VOLUME I.

STUDIES ON THE ELASTIC TISSUE OF THE SKIN AND ITS RELATION TO THE MAINTENANCE OF TISSUE TENSION AND TO LYMPHATIC DRAINAGE.

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STUDIES ON THE ELASTIC TISSUE OF THE SKIN AND ITS RELATION TO THE MAINTENANCE OF TISSUE TENSION AND TO LYMPHATIC DRAINAGE.

SECTION I.

A. GENERAL INTRODUCTION.

The skin is the largest and most extensive organ of the human body, yet it has a comparatively simple structure. On the surface there is the epidermis, a layer of stratified squamous epithelium, and developed from it are the hair follicles with sebaceous glands and the sweat glands which extend below the epidermis. Deep to it is the cutis vera, consisting of a thin layer of areolar tissue, and a broad band of fibrous tissue containing white connective tissue and yellow elastic fibres, these latter fibres being the special subject of this study. There are also non-striped muscles in relation to the hair follicles, blood-vessels, nerves, and nerve-endings. These structural elements vary in size and number in different situations according to requirements. The skin performs many different functions, some of which are carried out by the skin of the whole body, others being localised to definite areas. The different elements may function separately from one another, e.g. the sebaceous glands alone are concerned in the secretion of sebum, sensation of touch is conveyed by tactile nerve-endings: or they may combine to perform one function - e.g. hairs, sweat-glands and small blood-vessels all act together in the regulation of body temperature. Several of these elements and their functions have been studied fairly fully by various workers, but the significance of the presence of the dense layer of fibrous tissue, and especially of the yellow elastic fibres in it, has received little attention.

While the skin is the outpost for receiving impressions from the outer world, and the first line of defence against injury from without, it is also the outermost limit to the internal forces of the body, and as far as concerns this paper, the chief source of internal energy is the heart. The heart sends the blood out into the arteries with considerable force: most of this force is spent in the vascular system, a small amount, however, passing beyond to the tissues. After being 'buffered' in the filtration and reabsorption process in the capillaries any excess of force must be absorbed by the elastic tissue of the skin. Again, when an incision is made through the skin, the cut edges retract very noticeably: the skin is under continual tension. Accordingly, it seems of some importance to inquire into the function of this tension set up by the elastic tissue and this thesis represents a study of this problem.

B. LIMITATIONS OF "ELASTOMETRY."

A method of studying the elastic response of the skin to variations in the fluid content of the subcutaneous tissues has been introduced by Schade, using an instrument which he called the Elastometer. A weight, usually about 50 gm., is placed on a tactile disc lying on the skin, preferably on an area with little soft tissue below, e.g. the back of the wrist or the forehead, and left for a stated time - usually one minute - then removed: the effect of the weight is drawn by a pointer from the disc on a revolving drum, and from the resulting graph the "elasticity" of the skin can be compared with that of other subjects' skin. The principle involved and the full method of use are explained by Schwartz (1916), and the results obtained by this method are compared with other investigations (disappearance time of intradermically injected salt solution, urinalysis and nitrogen retention) in cases of oedema by Kunde (1926).

A. Crosti (1933) gives a good résumé of the observations which have been made by this method in various pathological conditions and indicates the clinical uses to which the instrument can be put, while recognising its limitations in the precise study of both the elasticity of the skin and the amount of fluid in the subcutaneous tissues. The instrument gives information chiefly about the manner in which fluid can be pressed out of the tissues and its rate of return, and as these factors vary in normal, inflammatory, and oedematous cases and at different stages in oedema, this information can be used to compare cases and the progress of cases. By its use, a pre-oedematous state can be recognised.

The information, however, cannot be used to find the actual tension in the tissue spaces, nor the tension in the skin itself, because there are too many variable factors, e.g. the amount of subcutaneous tissue, temperature, degree of moisture, etc. And it is not the physical "elasticity" of the skin which is measured.

C. OUTLINE OF WORK.

In this work, various points in the histology of the skin are described, with special reference to the yellow "elastic" fibres, and the subcuticular network of reticular fibres. Macroscopic methods were employed to study the elasticity of the skin by stretching and the results obtained are given and discussed. A few observations are included on the combined findings of histological and experimental findings, bearing on whether the yellow fibres are the chief elastic elements or not - a point which has been the subject of discussion recently. The results obtained by the stretching experiments were found to dovetail in with, and to amplify, much work done recently on the forces concerned in capillary filtration and reabsorption: from a combination of the results of those workers and the findings given here it is believed that the problems of tissue tension and extravascular circulation (i.e. the tissue fluids and lymph) can be considerably clarified.

