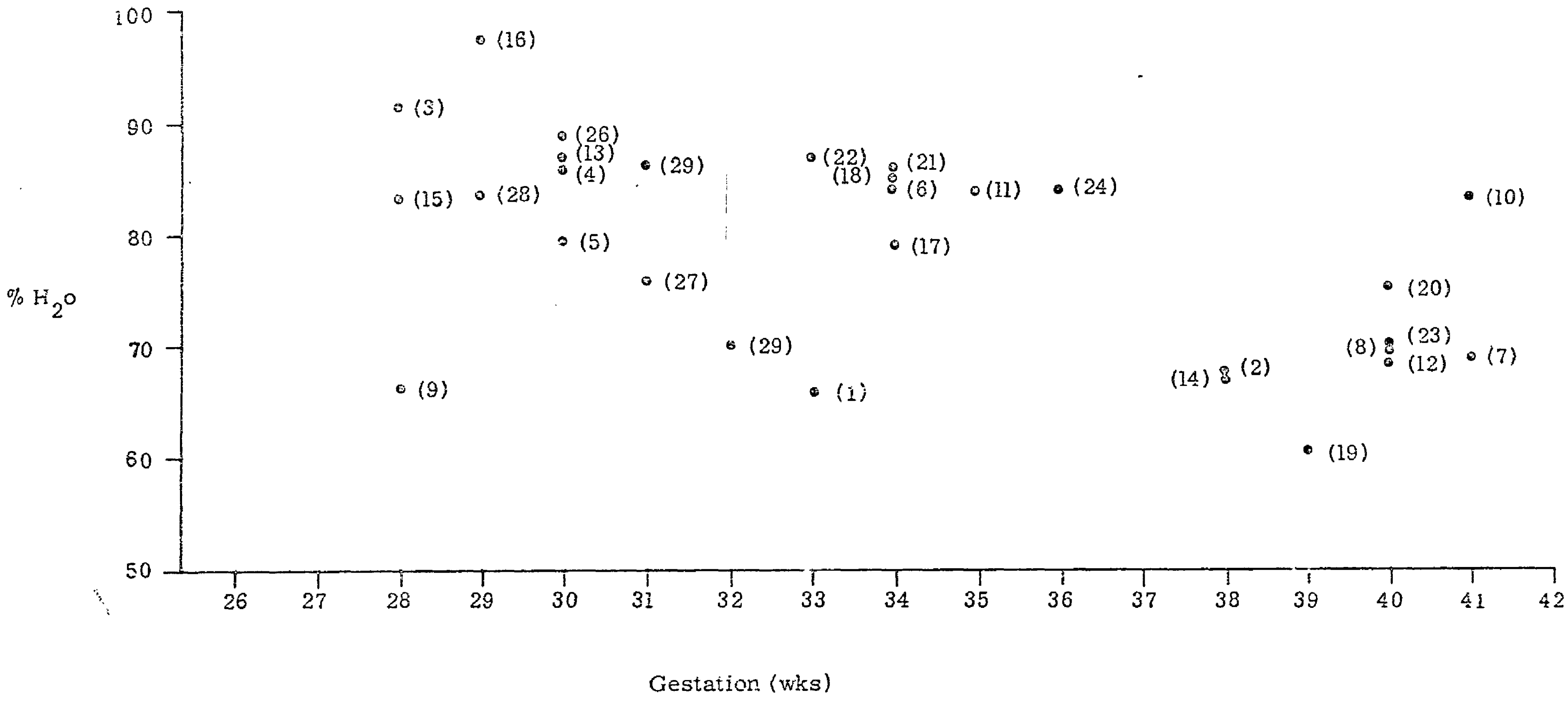


Fig. 21 - % H_2O in fat-free tissue against gestation (29 Males)

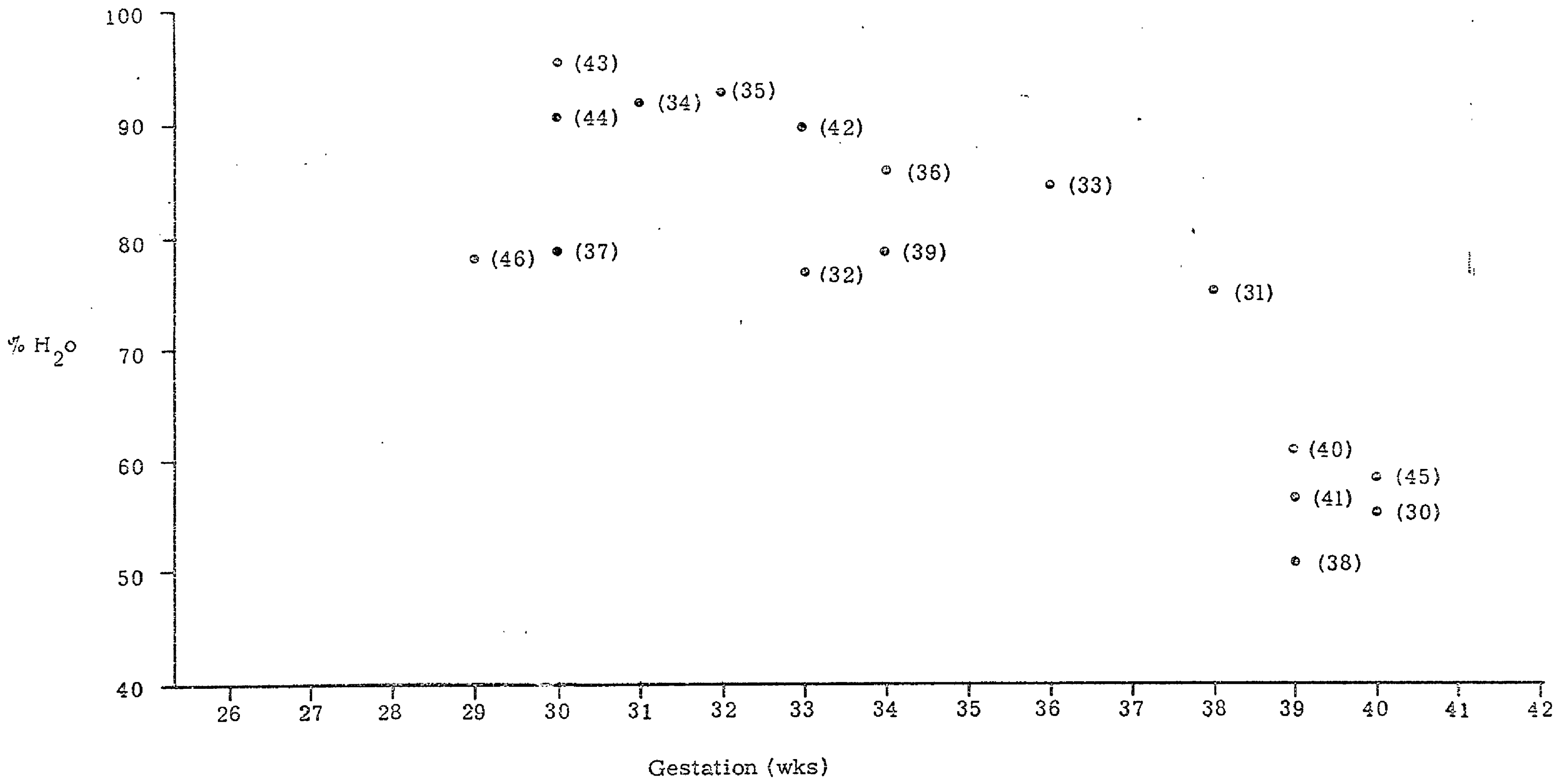


Fig. 22 - % H_2O in fat-free tissue against gestation (17 Females)

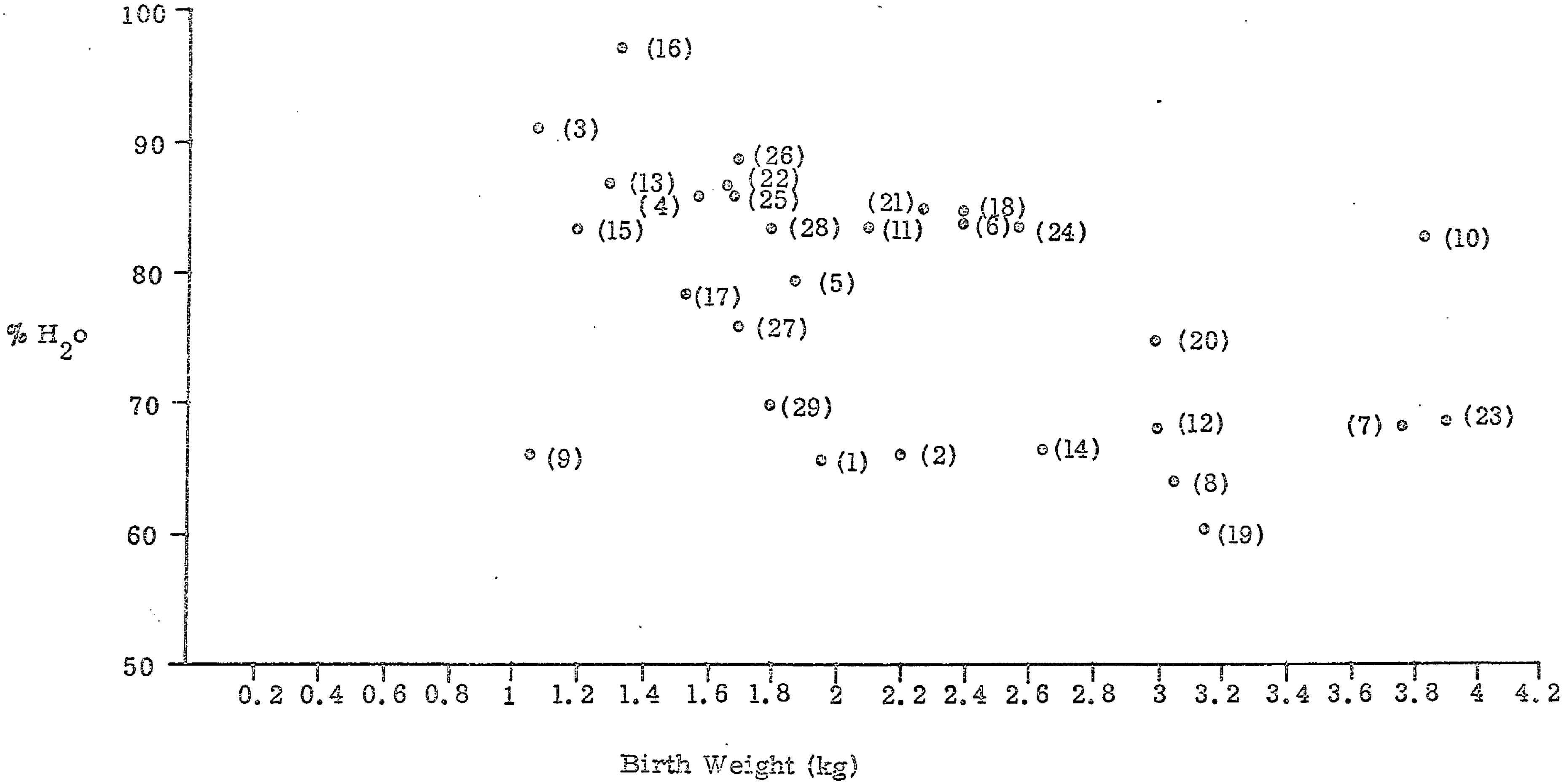


Fig. 23 - % H_2O in fat free tissue against birth weight (29 Males)

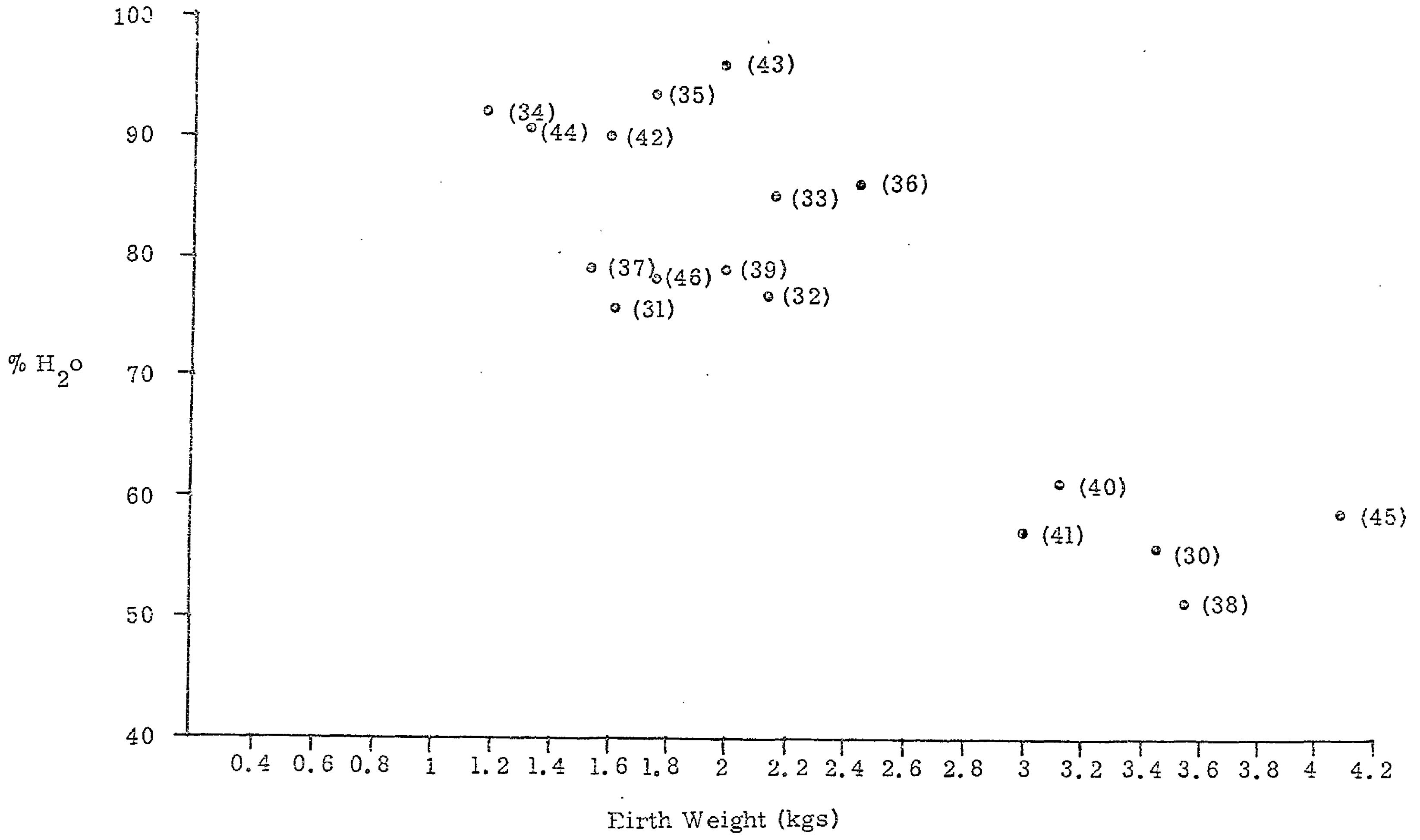


Fig. 24 - % H_2O in fat-free tissue against birth weight (17 Females)