SECTION II: HISTOLOGY:

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A. INTRODUCTION.

In the cutis vera there are both white connective tissue fibres and yellow elastic fibres - the latter in larger proportion than in any other tissue of the body, except the walls of blood-vessels. Previously, it has been accepted that it is these yellow elastic fibres which allow the skin to be stretched so easily, and that the white fibres play no part in this function. The return to the normal position after stretching is also attributed to the elastic fibres.

In an interesting article,"On the Elastic Fibres," Sternberg (1925) notes that those structures with many elastic fibres generally have extraordinary elasticity (used with the meaning that they are easily stretched and quickly resume something like their former shape, as rubber - not in accordance with the physicists' definition of elasticity). He goes on, however, to throw doubts on the accepted significance of these fibres. In many cases where he examined the elastic tissue of the skin, he found great alteration in this tissue histologically where he found no gross elastic change, and he states that dermatologists have already suggested other conceptions: Riehl and Kyrle have both expressed the view that the elasticity of the skin depends on the arrangement of tissues which make it up - the elastic fibres forming a supporting framework for the softer and more easily stretched white connective tissue fibres.

Sternberg further quotes the findings of Triepel that the modulus for stretching and that for solidity are much greater for collagen than for elastic fibres, whereas the amount of stretch required to produce a tear is less. Similarly, de Groodt (1930) states that the elasticity of the skin does not depend on the elastic tissue, but on the whole structure of the connective tissue.

Nevertheless, in a study of the elasticity of the skin it seems necessary to observe the different amounts of elastic tissue in the skin of different parts of the body. There must also be considered the variations in thickness in the different parts. The character, or quality, of the yellow fibres varies with age, and this introduces another point for consideration.

E. Lindholm (1931) has made some observations on several of the points raised. He examined the skin of the thorax and abdomen, and compared the number of elastic fibres present in these parts in infants and in adults. He finds that there are more fibres in infants and that this is often, but not always, accompanied by greater fineness of the fibres in early childhood. Also, there are, on the whole, more elastic fibres in women than in men. In male infants he finds fewer fibres in the abdomen than in the thorax, and similarly with men; but here there is more variation in the results. On the other hand, in women there are more fibres in the abdomen than in the thorax. He mentions that in women the number of fibres in the thorax corresponds closely with that in the limbs. A somewhat similar finding is observed in men. The fibres become more prominent, although fewer in number, from birth onwards.

Degenerative changes due to old age and exposure to weather have been fully described by various authors, e.g. Schmidt (1891), Kissmeyer and With (1922): and various aspects of the pathological histology by Ohno (1925).

In the present investigation, histological examination was carried out on portions of skin from various situations - abdomen, medial and lateral sides of the thigh and leg, foot, chest, forearm and arm, as well as more specialised areas such as eyelids and scrotum. As the experiments (to be described in Section III) on the capacity for stretching were performed on portions of skin from abdomen, thigh and leg, comparison between the histological and experimental results will be concerned chiefly with these areas of skin.

The age periods chosen for this investigation were:-

1. 0-5 years.*
2. 15-23 years.
3. 30-40 years.
4. Over 65 years.

* Most of the material in this group was obtained from subjects upon which autopsies were performed (at which I was present) in the Royal Hospital for Sick Children (Glasgow).

The areas mentioned in the preceding paragraph have been examined in every instance and sufficient subjects were taken in each period to demonstrate what could be regarded as the normal picture for males and females. In the first and last periods (infancy and old age) the skin of the different subjects in each period shows a remarkable similarity in the quantity and characteristics of the elastic tissue content, and a general impression of the typical findings is easily obtained. In the middle age periods (viz. 15-40 years of age), however, there is considerable divergence of results, individual cases varying in the amount of elastic tissue present: the typical findings illustrated for these periods are therefore to be regarded as averages. Table I gives the number of cases in which all the situations mentioned above were examined.

Table I.