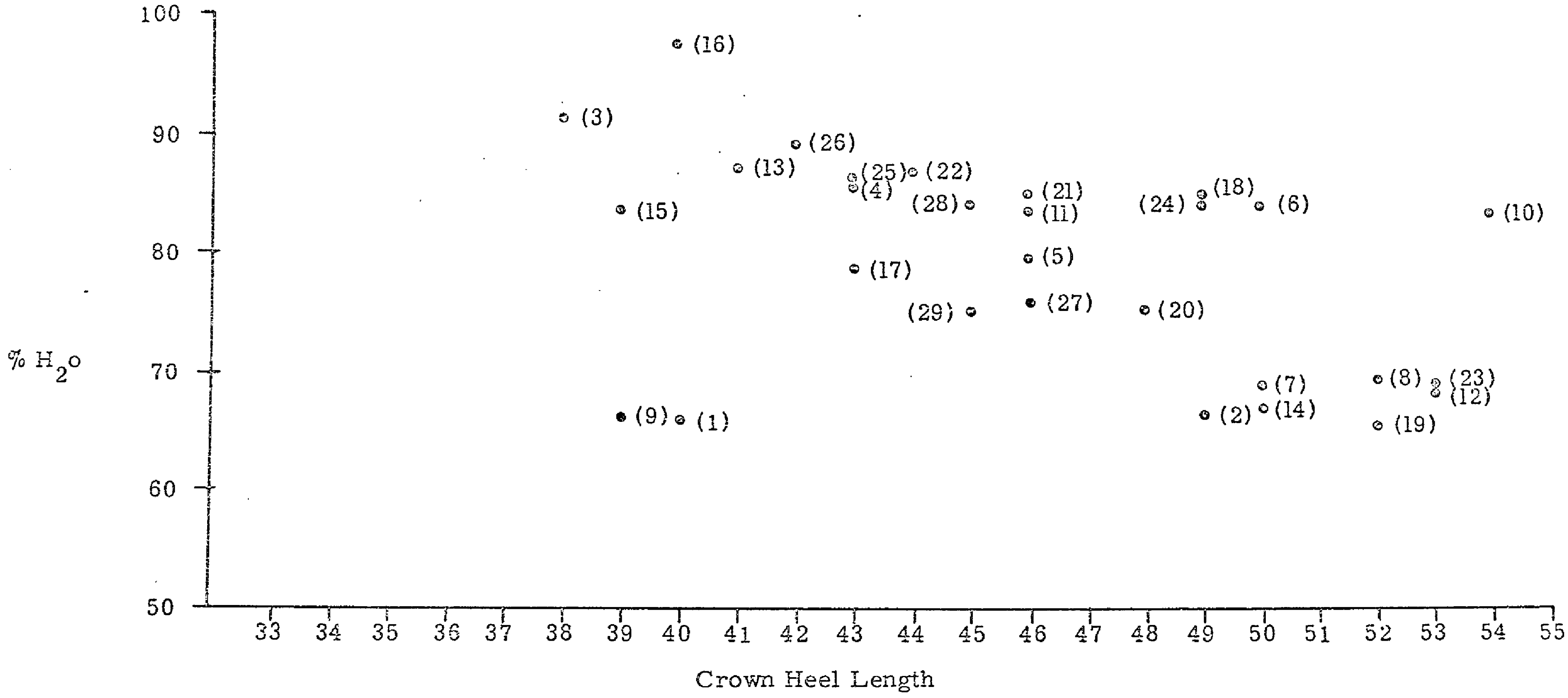


Fig. 25 - % H_2O in fat-free tissue against crown heel length (29 Males)

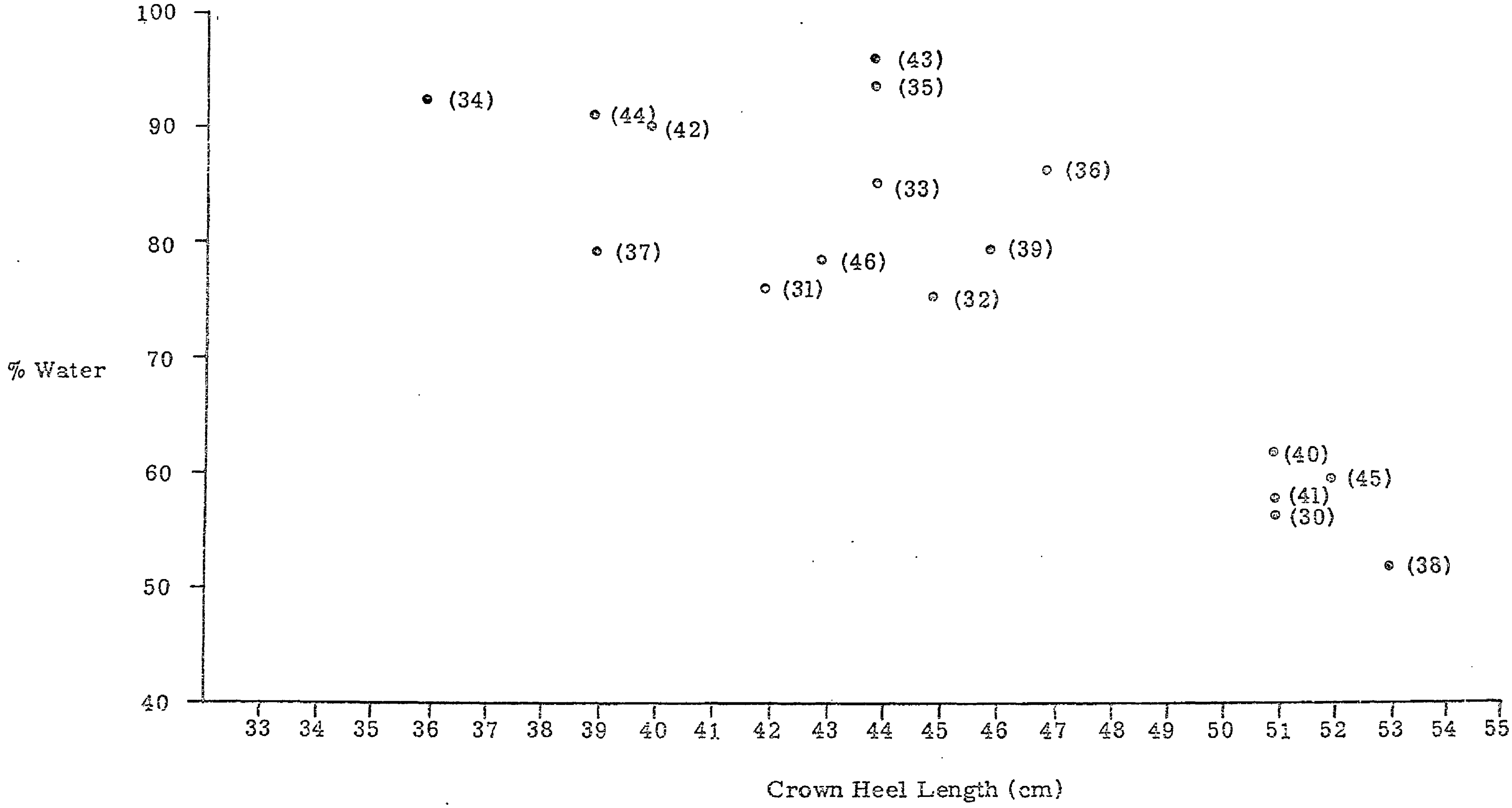


Fig. 26 - % H_2o in fat-free tissue against crown heel length (17 Females)

than all males. These values in female term infants average 56 per cent whereas values for the male appear to be about 68 per cent. Consideration of the particular infants isolated from appendices 6 and 7 as being "dysmature" or "twin" suggests that these infants tend to occupy upper positions on the graphs i. e. to have higher levels of water towards term (see numbers 6. 18 and 21 among the males (Fig. 21) and numbers 31, 33, 35 and 42 among the females (Fig. 22)). Caution must remain however about any emphasis on individual cases since reference to the maternal distribution (not presented) showed an over-representation of young unmarried primigravida - a group liable to be mistaken about their menstrual data, and hence the gestational ages of the infants.

Experiment 8 Estimation of Total Percentage of Fat by Weight

Again the values in all 46 infants were first of all examined. Percentages of total fat in the dehydrated specimens were plotted against gestation (Fig. 27) birth weight (Fig. 28) and crown heel length (Fig. 29). It can be seen from these illustrations that there is no convincing trend. There is certainly no steady increase in fat throughout the last ten weeks of pregnancy, values being spread between 30 and 60 per cent throughout. Separate values of fat for males and females were plotted and exhibited the same lack of discernible pattern. For this reason only the relationship between total fat and crown heel length is presented. Figure 30 shows the percentage of fat in dried tissue against crown heel length in 29 males and Fig. 31 the same in 17 females. Comparison of male and female term infants showed no marked difference between male

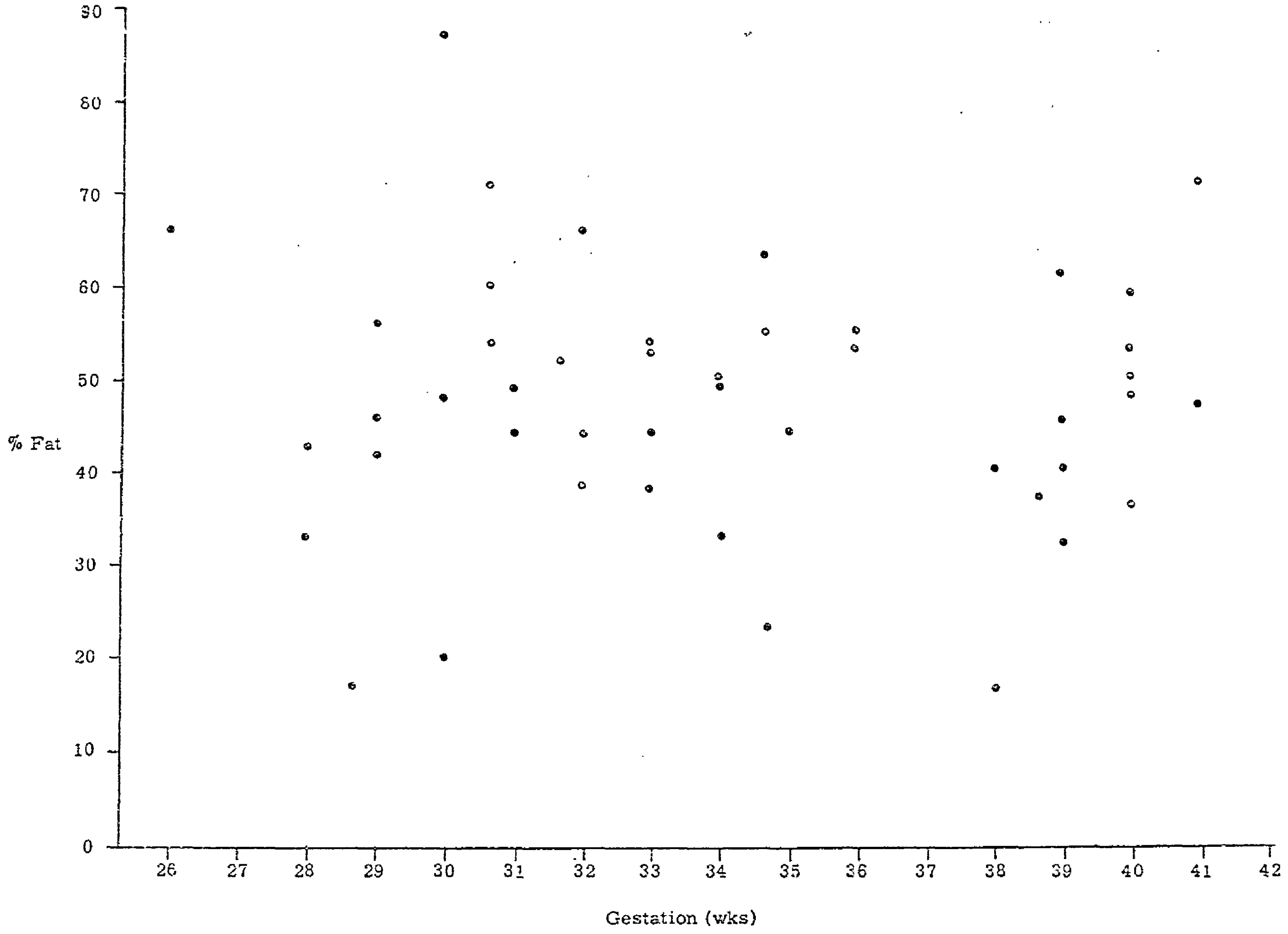


Fig. 27 - % Fat in dried tissue against gestation (46 Cases)

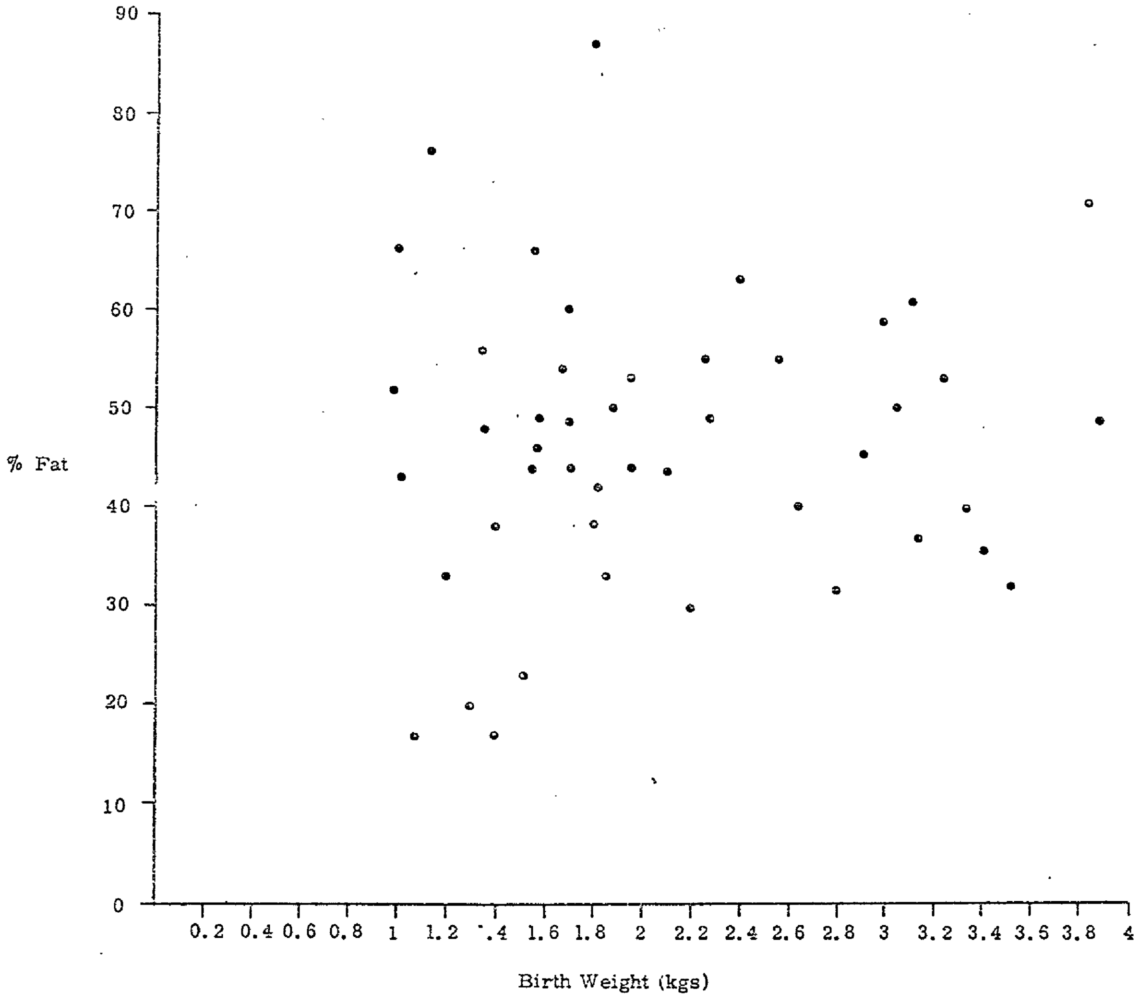


Fig. 28 - % Fat in dried tissue against birth weight (46 Cases)

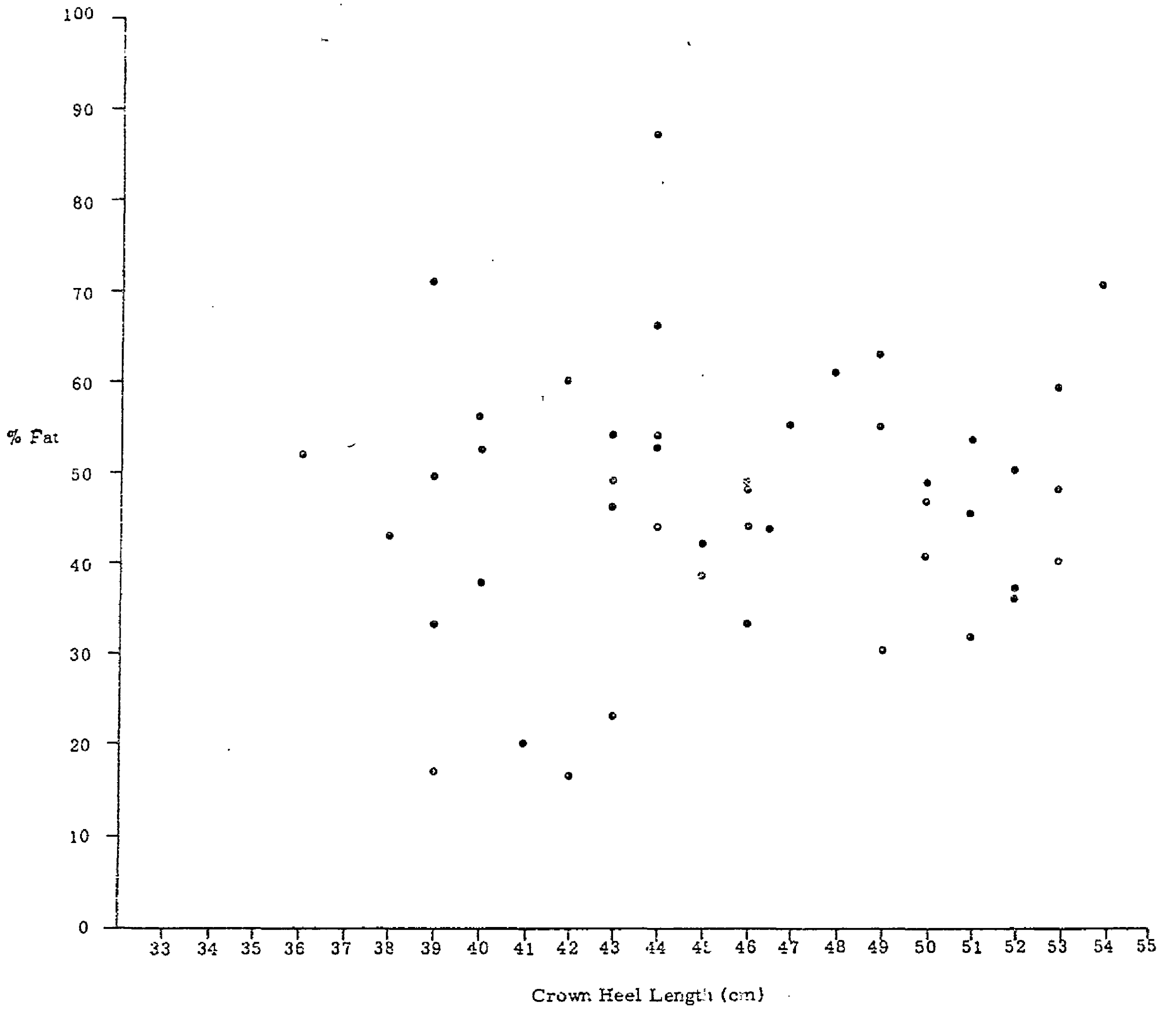


Fig. 29 - % Fat in dried tissue against crown heel length (46 Cases)

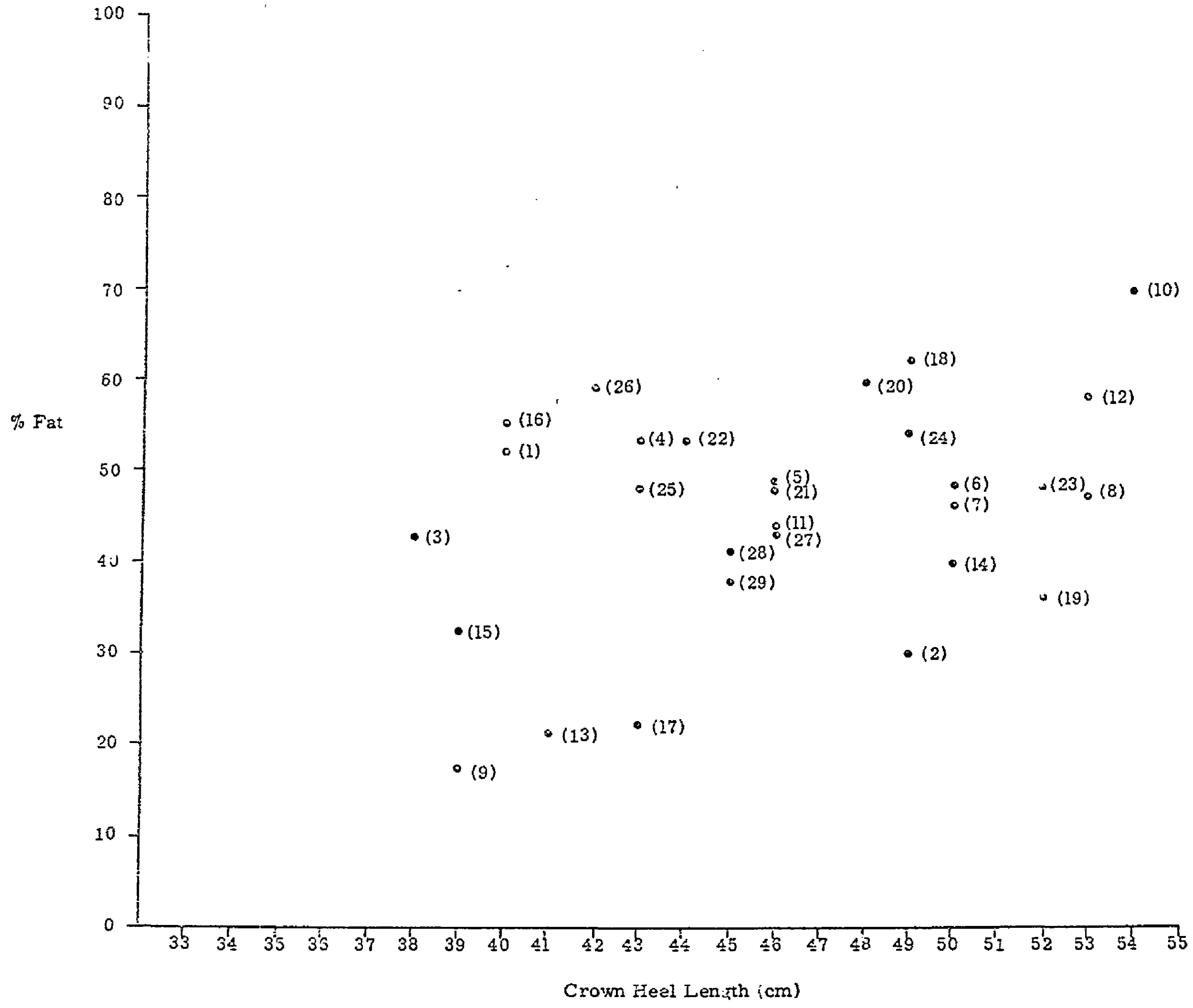


Fig. 30 - % Fat in dried tissue against crown heel length (29 Males)

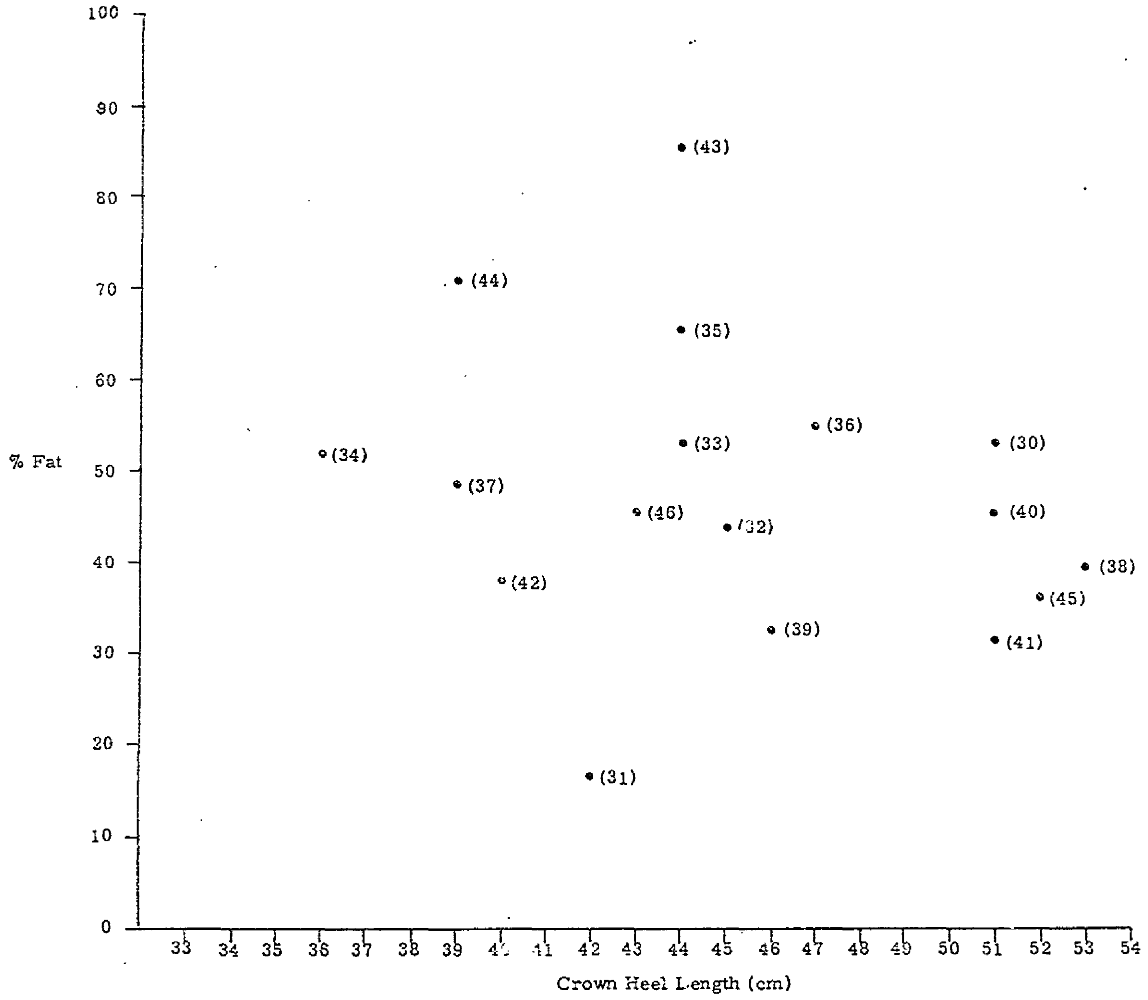


Fig. 31 - % Fat in dried tissue against crown heel length (17 Females)

and female fat values, the average being 41.5 per cent in females and 44.6 per cent in males. Again isolation of individual infants from reference to appendices 6 and 7 shows that male infants numbers 2, 13, and 17 have relatively low amounts of fat and numbers 6, 18, and 21 medium or high amounts (Fig. 30). Reference to the female infants shows that the dysmature infants numbers 33 and 35 occupy relatively high positions i.e. have high fat values, number 42 a position in the middle range, but twin number 31 a very low position. Again one must be wary about the true gestational ages of these infants.

Finally, since percentages of water and fat are of course interdependent, the relationship between the amounts of water and fat in the total specimen are presented together for the 29 males (Fig. 32) and the 17 females (Fig. 33). Figure 32 shows the familiar decrease in water with increase in gestation, and the linear type of spread echoes the pattern in the whole group. The water falls in value from about 77.5 per cent at 29/52 to 50.8 per cent at 39-40/52. Over the same time, the fat rises in value from approximately 7 per cent at 29/52 to 24.8 per cent at 39-40/52. Figure 33 (water and fat against gestation females) does not mimic that of the males. Progressions of both fat and water appear to remain at a relatively constant level from 30-36/52 and then a marked fall apparently occurs in the water value. Fat values scarcely alter although a slight rise occurs at term, again apparently precipitately. The water falls in value from 69.7 per cent at 30 weeks to 42.8 per cent at 39-40 weeks. Over the same time the fat rises in value from

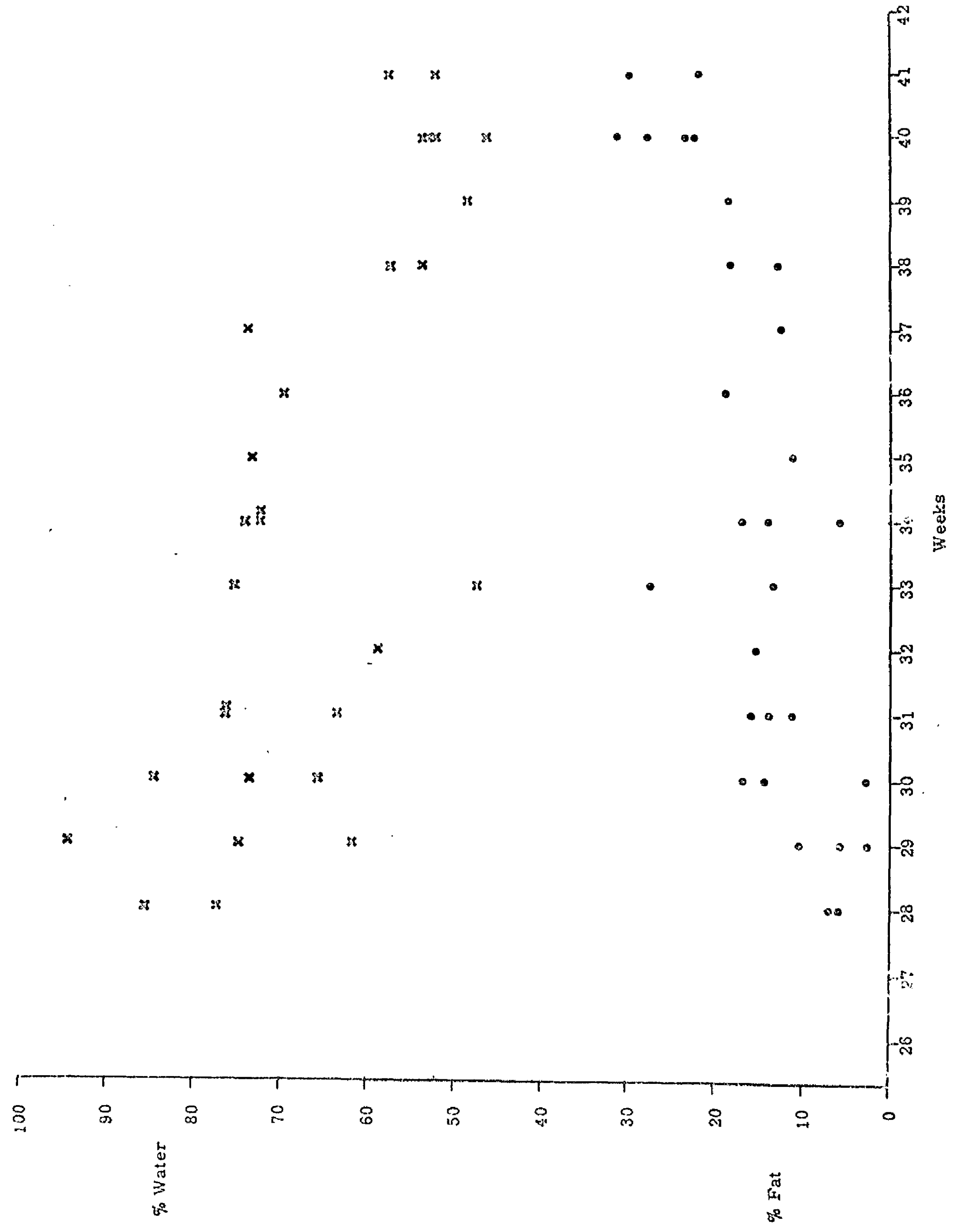


Fig. 32 - Percentage of water and fat in total SF specimen against gestation (29 Males)