Age.	Males	Females	Total
1. 0-5 years.	4	3	7
2. 15-23 years.	4	5	9
3. 30-40 years.	5	3	8
4. Over 65 years.	4	4	8
Totals:	17	15	32

Other situations were examined and special methods of technique were used on some of these subjects and in numerous others.

B. TECHNIQUE.

Small rectangular portions of skin and subcutaneous tissue, about 2 x ½ cm. in size, were taken from the situations to be examined. These specimens lay in transverse and longitudinal directions to the long axis of the body (occasionally a portion in only one direction was taken). In the foot, various parts of the sole were examined but from the dorsum the piece was always from the centre of the area. In the limbs, the portions examined were selected from mid-way along the legs, thighs, forearms or arms. In the abdomen and chest the specimens were taken from the mid-line, in the middle of the epigastrium and over the junction of the manubrium and body of the sternum. In a few subjects small square blocks from various situations were cut parallel to the surface in serial sections.

Circles of skin - fixed, stretched and loose.

As the skin contracts when an incision is made into it, it was thought that the histological appearance might be distorted by this contraction. An experiment was therefore carried out in which any contraction before fixation of the part to be examined was prevented, and sections so fixed were compared with sections from parts cut out and fixed in the usual way. A medium-sized thin cork was obtained, and a circle 1 cm. in diameter was drawn on it. Fine needles (8-10 in number) were pushed through the cork round the circle in such a way that their sharp points were all projecting a similar distance (about ½ cm.) through the cork. These sharp points were pushed well into the area of skin to be examined before any incision had been made. This area as well as the surrounding skin for at least 1 cm. beyond the needles was then excised, retaining the needles in position, and fixed in corrosive sublimate. After fixation, the central part was taken for examination - it had been held by the needles in the position in which it was on the body and therefore was not distorted by the contraction due to incising the skin. The result of this experiment was definite - there was no obvious difference in the appearance of the elastic tissue in sections fixed in this way from that of sections fixed in the ordinary way, and no special advantage was to be obtained by this special method. It was noticed, however, that the larger folds of the skin were flatter in the specially fixed sections - but the individual features showed no appreciable difference.

Fixation was carried out in corrosive sublimate solution and the blocks embedded and cut in paraffin. Sections of each block were stained by haemalum and eosin and by Weigert's method for elastic tissue. The elastic tissue stain proved difficult to make up satisfactorily unless great care was taken with the method: Gurr's basic fuchsin and Liquor Ferri Perchloridi (B.P. 1914) were used and it was found that methylated spirit could be substituted for absolute alcohol in the final stage: the time of staining in the Weigert's solution varied from ½-2 hours. Counter-staining by carmalum or saffranin was used.

A striking feature of the elastic tissue in the normal skin is its twofold arrangement (Figs. 1 and 2). First there are the main fibres in the deeper layer of the cutis vera: these are the more important ones in connection with the gross physical property of elasticity of the skin. But there is also a network of smaller and finer fibres and fibrils in the papillary, or subcuticular, layer extending into the papillae and lying fairly closely under the epidermis. Even more than the main fibres, this latter network shows marked variations in structure and amount, for different sites of the body and for different ages, and, as it is of considerable interest, it will be dealt with in a separate section (p. 23) after the distribution of the main fibres has been described.

C. MAIN ELASTIC FIBRES.

1. Arrangement.

The main elastic tissue in the cutis vera consists of large fibres of considerable length, running practically parallel with the surface of the skin: they are slightly tortuous, but considerable lengths are seen in sections 8 μ in thickness (Figs. 2 and 3). They run between and close beside the white fibres. In sections cut parallel with the surface of the skin (Figs. 4 and 5) they are seen to run between the bands of white fibres, often with a majority running in a definite direction (transverse or longitudinal to the long axis of the limb). The number and size of the fibres vary considerably with the site examined. There are also variations in their arrangement throughout the thickness of the skin: sometimes they are distributed evenly (Fig. 3): sometimes they are more numerous and larger superficially (Fig. 2): at other times they run in fairly dense bands with few elastic fibres between the bands (Fig. 7): again, the majority of fibres may run in one direction superficially, and at right angles deeper (Fig. 22).