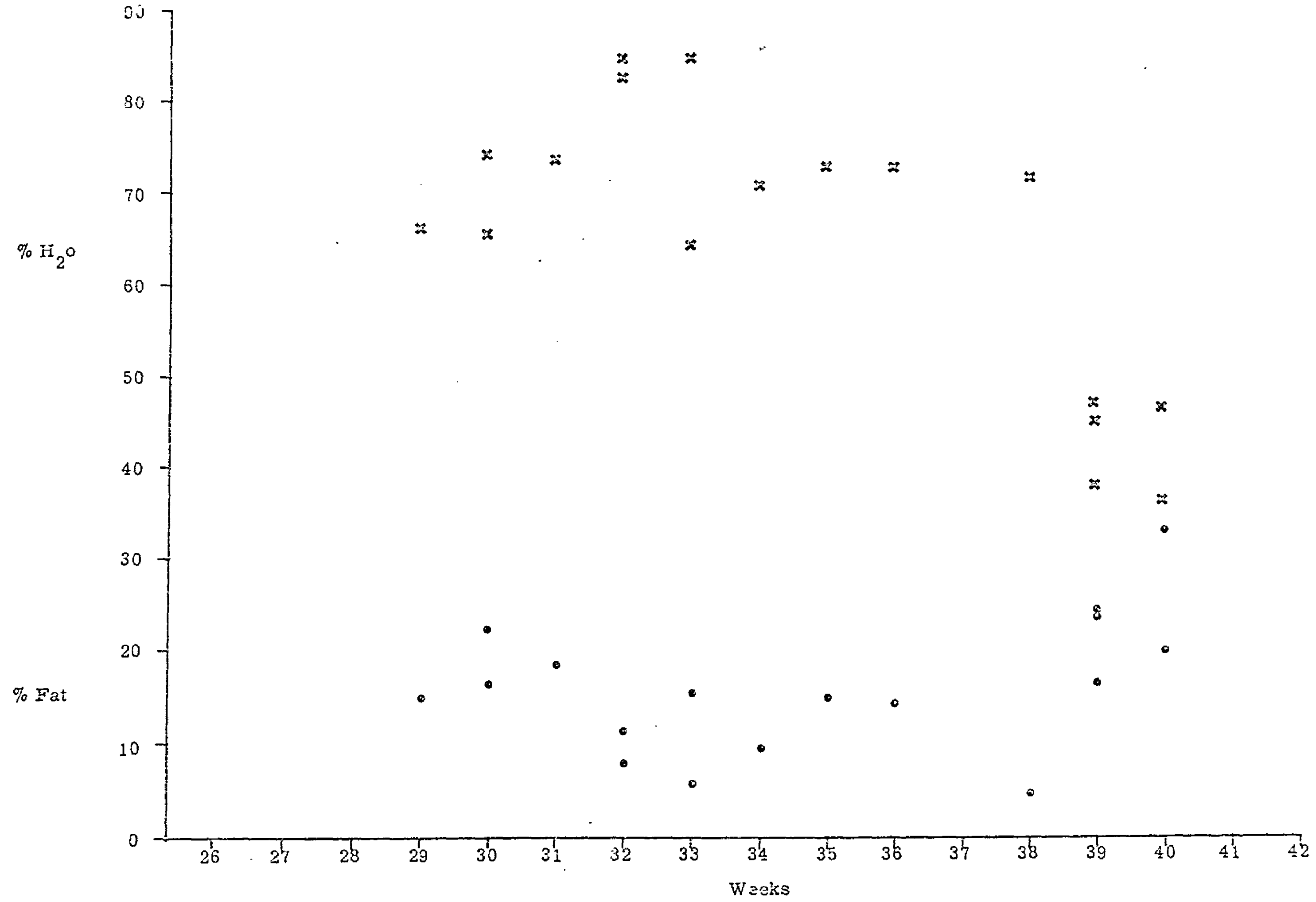


Fig. 33 - Percentages of water and fat in total SF specimen against gestation (17 Females)

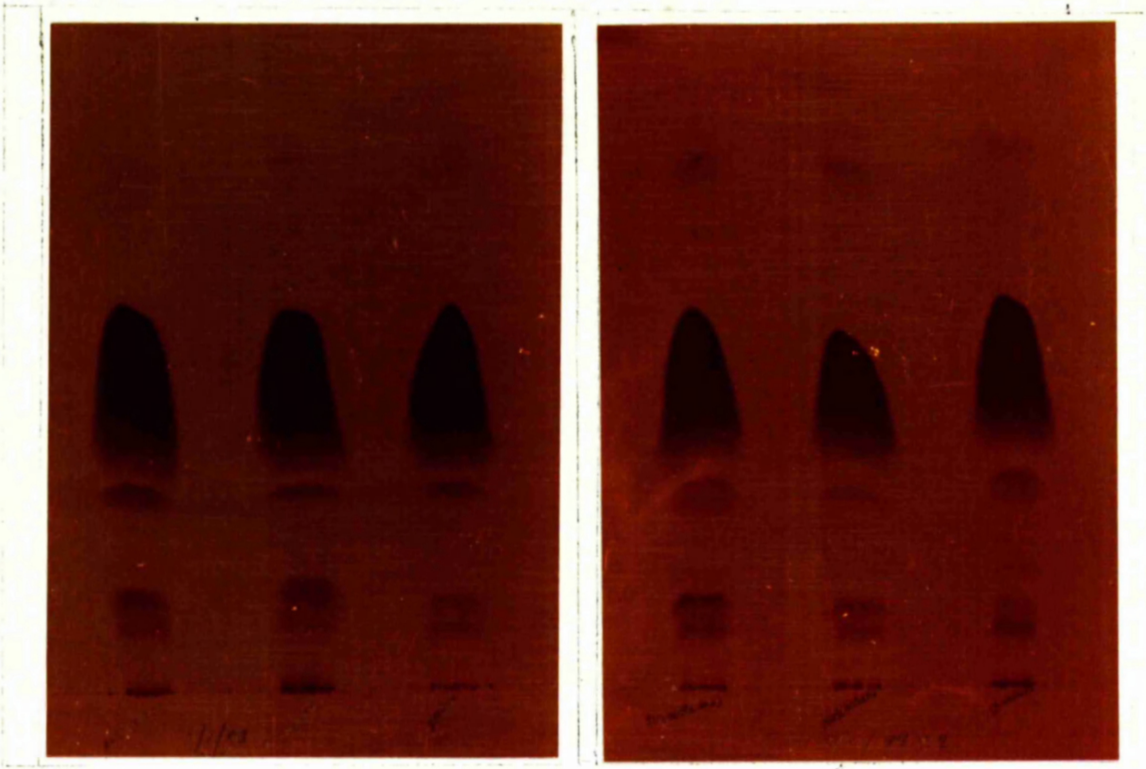
19.5 per cent to 22.6 per cent. There is also some suggestion of a rise in water at 32 weeks and a fall in fat at the same time.

Experiment 9 To Determine if any Gross Differences in Lipid Patterns Exist in Various Groups

A representative selection of the photographs taken of freshly developed lipid chromatographs is presented in Figs. 34 and 35. Freshly-run lipid markers are shown in the photograph in Fig. 36. These photographs illustrate the following conclusions which are however based on the chromatographs of the 46 infants and not merely on the eleven demonstrated.

1. Reference to the lipid standards (Fig. 36) suggests that the identities of the lipid fractions in descending order of R_F values are: cholesterol ester; triglycerides; fatty acid : 1-3 + 1-2 diglycerides and monoglycerides: phospholipids.
2. The spot identified as cholesterol ester running near the solvent front appears regularly in the premature infants (Fig. 34) but not in the term infants. There may be slightly more of this fraction in male pre-term as opposed to female pre-term infants. There may also be some variability in the extent of the fatty acid fraction.
3. No gross qualitative differences were demonstrated between male and female infants at term (Fig. 35).

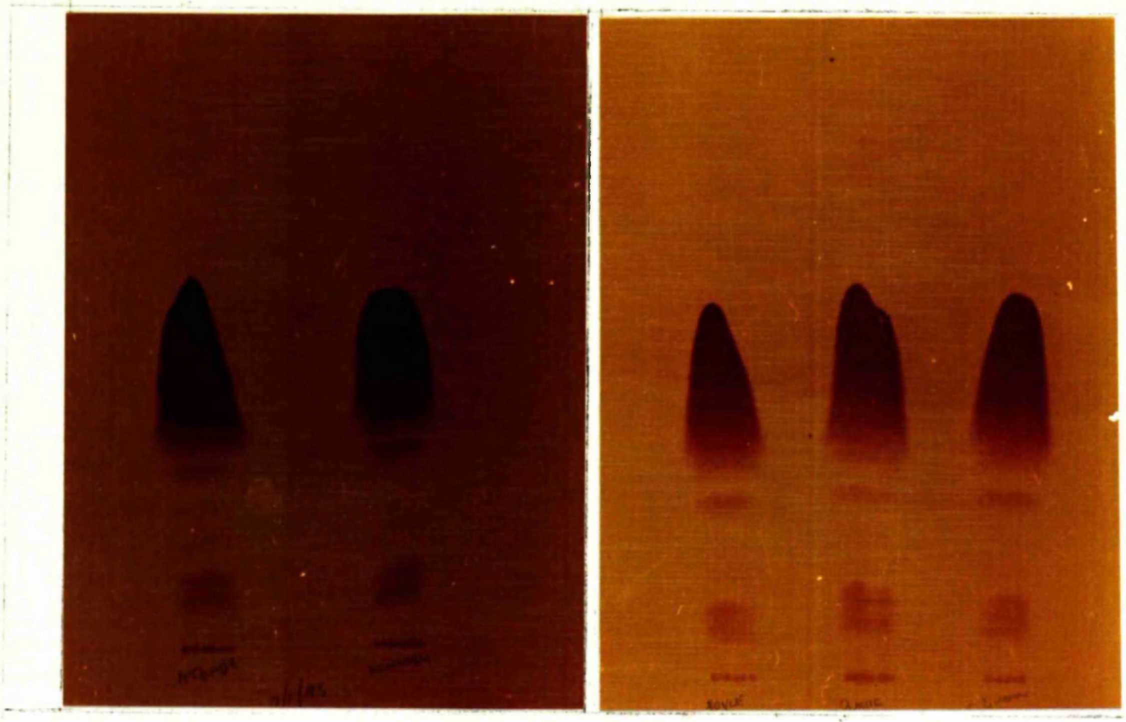
The writer is not qualified to draw any further conclusions from this experiment but a sample chromatograph was prepared in identical fashion and given to one of the MRC group in Reproductive Biochemistry for professional analysis. For the reader's interest, this report is given in Appendix 8.



P.M. No.	46	44	43	25	29	22
Sex	F	F	F	M	M	M
Gest^{n}.	29	30	30	31	32	33
B.W.	1.57	1.14	1.80	1.70	1.80	1.67

FEMALE MALE

Fig. 34 Thin Layer Chromatographs - Pre-Term Infants.



P.M.					
No.	45	41	19	23	20
Sex	F	F	M	M	M
Gest.^{n}	40	39	39	40	39
B.W.	3.88	2.80	3.14	3.90	3.03

FEMALE MALE

Fig. 35 Thin Layer Chromatographs - Term Infants.

- Cholesterol Ester
- Triglyceride
- Fatty Acid
- Mono and Diglycerides
- Phospholipid

Lecithin

Diglyceride

Fatty Acid

Cholesterol Ester

Triglyceride

1 - 2 Diglyceride

Monoglycerides

Fig. 36-Thin Layer Chromatograph of Pure Lipid Markers.

Chapter Fourteen

DISCUSSION OF EXPERIMENTAL RESULTS

The conclusion reached as a result of the experimental work in Section 1 was that the differences between duplicate measurements of skinfold thickness at the same site over the period of one hour are likely to be due to clinically imperceptible tissue changes - a conclusion which immediately provokes the question, 'What tissue changes ?'. The findings of Section 11 which show firstly that skinfold thickness values are greater in term infants than in pre-term and secondly that they are greater in female term infants than in male provide a focus for the above question. What tissue differences underly the differences in caliper measurements in these groups of infants ? Are there variations in the quantity of water or of fat in the skinfolds ? Alternatively is there a qualitative difference in the fat ? The experiments of Section 111 just described, attempt to answer these questions. The result of Experiment 7 to determine the amount of water in skinfold tissue showed that the percentage of water by weight in fat-free skinfold specimens as measured by desiccation, decreases steadily towards term. This trend is maintained whether increasing maturity is denoted by post-menstrual dates (Fig. 18), by increasing birth weight (Fig. 19) or by increasing crown heel length (Fig. 20). The data indicates that the water content in babies of 30 weeks is about 86% fat-free tissue and in babies of 40 weeks is about 65% Thus term infants apparently have less water in skinfold tissue than do premature babies.

Consideration of water as per cent of total specimen (Figs. 32 & 33) although varying with the percentage of fat emphasises this decrease towards term. Seperate plotting of male and female water values in fat-free tissue against gestation (Figs. 21 & 22) birth weight (Figs. 23 & 24) and crown heel length (Figs. 25 & 26) illustrates the same overall patterns of decrease. There is perhaps a steeper decline in females from higher values than the male around 32 weeks to lower values than the male around 39 - 40 weeks. That all female infants at term have lower skinfold water values than males is patent. These values in female term infants appear to be around 56%, whereas values for males at term appear to be about 68%. Isolation of individual cases picked out as "dysmature" or "light-for-dates" in the appendix shows that a sizeable number of them occupy upper graphical positions i.e. have higher water values. Uncertainty about the gestational ages of some of these infants however does exist. Experiment 8 to determine the percentage of fat in skinfold tissue by the method of Folch, Lees and Sloane-Stanley (53) produced values of total fat by per cent weight of dried specimens which were on the whole similar at 30 weeks of gestation and at term. A range of values between 30-36% appeared at both gestational ages, whether these were adjudged by menstrual dates (Fig. 27), birth weight (Fig. 28) or crown heel length (Fig. 29). When fat was considered as per cent of whole specimen however, (Figs. 32 & 33) an increase was noted in male infants from about 7% at 29 weeks to 24.8% at 39-40 weeks. This rise was less marked in the females being of the order of 19.5% of the total specimen at 30 weeks to 22.6% at 39 weeks. This suggests that the increase in fat was apparent rather than real and mainly due to diminution of water. No marked difference between male and female fat values at term was evident. The values average 22.6% in females and 24.8% in males in the whole specimen and 41.5% in females and 44.6% in males in the dried specimen. Experiment 9 was undertaken to produce chromatographic evidence of any differences in the patterns of the lipid constituents of skinfold fat. Comparison with chromatographs of pure lipid markers showed that triglyceride was the outstanding lipid constituent and no difference in its amount was seen either in term or pre-term infants, or in male or female term infants. A difference was noted in the cholesterol ester which decreased from 30-40 weeks gestation. This constituent was obviously minimal in quantity, reportedly (72) less than 2% at its maximum. Corroboration of this rather more specialised exercise was made available to the writer and appears in Appendix 8. The evidence from these experiments can be summarized as follows:

Differences between Term and Pre-term Infants

1. The quantity of skinfold water is less in term infants than in pre-term.
2. The quantity of skinfold fat is about the same in term infants as in pre-term.
3. The composition of skinfold fat remains largely the same in term infants as in pre-term infants.

Differences between Male and Female Term Infants

1. The quantity of skinfold water is significantly less in female term infants than in male.
2. The quantity of skinfold fat appears to be almost the same in female and in male term infants.
3. The composition of skinfold fat appears to be the same in female and male term infants.

It can be seen therefore that the most striking differences in the chemistry of term vis-a-vis pre-term skinfold tissue, and of male vis-a-vis female skinfold tissue lie in the water values. Is it possible that paradoxically, higher caliper measurements are accompanied by lower tissue water values. Presented in Figure 37 is a graph in which the progression of SFT values with gestation in the 43 premature infants considered in Chapter Seven is superimposed on the progression of water values with gestation obtained in the 46 infants of Experiment 7. This illustrates the possible relationship existing between these two measurements. Finally, although chemical values in post-mortem skinfold tissue cannot of course be assumed to correspond directly to skinfold thickness values in living babies, the fact that the substantial differences occurring in skinfold water parallel the mechanical differences occurring in the same two groups of living infants must be regarded seriously.

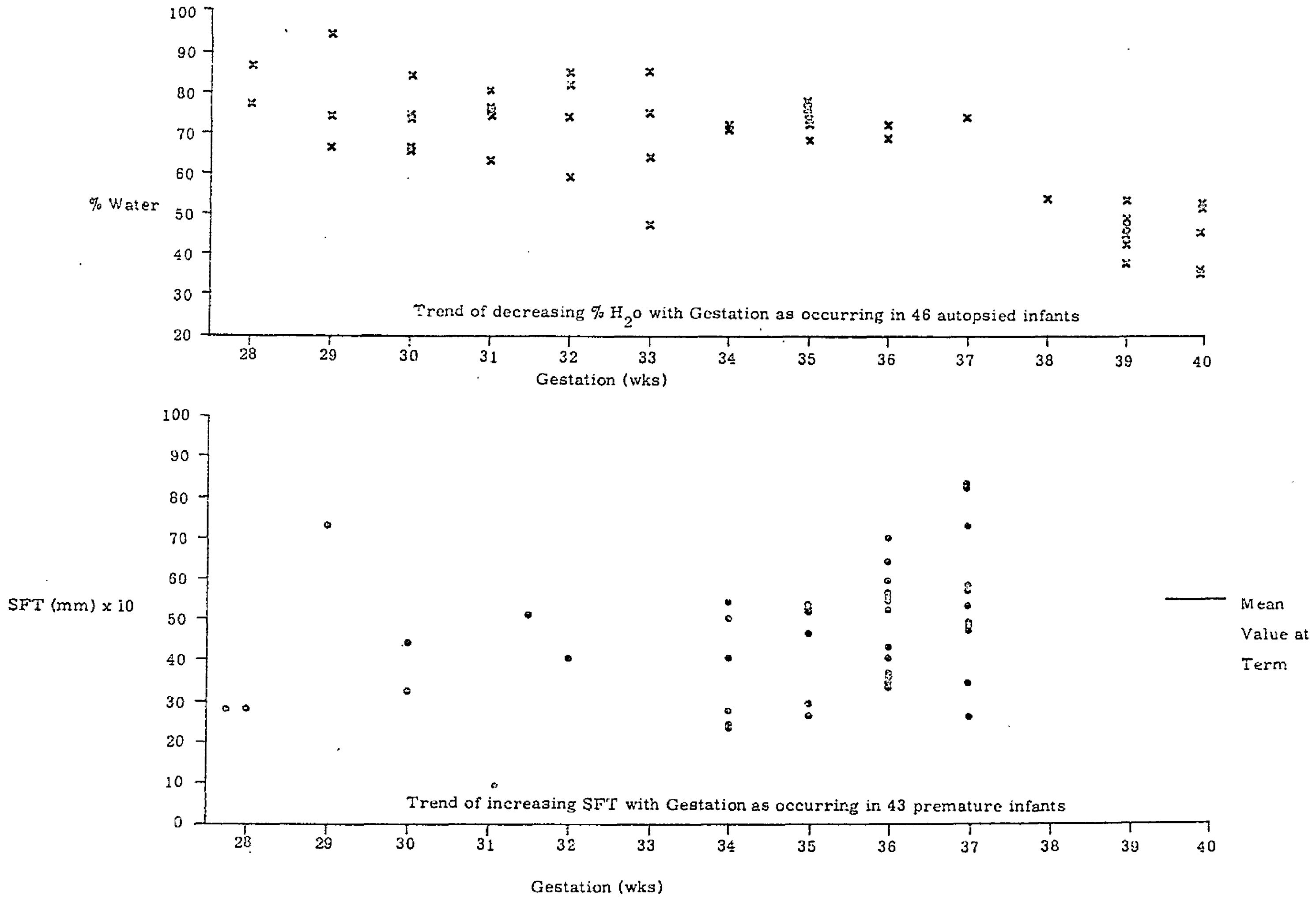


Fig. 37 - Comparison of S. F. T. trend with gestation and % water trend with gestation

Chapter Fifteen

A HYPOTHESIS

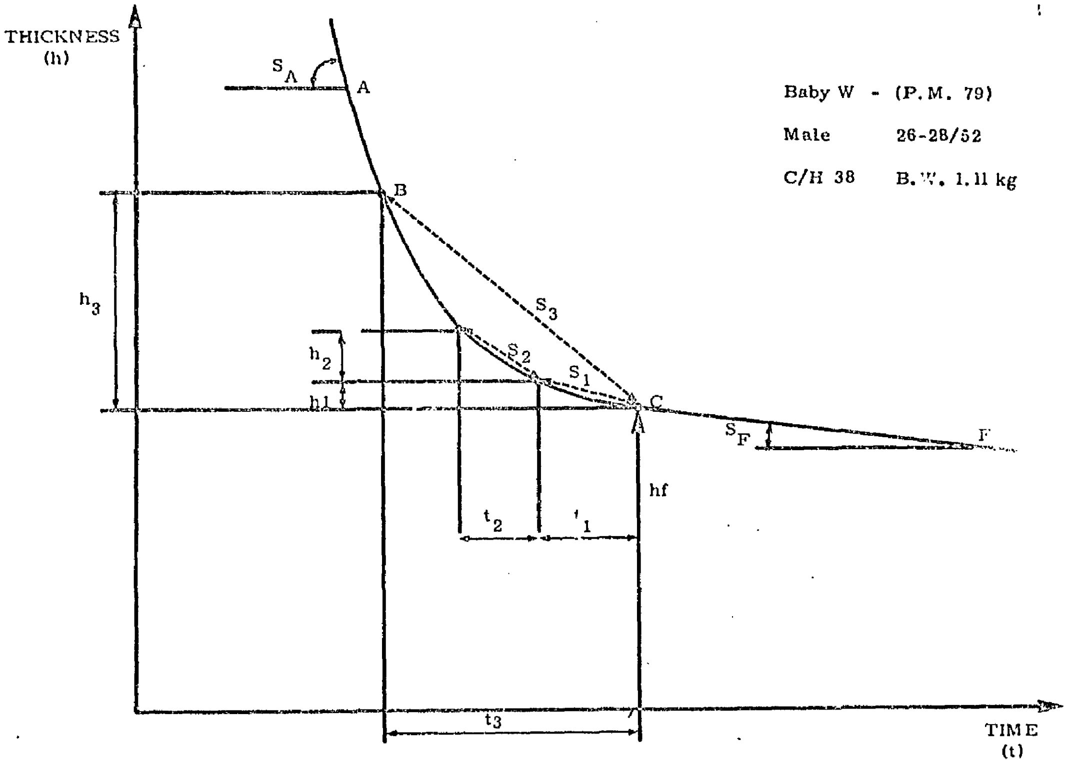
- That higher skinfold thickness values reliably accompany lower skinfold water values and further that they result from them.

Experiment 10 An Initial Test of the Hypothesis

It was decided to perform a small initial test of the above hypothesis by examining the compression curves and skinfold thicknesses in infants prior to death and comparing them with the water values after death.

Materials and Methods

Selection of the infants was based prospectively on the total number of moribund infants in the Paediatric department, Glasgow Royal Maternity Hospital in one week. Two infants fell into this category. The writer was notified by telephone of the impending neonatal death and in turn notified the Bio-engineer. Using the instrumented Harpenden Caliper attached to a Bryans X-Y plotter as described previously, graphical illustrations of skinfold distortion at the Supra-iliac site were obtained. This was done within half an hour before the deaths of the two infants. Mathematical analysis of their respective curves was completed and is presented in Figs. 38 and 39, together with the key diagram. Postmortem permission was obtained and autopsy specimens taken as described in Chapter Twelve. Percentage water and fat values were obtained in the two specimens as described in the same Chapter.



SA	11.22 mm/sec.	S_3	2.04 mm/sec.
SF	0.04 mm/sec.	t_1	0.30 sec.
h_3	1.0 mm.	t_2	0.12 sec.
t_3	0.49 sec.	S_1	1.13 mm/sec.
		S_2	2.78 mm/sec.

SFT = 3.0h_f = 3.06 mm.

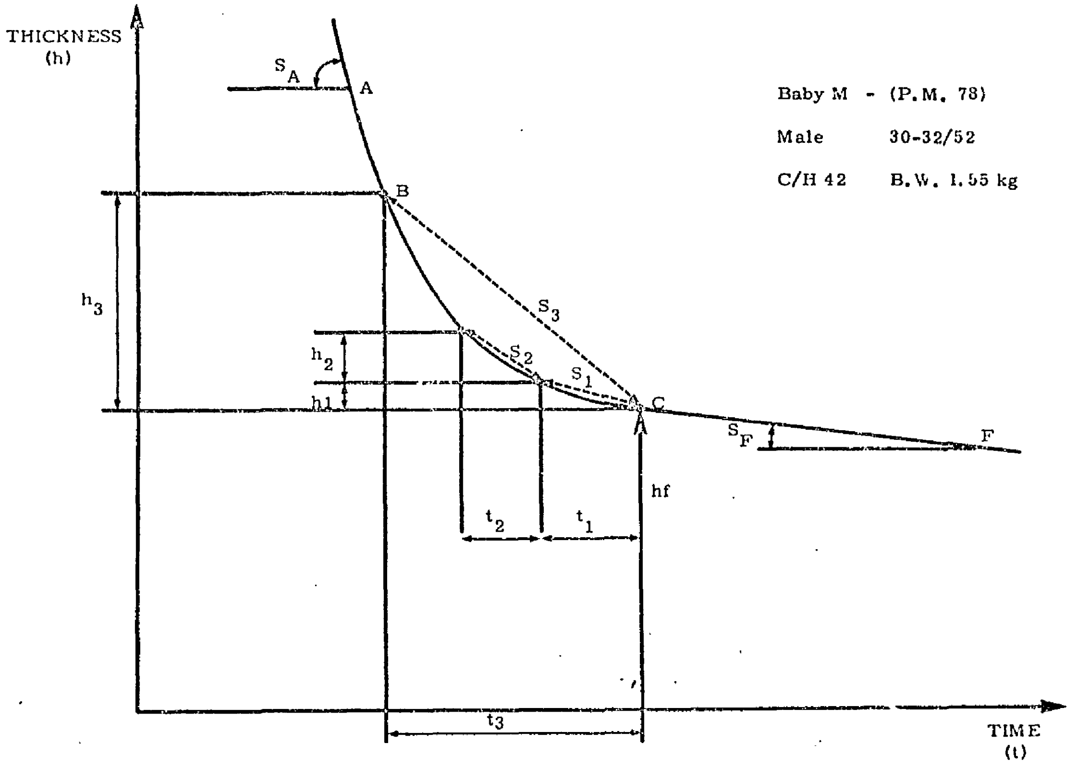
% Water = 84.61% Whole specimen

= 94.17% Fat-free specimen

% Fat = 10.15% Whole specimen

= 66.01% Dried specimen

Fig. 38 - Description of SFT Curve Components, and SF Chemistry in Baby W



SA	17.60 mm/sec.	S_3	0.54 mm/sec.
SF	0.04 mm/sec.	t_1	0.37 sec.
h_3	0.87 mm.	t_2	0.07 sec.
t_3	1.60 sec.	S_1	0.89 mm/sec.
		S_2	4.83 mm/sec.

SFT = $3.8h_f$ = 3.80 mm.

% Water = 78.32% Whole specimen

= 86.48% Fat-free specimen

% Fat = 9.44% Whole specimen

= 43.56% Dried specimen

Fig. 39 - Description of SFT Curve Components, and SF Chemistry in Baby M

Results

The results are presented in Figures 38 and 39 together with details of the infants involved. It can be seen from Fig. 38 that baby W of gestation 26-28 weeks has a water percentage of 84.61% whole specimen and 94.17% fat free specimen and a fat percentage of 10.15% whole specimen and 66.01% dried specimen. The SFT equal to h_f value is 3.0 ± 0.06. Baby M of gestation 30-32 weeks has a water value of 78.32% whole specimen and 86.48% fat free specimen and a fat percentage of 9.44% whole specimen and 43.56% dried specimen. The SFT equal to h_f value is 3.80. A decrease in the percentage water with increased gestation is accompanied by an increase in SFT.

This prospective experiment, would seem to lend support to the above hypothesis. As a pilot study it provides support and encouragement to further testing.

COMMENTARY

This thesis consists of the examination of a measuring technique with regard to its applicability in neonates, of the values obtained by its use in different groups of infants and of the chemical significance of these values.

The Technique - Section I

Measurement of skinfold thickness using a spring tension caliper was already known to be a simple way of assessing body fat in adults and older children through the use of regression equations. There seemed however to be many potential sources of error and such studies as were reported in newborn infants presented conflicting views about the usefulness of the technique, largely in the absence of standardized method and error appraisal. Section I of this thesis has consequently been devoted to examining the reliability of the technique. The sources of error were examined under five headings:

1. Errors inherent in the instrument
2. Errors in site selection
3. Variation in handling of skinfold and application of the caliper
4. Tissue variability
5. Errors in reading the gauge.