Hair follicles and sweat glands interrupt the continuity of the fibrous tissue bundles in the dermis. In Figs. 4 and 37, there is seen to be little elastic tissue in the vicinity of the appendages. In Fig. 4, the fibres are seen to sweep around a sweat gland leaving the immediate vicinity free of elastic tissue, although from Fig. 37 it would appear that the fibres merely come to an abrupt end near the hair follicle. In Fig. 5 - a section parallel to the surface and nearer the surface than Fig. 4 - there is a considerable amount of elastic tissue fairly close to the hair follicles, and this finding is constant for the upper parts of the follicles. Very often also, the fine elastic plexus is well developed around the epithelium of the follicles and may form dense condensations, especially in old skin (Figs. 22, 50, 23); these denser areas are often connected with the insertions of erectores pilorum (Fig. 15).

2. Direction.

In certain areas of the skin there is a tendency for the elastic fibres to be arranged in a definite direction. This can be studied by taking sections in planes both longitudinal and transverse to the long axis of the body and noting the direction of the majority of the fibres. Most transverse sections from the medial sides of the limbs show the entire length of the bulk of the fibres - i.e. they run transversely on the body (Fig. 2). In other areas, e.g. the lateral sides of the limbs (Fig. 3) the fibres cut transversely and longitudinally are roughly equal in number. These features were found consistently in all the cases examined. In the other situations examined (chest, abdomen) the direction of the fibres varied in the different subjects.

Special areas have distinctive arrangements of the fibres in special directions, and these will be described later.

3. Deep Connections.

Over most of the trunk and limbs, the skin can be moved fairly freely on the deep tissues. The connections consist of bands of connective tissue (white and yellow fibres) surrounding blood-vessels, etc. in their course through the subcutaneous fat. Illustrations of these can be seen in Figs. 7 and 10. They allow of considerable range of movement of the skin, as can be easily shown on the living body. In the palm of the hand and sole of the foot, the subcutaneous fat is replaced by dense connective tissue, chiefly of white fibres which bind the skin firmly to the deep tissues.

4. Sex.

In the number, size and arrangement of the elastic tissue fibres there is little to distinguish between the skin of the different sexes. The skin of females is of finer texture, often with finer and fewer hairs, and is supported by a much firmer layer of subcutaneous fat than that of males. Occasionally, however, it can be recognised that the skin of a female is thinner and contains slightly fewer elastic fibres than that of the males of the same age group. This supports the findings of Lindholm (1931), who counted the number of elastic fibres in the thickness of the skin in male and female subjects, and, although there were large variations for different cases, the average number was found to be slightly fewer in the female cases.

5. Age Variations.

These changes will be considered by examining sections from 6 different areas in each of the age groups studied.

(a) First Age Group (0-5 years). In the skin of infants the elastic fibres are always very numerous, well-formed and fairly large (Figs. 6-11). (See also Figs. 18-23 for comparison with adult skin from corresponding situations).

In the sections shown, it can be seen that the fibres are fairly evenly distributed, except for the spaces round sweat ducts and hair follicles: and in the sections from the limbs (Figs. 6-9) most of the fibres are found to run transversely to the body axis. In the skin of the lateral side of the leg (Fig. 7), however, there is a tendency for the elastic tissue to be arranged in bands of longitudinal and transverse fibres from the surface downwards. The downward projections of the cutis vera into the subcutaneous tissue, so marked in the skin of the lateral side of the limbs, are seen to contain an abundant quantity of elastic tissue.

The skin of the leg is noticeably much thinner than that of the thigh, but contains an equal proportion of elastic tissue. The lateral side of the thigh has skin as thick as that of the abdomen, but contains a very much greater proportion of elastic tissue: in the abdomen, the elastic fibres are rather fewer and finer in quality than in the limbs. But the chest skin is also different: its elastic fibres are very numerous, and fine in quality: there do not seem to be many fibres of any great length present.

(b) <u>Second Age Group (15-23 years)</u> - Figs. 12-17. The skin in all areas is at this age very much thicker than in the infant. But the relative thicknesses of the various parts are still maintained. The elastic tissue is not in so large a proportion as in the skin of a younger person: the fibres are fewer in number, and are not so well-formed: they are of uneven thickness, and the edges are often slightly curled. These changes are well seen in Figs. 14 and 15.

In the medial side of the thigh (Fig. 14), too, the fibres are more numerous in the superficial layer than deeper. On the other hand, in the skin of the abdomen (Fig. 16) the fibres are small, fairly numerous, and well-formed throughout the thickness of the skin.