Three different calipers were examined but the Harpenden caliper recommended for use in adults and older children by the M.R.C. trial (45) was substantially the best choice in infants also. The writer retains some reservations about its manoeuvrability inside incubators, but on grounds of accuracy, no other caliper could have been employed. After calibration by the Bio-engineering department, a simple Harpenden caliper was used throughout the remainder of the work.

Measurements were attempted at different sites and the most constant results obtained at the supra-iliac and quadriceps sites. These were preferable also on grounds of accessibility and were subsequently used as standard method. Despite these initial precautions, the error attached to the technique as judged by duplicate measurements in the same infant after an interval of one hour was substantial - 15% at 95% confidence limits i.e. 0.3 to 0.7 mm at jaw openings of 5.7 mm. This compares with that recorded in the M.R.C. study (45) in adults and older children of 0.3 to 0.6 mm at jaw openings of 7 mm. No such comparable figures can be traced for newborn infants. Wagner et al (153) in 1967 made some attempt at error count by recording correlation coefficients for one observer and two replications of the order of 0.97 to 0.99 but although this established a close relationship between duplicate readings, it gives no indication of actual error magnitude or of the reasons for the error. Although Vincent and Hugon (152), Gampel (58), Farr (47), Usher and McLean (149) carried out studies on SFT measurement in neonates, they did not investigate margins of error. However, despite the sizeable quantitation of error measured here, it appeared from an initial pilot study of about 100 babies that meaningful measurements could be obtained for comparison of newborn infants who were obviously of different sexes, gestation and clinical conditions. Further exploration of the sources of error was indicated.

It was suspected that the largest single error component would occur in the subjective part of the technique i.e. in the location of sites, in applying the caliper and in reading the gauge. The error component attributable to site selection was measured by examining the effect on error margins of marking skin sites before duplicate readings. Almost no difference in error quantity was found suggesting that the contribution made by this source was negligible. Perceptible difficulties however had been noted in reading off values from the dial, particularly in larger infants. This same problem was encountered by Fletcher (52) who recorded a percentage change of 4.6% in dial reading by means of a cine film. It was reported by Tanner (141) who suggested the remedy of reading immediately after application of the caliper without waiting for the needle to settle. This remedy was adopted as standard procedure through the succeeding work. Lewis and co-workers (82) in 1965 working in adults also encountered this difficulty observing that when the Harpenden is applied, the jaws do not come to a complete stop immediately after they close on the skinfold, but that they " drift " together at a very much slower rate for 3 to 5 seconds. They suggested that this drift might reflect the presence of extracellular fluid in the subcutaneous tissues whose behaviour appeared to vary with tissue hydration. Robertson et al (114) in 1969 using sophisticated electronic apparatus, derived a mathematical index based on tissue displacement traces in oedema of pregnancy. Their preliminary data appear to confirm that changes in their derived index reflect changes in skin hydration. In any case, since it was likely that the reading difficulty constituted a major factor in producing the error under examination, a study was made, of the actual mechanics of the recording of skinfold deformation by the caliper. This was done by using a Harpenden caliper provided with a direct write-out. The tissue response to compression proved to be bi-phasic in character and it was also found that the value declared as the skinfold thickness by the operator was related to the interpoint between these two phases. It was further found that no difference existed between the subjective readings of SFT declared by two operators and the simultaneous objective interpoint values read from the plotter. From this experiment it would appear that subjective error is not a large factor and that SFT values depend largely on the first rapid compression phase and this in turn on the displacement of the most mobile tissue constituent - logically fluid. The experimental work undertaken in Section 1 provides evidence that the error attached to this technique cannot be levelled at the instrument, or at the operator and must by exclusion be attributable to the tissue. More specifically these experiments suggest that the so-called error attending this technique in fact is a reflection of tissue behaviour and that this behaviour can alter in the same infant over the period of one hour.

To the writer's knowledge, no other comprehensive examination of the error involved in this measurement in neonates is available for comparison. The interpretation of the time-dependent profile as being initially a function of tissue fluid agrees however with the opinions expressed in 1969 by Robertson et al (114) and in 1965 by Lewis et al (82) working in adults.

The Values - Section 11

Three main groups of infants were studied in a survey of the values obtained by the use of the technique. These comprised a statistically selected normal group, a group of premature infants and a group of infants considered to be light-for-dates. The 231 normal infants were mainly of more than 37 complete weeks of gestation and ranged from the Aberdeen 10^{c} (146) upwards in birth weight, but included 19 premature and 22 light-for-dates infants as inevitable in the average population.

SFT and Birth Weight in Normal Infants

Strong correlations emerged between SFT values and the infants birth weight. This is in keeping with the bulk of previous work e.g. Vincent and Hugon (152) Gampel (58) and Usher and McLean (149). The correlation coefficients recorded in this study are in fact 0.60 for males; 0.57 for females at the Supra-iliac site and 0.72 for both males and females at the Quadriceps site, a figure of more than 0.4 being highly significant. The only comparable values in the literature are a figure of 0.53 for both umbilical and quadriceps sites reported by Wagner et al in 1967 (153) and figures of 0.42 at an abdominal site and 0.65 at a thigh site reported by Farr in 1966 (47). Neither of these studies considered the sexes separately.

SFT and Birth Length in Normal Infants

SFT values in the normal sample reported here also related closely to the crown heel and crown rump lengths of the infant.

The correlation coefficients are shown below in tabular form.

Site	Male		Female	
	C/H Length	C/R Length	C/H Length	C/R Length
Supra-iliac	0.47	0.49	0.30	0.42
Quadriceps	0.50	0.59	0.40	0.58
	>0.3 significant		>0.4 highly significant	

No exact figures for comparison can be traced, although Wagner et al (153) report a correlation for umbilical and quadriceps skinfolds against weight/length ratio nearly equal to that against weight alone, i.e. 0.53.

SFT and Gestation in Normal Infants

No correlations between SFT and gestation existed in this normal group. The figures obtained of 0.14 at quadriceps site and 0.09 at supra-iliac sites parallel those of Farr (47) in 1966 of 0.18 at an abdominal site and 0.30 in a thigh site. Her figures however illustrate a steady increase in mean SFT over a wider range of gestational ages as do those of Vincent and Hugon (152) and Gampel (58), and Farr (47) reports that this increase tends to lessen between 38 and 40 weeks. Gampel also describes an increase in female SFT which may continue after term, the rise being very small. Paradoxically, he describes a slight and insignificant fall in SFT in post-term males. The vexed question of true gestational age has been discussed in detail earlier, and the widespread pessimism as to the accuracy of values mentioned. Correlations with such values must be viewed with reserve. Given the probability that foetuses mature at different rates and the fact that not all gestations last 40 weeks, the difficulty of correlating SFT with gestation within the narrow range of 37 to 41 weeks is not surprising.

SFT in Male and Female Normal Infants

Findings in this sample of normal infants also confirmed those of the initial pilot study, done as part of the investigation into technique, in that highly significant differences existed between SFT measurements of males and females. A p value of less than 0.05 was obtained at the quadriceps site and of less than 0.005 at the supra-iliac site (where p less than 0.05 is significant and p less than 0.01 is H.S.). The comparison between males and females also produced the expected differences in birth weight, (p less than 0.05) and in crown heel length (p less than 0.001). It seems that males are longer, heavier and have thinner skinfolds at birth than the females. This sex difference in SFT values has been reported with varying degrees of emphasis by other authors. In 1962 Vincent and Hugon (152) found that sexual differentiation in SFT clearly emerges from a weight of 2kgs. onwards, females showing significantly greater values as subscapular and triceps sites. In 1963 Parizkova (107) found SFT values at a "hip site" significantly greater in females than in males. In 1965 Gampel (58) found girls to have a slightly higher subscapular and a slightly lower triceps thickness than boys but neither difference to be significant. He did find the difference to be significant at the subscapular site in infants in the 3.0 to 3.49 kg weight group. In 1966 Farr (47) found that mean SFTs in the females were greater than in the males at all sites, although wide scatter about the mean existed. She also found that this difference was reversed for measurements over chest and abdominal wall in infants weighing less than 5 lbs. In 1967 Wagner et al (153) found no sex differences in his sample of 103 normal American infants. Usher and McLean in 1969 (149) did not consider the sexes separately. In general therefore reports seem to agree that, at least in heavier children, different sex patterns for SFT seem to exist although variations in statistical handling make exact comparisons impossible. In the present work however, the sex difference in values in term infants at the selected supra-iliac and quadriceps sites has been clearly established on a proper statistical basis.

Consideration of the abnormal infants is somewhat hampered by lack of numbers. The premature infants were described in Chapter Seven and consisted of 43 infants ranging in gestation from 28 to 37 completed weeks.

SFT and Birth Weight in Premature Infants

Even stronger correlations between SFT and birth weight were evident in this group of infants. At the supra-iliac site the correlation coefficient with birth weight was 0.65 as compared with 0.60 for males and 0.57 for females in term infants. At the quadriceps site, the correlation coefficient with birth weight was 0.83 compared with 0.72 for both male and female infants in the normal group.

SFT and Birth Length in Premature Infants

The relationship between SFT and crown heel length was also enhanced in these infants. The correlation coefficients of SFT against crown heel length were 0.55 at the supra-iliac site compared with 0.47 (male) and 0.30 (female) in the term infants. At the quadriceps site these figures were 0.67 as against 0.47 (male) and 0.30 (female).

SFT and Gestation in Premature Infants

In this group of infants however, a significant relationship emerged between SFT values and gestation. The figures were 0.44 at the supra-iliac site and 0.52 at the quadriceps site compared with 0.09 and 0.14 respectively in the normal infant. It is difficult to know whether this is a real relationship or a function of the wide range of ages considered. That there is an increase in SFT values generally with advancing pregnancy is accepted, (Farr (47), Gampel (58), Vincent and Hugon (152) and Usher and McLean (149)). The latter authors report in fact a $2\frac{1}{2}$ times increase in double skin thickness between 25 weeks and term in normally nourished infants. Farr however claims that the correlation between SFT and gestation becomes negligible when the effect of birth weight is eliminated. She produced a small series of graphs showing trends in particular birth weight groups of diminishing SFT values towards term. At least in the group of less than 5 lbs birth weight this, to the writer's mind, shows the trend of SFT with gestation in progressively lighter-for-dates infants, to the low values at term expected in low birth weight infants. In other words, she demonstrated the trends of SFT with gestation in abnormal pregnancy as opposed to normal. There is no doubt however that disentangling the relationships between the various growth features will require much more time and effort. It would seem that several years will be required to collect sufficient numbers particularly of premature females to allow valid comparisons of the sexes and firm conclusions about trends. The same problem of numbers prevents firm conclusions being drawn about the LFD infants. This group,described in Chapter Eight comprises 69 infants of birth weight < 10th^{c} Aberdeen (146) and of more than 37 completed weeks of gestation.

SFT in the Light-For-Dates Infants

It is interesting to note that the established relationships of SFT with birth weight and birth length existing in both the normal and premature infants are totally absent in this group and that no sex difference in values exists. This would suggest a rather more complicated growth pattern in these infants. It might have been expected in fact that growth retarded infants had the same intergrowth patterns as normal infants although on a lower scale. Perhaps the findings here are more suggestive of a defect in the growth process rather than a simple slowing of the rate of development. The writer therefore disagrees with Wagner (153) about his opinion that dysmature infants are miniature versions of normal.

In any case the very strong connection between SFT values, birth weight and crown heel length in the normal infants, and between SFT, birth weight, crown heel length and gestation in the premature infants, suggest that SFT measurements may eventually provide an additional growth parameter. Conversely, the absence of these steady relationships may be a pointer to abnormal growth states such as dysmaturity.

The Chemistry - Section 111

It was concluded in Section 1 that the differences existing in duplicate skinfold thickness measurements at the same site over the period of one hour, are likely to be due to clinically imperceptible tissue changes. The most obvious next question is: What tissue changes ? Is there a variation in the quantity of water or of fat in the skinfold ? Alternatively is there a qualitative difference in the fat ? A change from solid to oleous state or vice versa ? The experiments of Section 111 attempt to answer these questions. The most obvious direct approach to the question of what different tissue constituents underlie the different tissue thickness values, is of course by the examination of biopsy specimens immediately after caliper measurements. This being impossible for ethical reasons, autopsy specimens had to suffice. Although chemical values in post-mortem skinfolds cannot of course be assumed to correspond directly to skinfold thickness values in living babies, gross differences occurring in total water, total fat and in the various lipid fractions might exist sufficient to account for the mechanical differences occurring in live infants. In this connection, the findings of Section 11 which suggest firstly that skinfold thickness values are likely to be freater in term infants than in premature, in common with birth weight and birth length to which they are connected, and secondly that they are certainly greater in female term infants than in male, have provided a means of directional analysis. The chemical values are considered therefore under the twin headings of gestation and sex difference at term. Selection of the infants used was of course dictated by the availability of dead infants and although grossly congenitally abnormal infants, macerated stillbirths and neonatal deaths aged more than 7 days were excluded, the infants vary considerably in age and cause of death. Nevertheless interesting patterns emerged when gross levels of fat and water were estimated in the 46 infants considered.

Skinfold Tissue Water and Gestation

The result of Experiment 7 to determine the amount of water in skinfold tissue showed that the percentage of water by weight in fat-free skinfold specimens as measured by desiccation, decreases steadily towards term. This trend is maintained whether increasing maturity is denoted by post-menstrual dates (Fig. 18), by increasing birth weight (Fig. 19) or by increasing crown heel length (Fig. 20). The data indicates that the water content in babies of 30 weeks is about 86% fat-free tissue and in babies of 40 weeks in about 65%. Thus term infants apparently have less water in skinfold tissue than do premature babies. Consideration of water as per cent of total specimen (Fig. 32) although varying with the percentage of fat emphasises this decrease towards term.

Skinfold Tissue Water Male and Female

Seperate plotting of male and female water values in fat-free tissue against gestation (Figs. 21 & 22) birth weight (Figs. 23 & 24) and crown heel length (Figs. 25 & 26) illustrates the same overall patterns of decrease. There is perhaps a steeper decline in females from higher values than the male around 32 weeks to lower values than the male around 39-40 weeks. That all female infants at term have lower skinfold water values than males is patent. These values in female term infants appear to be around 56%, whereas values for males at term appear to be about 68%. Isolation of the individual cases in these graphs by reference to the appendix shows that babies who had birth weight less than the 10th^{c} Aberdeen tended to occupy the uppermost positions i.e. had the highest levels of water.

As has been stated, no exactly corresponding study can be traced which will provide evidence for or against the findings reported here. Meyer (87) studying skin water and Baker (8) studying subcutaneous adipose tissue from an abdominal site both found a decrease in water content with age and since in the present study, skinfold tissue includes both skin and subcutaneous fat, the results here are similar to those obtained by these observers. The fact that similar trends have been reported in total body water and in extracellular water by Widdowson and Spray (159), McCance and Widdowson (93) Friis-Hansen (55) and (56) and more recently by Clapp et al (29) and by Cassady (26) suggests that water changes in skinfold tissue echo those occurring in other water compartments. In fact total body water falls from 87% at 20 weeks to 78% at term and extracellular water from 62% at 20 weeks to 44% at term according to the figures presented in 1972 by Assali, Dehaven and Barrett as being the average values derived from recent literature based on " in vivo " studies. These figures correspond closely to those obtained by Widdowson and Co-workers (159) (93) based on post-mortem analyses i.e. 82.5% total body water in prematures of about 1.5kg weight and 68.8% in term infants of about 3.5kg weight. The close agreement between chemical determinations of water in dead infants and in vivo measurements in live infants has been remarked on by Cassady (26), Friis-Hansen (56) and Assali and Dehaven and Barrett (6) and enhances the usefulness of comparisons between skinfold thickness values in live infants and water values in dead ones as undertaken in this study.