In this group there are 2 cases in which the amount of elastic tissue is very small - the fibres are also very small, and appear to be broken up or to consist of only short lengths. This is a very striking finding, but no special reason could be found to explain it.

(c) Third Age Group (30-40 years) - Figs. 18-23. The illustrations are from one case - a woman aged 35 years - and her skin is slightly thinner than that of the males of the same age group. The elastic fibres are fairly numerous, and show slightly greater irregularity in size and thickness than in the previous groups. Sometimes they are fairly evenly arranged (e.g. Fig. 20), but very often there is irregular grouping of the fibres (e.g. Figs. 21, 23). Often there are seen small areas where there is practically no elastic tissue, or a great increase in the non-elastic area round hair follicles (Fig. 19), etc. Again, the elastic tissue in the abdomen and chest is rather less than in the limbs, and of a finer texture. In the abdomen (Fig. 22) the superficial area contains more elastic tissue than the deep layer.

To show the slight variations, but essential similarity, in different subjects from the same age group 4 illustrations (Figs. 47-50) of sections of abdominal skin from male adults between 28 and 39 years of age are shown. There is slightly less elastic tissue in Fig. 48 than in the other three, and the skin in Fig. 50 is thinner than in the others. On the whole, however, they all present very similar appearances.

(d) Fourth Age Group (Over 65 years) - Figs. 24-29. At this, the oldest age, the degenerative changes are well shown. The fibres are very irregular in thickness - there are rough thickenings and the appearance of broken ends coming off from the sides of the fibres, and the ends are irregularly fragmented. There is also condensation and conglomeration of elastic staining tissue around muscle bundles and hair follicles (see Figs. 24, 25, 28), sometimes with comparative or even complete absence of elastic tissue just beyond. There is obviously not the same continuity of structure as is present in the skin of younger cases, although the similarity can be seen in a general way, especially in Fig. 26. The relative thicknesses of the skin from the various parts are still the same, except that the skin from the abdomen in this case (Fig. 28) is very much thinner than in the other adult age groups: the elastic fibres are not arranged in planes of varying amounts, and, because they are so greatly broken up they do not appear at first glance to be running mainly parallel to the surface. In the chest (Fig. 29) there is only slight superficial condensation of the fibres: in the deeper layers there is a large number of large irregular ones present.

Exposure to the weather intensifies the degenerative changes in the elastic tissue, giving a yellowish colour and wrinkled appearance to the skin. Fig. 30 shows a section from skin from the lateral aspect of the forearm in this condition: the elastic tissue is greatly increased in amount and irregularly distributed, being condensed into amorphous masses superficially, but the fibres remaining separate in the deeper parts.

6. Special Areas.

The number, size, and arrangement of the elastic fibres in certain regions of the body call for individual consideration of these regions as there is a constant and definite alteration in the constitution of their elastic tissue as compared with that found in most areas of the body.

In the sole of the foot and palm of the hand there is almost complete absence of the main fibres (Fig. 31): there are very few running parallel to the surface between the bundles of white fibres: usually the fibres are seen to be running alongside blood-vessels and sweat ducts, and accordingly they run obliquely or perpendicular to the surface. There are large collections of elastic fibres, however, in bands immediately under the skin alongside the larger blood-vessels.

The skin of the plantar aspect of the toes is similar to that of the sole of the foot, in that there are few large elastic fibres in it: there is a considerable increase in the amount of the fine elastic fibrils immediately below the epithelium, forming in this situation, as already mentioned (p. 12), a fine plexus (Fig. 32).

In the groin (Figs. 33 and 34) the majority of the elastic fibres run obliquely, as the full length does not appear in transverse or longitudinal sections.

The largest number of large elastic fibres is found in the perineum (Figs. 36 and 37), being particularly abundant in the young child (Fig. 35), and around the anus. Most of the fibres in this region radiate from the anus. This is probably a mechanism to prevent over-distension of the parts during defaecation, etc..

The scrotum possesses practically no elastic tissue - even the fine sub-epithelial plexus is very scarce here (Fig. 38). Numerous rather short fibres are present in the skin of the penis and they are seen to run chiefly transversely (Figs. 39, 40).