Reference has only been made here to the more recent literature but the writer found Friis-Hansen's (55) earlier literature references so enjoyable that they are now reproduced.

Hippocrates	(± 400 B.C.) - " a child is blended of moist warm elements - - - the moistest and warmest are those nearest to birth ".
Galen	(± 150 A.D.) - " for always from his birth, every animal daily becomes drier ".
Razes	(± 900 A.D.) - " the blood of children in the same fashion contained more moisture than that of adult and old people ".
Katz	(1700 A.D.) - " it was the nature of children to sleep because of the greater amount of fluid in them ".

The "modern" references in Friis-Hansen's treatise (55) are also included here as he presented them:

Total Body Water in the Human Fetus, Measured by Desiccation in Per Cent of Body Weight (Calculated from the Literature)

Reference	Age in Lunar Months									
	1	2	3	4	5	6	7	8	9	10
Bezold (1857)					88					
Fehling (1877)	97.5			91.4	90.5	86.3	83.7	82.9		
Michel (1899)		93.8	90.2		87.3	85.1	84.7			
Schmitz (1924)		92.6	90.7	89.1	88.5	86.3				
Givens et al (1933)	90.0	88.9	89.5	87.5	83.2		83.4			
Iob et al (1934)		95.4	93.6	88.7	87.5	85.5	83.7	80.9		75.5
Average	93.8	92.7	91.0	89.2	87.5	85.8	83.9	81.9		75.5

Extracellular Water in the Human Fetus, in Per Cent of Body Weight

Reference	Age in Lunar Months			
	5	6	8	10
Harrison et al (1936)	62	60	53	43
Stearns (1939)		58	51	43
Average	62	59	52	43

Intracellular Water in the Human Fetus, in Per Cent of Body Weight

Reference	Age in Lunar Months			
	5	6	8	10
Harrison et al (1936)	25	26	29	32
Stearns (1939)		28	29	31
Average	25	27	29	32

It can be seen that the concept of decreasing total and extracellular water together with increasing intracellular water as growth proceeds is not new.

Mention has already been made of the comparatively higher graphical positions of light-for-dates infants,suggesting higher levels of water in their skinfold tissue towards term. It is interesting to note that recent studies in malnourished and intra-uterine growth retarded infants also report increased water levels. Davidson and Passmore in their textbook of " Human Nutrition and Dietetics " (31) state 'total body water has been measured in many children with protein calorie malnutrition and high ranges of 65 - 80% of body weight consistently found, whereas the value in normal children is 60%. The very high values around 80% have been reported in marasmic children whose body fat had been greatly reduced'. Support for this statement comes from Garrow et al (60) who found that marasmic infants had 121 - 125% expected amount of total body water and Kwashiorkor infants 81 - 82%. Smith in 1960 (133) also described a marasmic infant with no clinical oedema and gross loss of subcutaneous fat having a body water as high as a classical case of Kwashiorkor. More recently Cassady in 1970 (26) using Bromide space estimations stated that an expanded extracellular compartment characterizes the growth retarded group in his study of normal and dysmature infants and Cheek et al also in 1970 (27) report a disproportionately high extracellular volume relative to creatinine excretion and an elevated concentration of water in adipose tissue in infants suffering from protein calorie malnutrition.

As far as the sex difference in water values in concerned, infrequent indication of the sex of the infants studied has been given in previous reports. Smull (134) in 1958 in a study of 21 premature infants and Fink and Cheek (49) in 1960 studying 20 normal infants in the first day of life found no consistent variation due to sex in their measurements of the corrected bromide space (extracellular volume). Owen et al (105) in 1962 do however record a relatively greater content of water and exchangeable chloride in boys than in girls aged 4-9 months, but not aged 2 weeks to 4 months.

This study of water values in any case, demonstrates that term infants have less water in skin and subcutaneous tissue than do premature infants and that female term infants have a consistently lower water content in this tissue than do males.

Skinfold Tissue Fat and Gestation

Experiment 8 to determine the percentage of fat in skinfold tissue by the method of Folch, Lees and Sloane-Stanley (53) produced values of total fat by per cent weight of dried specimens which were on the whole similar at 30 weeks of gestation and at term. A range of values between 30-36% appeared at both gestational ages, whether these were adjudged by menstrual dates (Fig. 27), birth weight (Fig. 28) or crown heel length (29). When fat was considered as per cent of whole specimen-however, an increase was noted in male infants of from about 7% at 29 weeks to 24.8% at 39-40 weeks. This rise was less marked in the females being of the order of 19.5% of the total specimen at 30 weeks to 22.6% at 39 weeks. This suggests that the increase in fat was apparent rather than real and mainly due to diminution of water.

Skinfold Tissue Fat Male and Female

At term there occurs no marked difference between male and female fat values which as already stated remain at about 22.6% in females and about 24.8% in males for the whole specimen and about 41.5% in females and 44.6% in males for the dried specimen.

The evidence here suggests therefore that no definite upward trend in the fat content of skinfold tissue occurs during the time span of 30-40 weeks gestation. Also no gross differences in fat values at term exist between male and female infants.

Again the absence of counterpart studies in the literature prevents exact comparison. The fat values as obtained in this study do not however conform to the accepted views of steadily increasing deposition of fat in the foetus over the last trimester of pregnancy (33), (92), (125). These views are based however mainly on the work of Wilmer (161) in 1940 and of Widdowson and co-workers in the early fifties (93), (135), (158), (159). Wilmer's tables as quoted in Paediatric textbooks e.g. Dunhams " Premature Infants " describe a 35-fold increase in subcutaneous fat in grams per square centimetre of body surface. Wilmer's tables were however produced in 1940 by collating very early data on the total weight of skin and tela subcutanea from e.g. Von Leibig in 1874 and Bischoff in 1863 and calculating the mean weight per square centimetre by using the surface formulae of Scammon and Klein (121). The limitations of retrospective analyses of this kind are well recognised. The widely quoted figures produced by Widdowson and Spray (159), Widdowson (158) and McCance and Widdowson (93) were based on their own experimental data and record an upward trend in fat values from 3.5% in a 1.5kg. "premature" and 7.6% in a 2.5kg. "premature" to 16.2% in a 3.5kg. term infant. These figures represent fat as a percentage of whole body weight and are in fact "estimates of probable composition" based on findings in 19 infants (159). One actual infant however of weight 4.34kgs. is recorded as having as much as 28% of body weight in fat. The data was obtained by direct chemical analysis of whole cadavers using a method dating back to 1898 but not described in detail (135). In addition the use of body weight as an equivalent for gestational age has already been criticised as inadequate in the Introduction and formed one of the objections which led to the work presented in this Thesis. Perhaps the only apt comparison with the findings reported here is the work of Baker in 1969 (8). He measured the percentage of lipid in subcutaneous adipose tissue from an abdominal site in the human newborn infant and recorded a value of 45-46%. This report is probably closest both in terms and in values to the work reported here. None of these studies consider the sexes separately. In any case, it appears from the data obtained here that the quantity of fat in skinfold tissue remains relatively constant towards term and that the amounts in male and female term infants are similar.

Skinfold Lipid Constituents and Gestation

Experiment 9 was undertaken to explore any differences emerging with advancing pregnancy in the lipid constituents of skinfold tissue. Thin layer chromatographs were produced from the fat extracts in the 46 autopsied specimens and compared with the chromatographs of pure lipid markers. It was immediately recognizable that triglyceride was by far the most predominant lipid fraction in all 46 infants. No quantitative differences in triglyceride were evident in any cases. There was however a consistently larger amount of cholesterol ester in pre-term as compared with term infants. This can be seen from the examples presented (Figs. 34 and 35). It must be remembered here however that only relatively large quantitative differences can be displayed by this technique.

Skinfold Lipid Constituents Male and Female

No sex differences could be detected in any of the chromatographs whether of term or pre-term infants. Professional analysis of a sample chromatograph was undertaken by one of the MRC group in Reproductive Biochemistry at Strathclyde University. The various lipid fractions were scraped off separately and analyzed. Details of the findings are provided in the appendix 8 , and confirm the identifications made by the writer as detailed above.

Again literature references are meagre. The increased amount of cholesterol precursor in the pre-term infants accords roughly with Meyer's findings (87) of increased skin cholesterol in premature infants, and Hirsch's (72) report of increased cholesterol in premature subcutaneous adipose tissue. The predominance of triglycerides in the tissue fits with most recent accounts (18), (35), (72) as for example that of Pawan (108) in 1971 who states that more than 90 per cent of fatty acids are present in adipose tissue as triglyceride, about 0.5 per cent as phospholipids, less than 0.2

per cent as diglycerides and free fatty acids with traces of monoglycerides, cholesterol and other lipids. This evidence suggests that the composition of skinfold fat remains relatively constant towards term and is indistinguishable between male and female term infants. The decrease in cholesterol ester from pre-term to term infants in fact reflects a change in a constituent which reportedly (72) at its maximum makes up less than 2 per cent of the tissue.

This third section of the work was aimed at detecting any changes in tissue constituents with advancing gestation, and any differences occurring between the sexes at term which would account for the corresponding changes and differences occurring in the caliper measurement. The trend to increasing skinfold thickness values with advancing pregnancy demonstrated in Section II appears to be accompanied by a decrease in the amount of skinfold water, no change in the amount of skinfold fat and almost no change in skinfold lipid patterns. It is unlikely that alterations in cholesterol ester could affect the mechanical behaviour of the tissue before triglyceride, which makes up about 99 per cent of it (72). The significantly greater skinfold thickness values in female term infants demonstrated in Section II are accompanied by a significantly lower amount of skinfold water, similar amounts of skinfold fat and no qualitative difference in lipid constituents. Thus the chemical experiments of Section III provide evidence that the changes in caliper measurements from 30 weeks to term and the difference between the sexes at term are linked to changes and differences in tissue water rather than fat.

The most important supporting evidence for such a connection is probably the report by Brook in 1971 (17) of a correlation coefficient of 0.98 between total body water as measured by deuterium oxide and lean body mass as derived from skinfold thickness in children aged 1-11 years. The coexistence of substantially (43%) higher mean SFT values and significantly reduced total body water in infants of diabetic mothers reported earlier by Osler and Pedersen (102) also lends support. No other directly correlating studies can be traced. The absence of direct correlations between SFT values and fat in the form of serum lipids in the studies of Allbrink and Meigs (2) in 1965 and of Bhasin and Ahuja in 1972 (14) is also indirectly supportive.

CONCLUSIONS

From the data presented here the following conclusions can be drawn:

1. Measurement of skinfold thickness by the Harpenden caliper is a reliable technique provided reasonable standardization of method is maintained.
2. Skinfold thickness values depend on the first phase of the biphasic tissue response to caliper compression, and this is probably a function of tissue water content.
3. Skinfold thickness values, significantly related to birth weight and crown heel length increase towards term.
4. Skinfold thickness values fall below the mean in light-for-dates infants.
5. Skinfold thickness values are significantly greater in female term infants than in males.

6. The percentage of water in skinfold tissue decreases towards term.
7. The percentage of water is significantly lower in female term skinfold tissue than in male.
8. The percentage of water may be higher in light-for-dates infants towards term.
9. The percentage of fat in skinfold tissue remains relatively constant towards term.
10. The percentage of fat shows no great disparity between female term skinfold tissue and male.
11. The skinfold tissue lipid patterns remain relatively constant towards term. Cholesterol ester diminishes slightly in content but is probably insufficient in quantity to be perceptible mechanically.
12. The lipid patterns are indistinguishable between male and female skinfold tissue at term.

These conclusions inescapably lead one to the opinion that skinfold thickness values vary inversely with tissue water content. The fact that not one but three indications are evident of a connection or similarity between the behaviour of skinfold thickness values and that of tissue water is difficult to ignore.

In any case, this simple technique can be reliably used in newborn infants, is closely linked to other growth indices and may provide readily accessible information on the infants state of hydration.

Appendix 1.

Male Premature Infants (24)

Case No.	Gestation	B.W.	Length C/H	Length C/R	B.W. Position On Centile Chart
(From Normal Population Sample (14))					
1	36/52	3.10k	51.0	34.0	
2	34/52	1.99	44.5	28.9	
3	37/52	2.52	46.8	30.5	<10th^{c}
4	37/52	3.14	49.4	31.5	
5	36/52	3.48	49.5	33.8	
6	37/52	2.96	47.8	30.4	
7	37/52	2.35	45.7	29.6	<5th^{c}
8	37/52	4.30	53.0	35.9	>95th^{c}
9	37/52	3.86	49.0	32.7	>90th^{c}
10	36/52	3.40	51.2	31.8	
11	35/52	3.26	50.8	33.3	
12	37/52	3.26	49.0	31.5	
13	34/52	2.49	45	29.6	
14	34/52	1.60	40.5	26.0	<5th^{c} @ 34/52
(Clinically Selected (10))					
15	35/52	2.14	43.5	28.5	
16	35/52	1.42	40.8	25.2	<5th^{c}
17	36/52	2.80	47.7	31.7	
18	36/52	2.43	45.4	28.8	
19	37/52	2.43	46.4	30.5	<10th^{c}
20	26/52	0.80	32.8	21.3	
21	36/52	2.52	47.5	30.4	
22	36/52	2.61	47.4	-	
23	31+/52	0.97	36.0	-	
24	30/52	1.21	40.0	27.0	

Appendix 2.

Female Premature Infants (19)

Case No.	Gestation	B.W.	Length C/H	Length C/R	B.W. Position On Centile Chart
(From Normal Population Sample (5))					
25	37/52	3.02	46.6	32.1	
26	29/52	3.62	51.8	35.0	
27	34/52	1.26	39.4	26.0	< 5th^c
28	37/52	3.03	47.9	28.2	
29	35/52	2.07	44.5	29.8	< 10th^c
(Clinically Selected (14))					
30	32/52	1.40	40.0	-	
31	34/52	1.63	40.3	26.8	< 5th^c
32	36/52	2.72	48.4	31.2	
33	35/52	2.11	45.3	29.5	on 10th^c
34	37/52	2.41	44.9	29.9	
35	28/52	1.13	37.3	24.0	
36	36/52	2.72	47.8	30.4	
37	36/52	2.66	46.4	29.0	
38	36/52	2.53	45.3	28.5	
39	35/52	2.32	45.8	29.0	
40	34/52	1.39	41.9	26.9	< 5th^c
41	36/52	2.02	45.0	28.5	< 5th^c
42	31/52	1.14	37.0	26.0	
43	36/52	2.35	45.2	29.3	

Appendix 3.

Male Light For Dates Infants (37)

Case No.	Gestation	B.W.	Length C/H	Length C/R	Pregnancy No.
(From Normal Population Sample (12))					
44	39/52	2.74	48.5	31.0	1
45	39/52	2.46	46.2	30.5	1
46	40/52	2.66	49.5	32.0	1
47	40/52	2.92	48.2	31.5	2
48	41/52	2.92	47.9	31.0	5
49	?44/52	2.74	48.0	31.5	1
50	39/52	2.49	46.8	30.3	8
51	38/52	2.55	44.6	30.4	3
52	39/52	2.57	48.3	31.9	1
53	?44/52	2.63	47.8	30.5	1
54	38/52	2.55	47.5	30.3	1
55	41/52	2.71	48.0	-	1
(From Delivery Room Records (25))					
56	37/52	2.69	47.5	29.8	4
57	39/52	2.52	47.0	29.7	1
58	39/52	2.80	48.5	30.9	12
59	39/52	2.63	45.8	31.9	1
60	37/52	2.55	45.0	29.0	2
61	40/52	2.72	48.0	31.9	1
62	38/52	2.60	48.8	30.8	2
63	41/52	2.52	50.3	31.0	1
64	41/52	2.77	47.5	30.0	1
65	39/52	2.70	48.5	31.0	1
66	39/52	2.89	49.0	31.8	2
67	39/52	2.83	49.9	32.5	1
68	38/52	2.69	48.4	31.4	6
69	37/52	2.83	46.8	29.9	1

Appendix 3 (cont'd).

Case No.	Gestation	B.W.	Length C/H	Length C/R	Pregnancy No.
70	42/52	2.97	49.0	37.0	8
71	41/52	2.94	47.3	29.8	3
72	37/52	2.38	44.3	29.6	2
73	39/52	2.36	47.0	29.8	2
74	42/52	2.61	48.2	31.5	1
75	41/52	2.72	49.7	32.3	3
76	38/52	2.68	48.0	30.7	3
77	37/52	2.63	48.8	31.8	2
78	37/52	2.46	46.5	30.5	3
79	37/52	2.56	48.5	31.6	1
80	40/52	2.94	49.8	32.0	5

Appendix 4.

Female Light For Dates Infants (32)

Case No.	Gestation	B.W.	Length C/H	Length C/R	Pregnancy No.
(From Normal Population Sample (10))					
81	41/52	2.57	47.3	30.7	2
82	38/52	2.52	46.6	30.7	1
83	43/52	2.80	48.5	31.5	2
84	40/52	2.72	45.5	30.6	4
85	41/52	2.63	49.4	31.4	2
86	39/52	2.57	47.4	31.5	5
87	40/52	2.55	47.3	29.5	2
88	41/52	2.80	47.0	29.0	3
89	42/52	2.27	45.6	28.3	2
90	42/52	2.74	48.1	30.4	1
(From Delivery Room Records (22))					
91	41/52	2.86	49.0	31.3	1
92	40/52	2.57	47.6	31.2	10
93	40/52	2.07	46.0	28.9	1
94	41/52	2.72	48.4	31.0	5
95	38/52	2.43	44.7	29.7	2
96	40/52	2.50	45.0	31.1	3
97	37/52	2.14	44.5	28.8	1
98	40/52	2.80	46.4	30.8	2
99	40/52	2.39	47.0	29.2	1
100	38/52	2.52	46.4	30.0	1
101	41/52	2.75	50.0	32.6	2
102	40/52	2.55	46.6	29.9	1
103	42/52	2.63	48.7	31.5	1
104	39/52	2.43	47.0	29.1	7
105	37/52	2.45	45.0	28.0	1
106	39/52	2.66	47.7	32.0	1

Appendix 4 (cont'd).

			Length	Length	
Case No.	Gestation	B.W.	C/H	C/R	Pregnancy No.
107	42/52	2.75	44.5	29.8	6
108	40/52	2.80	50.6	32.7	6
109	41/52	2.55	49.4	32.3	1
110	38/52	2.07	44.0	29.3	6
111	38/52	2.54	47.6	30.9	1
112	39/52	2.63	49.3	32.2	1

Appendix 5

Apparently normal term infants used to demonstrate

Time/deformation curves (21)

MALE

Case No.	Birth Weight	Age of Infants (days)
113	2.80	2
114	2.82	4
115	3.05	2
116	3.10	3
117	3.11	3
118	3.20	2
119	3.62	2
120	3.52	4
121	3.72	4
122	3.82	3
FEMALE		
123	2.45	4
124	2.69	3
125	3.02	4
126	3.11	3
127	3.14	2
128	3.18	2
129	3.21	4
130	3.64	3
131	3.76	3
132	3.99	3
133	4.04	3

Appendix 6

Autopsy Specimens For Chemical Analysis - Details Of Male Infants (29)

PM No	Gestation (wks)	SB/NND (hrs)	BW DW	Length C/H(cm)	Pathology
1	33	S.B.	1.96	40	R.D.S.
*2	38	S.B.	2.20	49	Twin Asphyxia Abruptio Placentae
3	28	NND 5	1.08 1.11	38	Abruptio Placentae Intracranial Haem.
4	30	NND 61	1.58 1.52	43	R.D.S. Pulm. Haem.
5	30	S.B.	1.89	46	A.P.H. I.U.D.
*6	34	NND 47	2.41 2.40	50	R.D.S. Dysmaturity
7	41	S.B.	3.88	50	Cord Round Neck Asphyxia
8	40	NND 14	3.05 "	52	Coarctation Aorta Congen. Cystic Dis. Lungs
9	28-29	NND 12	1.07 1.06	39	Asphyxia Intraventricular Haem.
10	41	NND 29	3.85	54	Asphyxia Intracranial Haem. Adrenal Haem. Coagulation Defect
11	35	NND $8\frac{1}{2}$	2.10 "	46	Abruptio Placentae Intraventricular Haem. Dissem. I-V Coag.

Appendix 6 (cont'd)

P.M. No.	Gestation (wks)	S.B./NND. (hrs)	B.W. D.W.	Length C/H(cm)	Pathology
12	40	NND. 55	3.00 2.92	53	Haemorrhagic Pneum. Cerebral Oedema Endocrine Abnorm.
*13	30	NND. 36	1.30 1.28	41	R.D.S. / Prematurity Dysmaturity
14	38	S.B.	2.64	50	Abruptio Placentae I.U.D.
15	28	NND. 4	1.20 1.18	39	Intracranial Haem. Abruptio Placentae Atelectasis
16	28-30	NND. 17	1.34 1.32	40	Intraventricular Haem. Atelectasis Hyaline M. Dis.
*17	34-35	S.B.	1.52	43	Twin Asphyxia Abruptio Placentae
*18	34-35	S.B.	2.4	49	Twin Abruptio Placentae
19	39	S.B.	3.14	52	Asphyxia Placental Insuff. Coagulation Defect
20	39-42	NND. 58	3.03 3.12	48	Breech Intracranial Haem.
*21	37	NND. 21	2.28 2.26	46	Pulm. Hypoplasia Renal Agenesis
22	33	NND. 35	1.67	44	Intracranial Haem.
23	40	S.B.	3.90	53	Asphyxia Placental Insuff.
24	36	NND. ½	2.57 "	49	Asphyxia Abruptio Placentae Pulm. Hypoplasia

Appendix 6 (cont'd)

P.M. No.	Gestation (wks)	S.B./NND. (hrs)	B.W. D.W.	Length C/H(cm)	Pathology
25	31	NND. 2	1.70 1.38	43	Asphyxia Renal Agenesis
26	30-31	NND. 20	1.70 1.62	42	Asphyxia Intraventricular Haem.
27	31	NND. 6	1.71 1.64	46	Atelectasis Hyaline M. Dis.
28	29	NND. 39	1.81 1.86	45	R.D.S. Pneumothorax Intraventricular Haem.
29	32	S.B.	1.80	45	Asphyxia Abruptio Placentae

* Numbers	2, 17, 18	Twin
* "	6, 13	Pathologically dysmature
* Number	21	<10th centile

Appendix 7

Autopsy Specimens For Chemical Analysis - Details Of Female Infants (17)

P.M. No.	Gestation (wks)	S.B./NND. (hrs)	B.W. D.W.	Length C/H(cm)	Pathology
30	40	NND. 9	3.25 3.185	51	Congenital Heart Dis.
*31	38	S. B.	1.42	42	Twin Asphyxia Abruptio Placentae
32	33	NND. 48	1.94 1.91	45	Hyaline M. Dis. Pneumonia Intraventricular Haem.
*33	36	NND. 16	1.96 "	44	Asphyxia / R. D. S. Intraventricular Haem.
*34	31-32	NND. 96	0.99 0.92	36	Triplet Intraventricular Haem.
*35	32	NND.144	1.56 1.40	44	Twin Hyaline M. Dis. Pneumonia
36	34-35	NND. 33	2.26 2.23	47	Rt. Pneumothorax Hyaline M. Dis. R. D. S.
37	30	NND. 10	1.35 1.32	39	Intraventricular Haem. Pulm. Hypoplasia Hyaline M. Dis.
38	39	NND. $\frac{1}{2}$	3.35	53	Asphyxia Atelectasis Pulm. Haem.
39	34	NND. 3	1.85 1.84	46	Intracranial Haem. Congenital Heart Dis. Asphyxia Tracheal Aplasia

Appendix 7 (cont'd)

P.M. No.	Gestation (wks)	S.B./NND. (hrs)	B.W. D.W.	Length C/H(cm)	Pathology
40	39	S.B.	2.92	51	Breech Intracranial Haem. Rt. Tentorial Tear
41	39	S.B.	2.80	51	Asphyxia L.U.C.S. for Foetal Dis.
*42	33	NND. 4¼	1.40 "	40	Asphyxia Atelectasis
43	30	NND. ½	1.80 "	44	Asphyxia Atelectasis
44	30-31	NND. 96	1.14 1.06	39	Coag. Defect Intraventricular Haem. Haem. Infarct Bowel Peritonitis Septicaemia
45	40	NND. 57	3.88 3.42	52	Breech Asphyxia Intracranial Haem.
46	29	NND. 72	1.57 1.40	43	R.D.S. Intraventricular Haem. Bilateral Pneumonia

* Numbers 31, 34, 35 Twin

* " 33, 42 <10th centile

Appendix 8

Professional Analysis of Sample Chromatograph

1. By Zinzadze reagent phospholipid was located only at the origin.

2. The major spot on all chromatograms was triglyceride by elution and further chromatography with marker.

3. Cholesterol was detected by elution and sulphuric acid treatment in the spot running to the front.

Courtesy of Mr. J. O'Grady
M.R.C. Group
Biochemistry of Reproduction
University of Strathclyde.

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The work involved in Section 1 of this thesis has been published in the journal 'Biology of the Neonate' and Dr. James MacGregor of the University of Stratholyde was the second operator in Experiment 4. Dr. Frank Bell produced the mathematical analysis of compression curves in Chapter 9.

SUMMARY

This thesis concerns the Caliper Measurement of Skinfold Thickness in newborn infants. The technique has been used in adults for about eighty years and provides values which have been shown to be closely related to body fat as calculated from volumetric analysis, densitometry and roentgenogram measurements. Nomograms and regression equations allowing the direct calculation of total body fat from skinfold thickness measurements have subsequently been developed. Durnin in the University of Glasgow has extended the use of the technique to adolescents and Tanner has pioneered its use in children aged 1 month to 4 years. Its application however has been extremely limited in newborn infants. The reasons for this are probably two-fold: the first is the suspected unreliability of the technique, many potential sources of error existing, the second is lack of knowledge as to the exact clinical significance of the values.

The work presented here seeks to improve this position and is described in three sections. Section I consists of an examination of the technique as applied to neonates. Section II examines the values in normal, premature and light-for-dates infants and Section III describes the gross chemistry of skinfold tissue in autopsied infants.

The Technique - Section I

Three different calipers were examined with regard to ease of manipulation, size of scale, accuracy etc. The instrument preferred and used throughout was the Harpenden caliper. Different sites for measurement were considered and particular ones selected for reasons of accessibility and low error content.

Measurements were attempted in different order and with the infant in different positions. A standard technique was developed.

The error attached to the technique was calculated from duplicate measurements in the same infants after a period of one hour. The magnitude of the error was defined as 15% at 95% confidence limits. The sources of this sizeable error were examined as originating from the instrument, from the operator or from the tissue. The accuracy of the Harpenden caliper had been reported as adequate in the MRC study in 1951 and the error recorded there was of the same order as found here. The particular instrument used was of course calibrated first. The subjective aspect of the technique was examined for error content by comparing the standard error detailed above with that obtained when marked skinfolds were measured after one hour. No appreciable difference in error was demonstrated. The subjective aspect of the technique was further examined by experiments with an instrumented Harpenden caliper attached to an XY plotter. Operator readings were compared with those on the plotter. The readings of two operators were also compared with plotter values. Little difference in values was evident. Thus, none of these experiments pinpointed the exact location of the error which must by exclusion be levelled at tissue behaviour. The first experiment with the instrumented caliper portrayed the response of the tissue to caliper compression as a curve which was bi-phasic in character. Further examination of compression curves was undertaken later to detect any changes in tissue behaviour in different babies.

Comparison of compression curves in these infants did not show a link between skinfold thickness values and the rate of compression as defined by millimetres per second decrease in tissue thickness. If the time of reading is constant, as should be the case if successful standardization has been achieved, this suggests that alterations in the quantity of some tissue constituent may exist. The suggestion is made that this tissue constituent is in fact fluid and literature support for this view is presented.

The Values - Section II

Skinfold thickness values were recorded in a statistically selected normal group of infants, in a group of premature infants and in a group of light-for-dates infants. In the normal group of infants, strong correlations were obtained between skinfold thickness values and the infant's birth weight and crown heel length, but not with its gestational age. A highly significant difference also emerged between male and female values, male values being smaller. In the premature infants,the same relationships with birth weight and birth length emerged but in this group significant correlations appeared between skinfold thickness values and gestation,a trend to increasing values with advancing pregnancy being apparent. There were insufficient numbers to consider the sexes separately. In the "dysmature infants", all skinfold thickness values fell below the mean values recorded in the normal group. The relationships with the other growth indices and the differences between male and female values were absent. Findings in the few corresponding reports in the literature are compared.

The Chemistry - Section III.

This section describes the chemical analysis of autopsied skinfold tissue. Specimens consisted of the portion of tissue enclosed by the caliper blades at the standard site and were dissected by the writer personally. The percentages by weight of total water in fat-free specimens and of total fat in the dehydrated specimens were estimated. The fat extracts were subjected to thin layer chromatography. Changes with gestation and differences in male and female values at term were sought as explanations for the changes and differences found in the corresponding caliper values. A trend to decreasing water values with increasing gestation was evident and female infants had significantly less water than male infants at term. No such obvious trend was seen in fat values and no significant sex difference occurred. Thin layer chromatographs showed that triglyceride was by far the largest constituent of all fat extracts and that similar lipid patterns occurred from 30 - 40 weeks. No sex differences were apparent. No exact replica of this approach where skin and subcutaneous tissue are treated as a single organ has been found in the literature.

CONCLUSIONS

It is thus concluded from the evidence collected here;

A. That measurement of skinfold thickness in the newborn by the technique described is reliable and that the "error" in fact reflects a change in tissue behaviour and probably its water content.

B. That skinfold thickness values are closely related to the infant's birth weight and crown heel length, that they increase with gestation, and that female values are significantly greater than male values at term.

C. That the percentage of water in skinfold tissue declines with increasing maturity whether denoted by birth weight, crown heel length or gestational age; That female water values at term are significantly lower than male ones; and that no such trend or difference exists in percentage fat nor in lipid patterns as visualized in thin layer chromatographs.

Of particular interest in these findings is the recurring link between skinfold thickness and tissue water - in explaining the error; in the opposite but matching trends with gestation; and in the opposite but matching sex differences at term. The possibility must be raised that skinfold thickness values reflect tissue water in an inverse way .

In any case, this simple technique can be reliably used in newborn infants, is closely linked to other growth indices and may provide readily accessible information on the infants state of hydration.