The skin of the back is very thick and contains a large number of elastic fibres (Fig. 41). There are numerous long prolongations into the subcutaneous tissue, but these do not contain so much elastic tissue as the superficial parts of the skin. The elastic fibres are seen to stop short of the hair follicles and sebaceous glands, leaving a small clear area around each.

On the posterior surface of the elbow there are numerous large elastic fibres in the cutis vera (Fig. 42). Here there is a great increase in number of the folds of the skin, with numerous groups of large papillae and there is little development of the finer fibres in these papillae.

Although there is a great increase in number of the hair follicles in the scalp, consequently breaking up the continuity of the bands of elastic tissue, yet the latter is present in considerable quantity, especially in the more superficial part of the dermis.

The eyelids and eyebrows provide a curious contrast in their elastic tissue content. The eyebrows (Fig. 43) are similar to other parts of the face, as described by Ohno (1925) in that there is a large amount of the elastic tissue and it is subject to the excessive degenerative changes occurring with advancing age and exposure to the weather: the tissue becomes condensed into masses, staining densely with Weigert's stain, and situated immediately below the epidermis. Whereas in the eyelids (Figs. 44 and 45) there is only a trace of elastic tissue in relation to hair follicles and blood vessels. The sharp boundary zone between these parts is shown in Fig. 46.

D. SUB-EPIDERMAL PLEXUS OF FINE ELASTIC FIBRES.

1. Different Sites.

The characteristic appearance of the fine elastic plexus in the skin on different parts of the body will be described with illustrations as far as possible from one case, with examples from others for a fuller comparison. The plexus varies considerably, even in one section, especially in relation to the dermal papillae: thus, between the papillae the plexus is often of nondescript structure, consisting of only a narrow line of small fibres running parallel to, and a little deeper than the bases of the epithelial cells with a few fine fibrils at right angles, traversing part of the space towards the epithelial cells. In the papillae, on the other hand, the plexus opens out and it is in these parts that forms more or less characteristic for the different parts of the body can be determined.

The plexus in the skin of the toes is very plentiful and dense: in the plantar aspect (Fig. 51) it is like that of the dense parts of the sole of the foot. Similarly the dorsal aspect gives a structure very like that of the dorsum of the foot. The only difference is that both fine plexus and main fibres are increased in amount in connection with the folds of skin over the joints of the toes.

The skin of the sole of the foot presents a varying structure depending on the part of the foot examined. On the arch of the sole there is practically no fine elastic plexus, whereas on the ball and heel the plexus is very well developed. Even on the latter parts, however, it is not continuous: it is dense, consisting of closely-packed fibres and fibrils in the papillae and especially towards their bases as shown in Figs. 52 and 53, for several adjacent papillae, and then is loose and slight in amount in the next few papillae. It seems probable that this irregular development and distribution of the plexus in these areas is connected with the stress put on the parts in walking. On the dorsum of the foot, the papillae occur in groups of 2 or 3 separated by stretches of level epithelium. In the level stretches the fine plexus is slight in amount, and irregular in form. In the papillae a beautiful digitate appearance is presented, with a line of small fibres forming a fairly regular arc of a circle, parallel to the epidermis, and from this a small number of single, long, thin fibrils run out towards the epidermis (Fig. 54). In Fig. 55 this arrangement is shown again, but is slightly obscured by the thickening of fibres and clumping and thickening of fibrils found in old age.

Figs. 56 and 57 show the plexus on the medial side of the leg: it varies in the calibre of the fibres in different sections of the same subject, and there is nothing very striking about its shape. The fibrils are fairly short, and not numerous. In comparison with that on the medial side, the skin on the lateral side (Fig. 58) presents a thicker set of fibres which is much closer to the epidermis: the fibrils are short and indistinct. In these areas the skin papillae are very small and few in number.

On the medial side of the thigh (Fig. 59) the papillae are large, fairly numerous, and rectangular. The plexus assumes a distinctive form in them. The small fibres are grouped at the base of the papillae and the fine fibrils run out in long wavy bundles towards the upper corners and apex. Between the papillae, the structure is seen in Fig. 60. Again, turning to the lateral side of the thigh (Fig. 61) the fibres are thicker and form a basal layer some distance from the epidermis with loops of varying length up to the small squat papillae, and from these loops a few long thin fibrils run towards the epidermis.

Figs. 62 and 63 show the spidery-like appearance found on the abdomen. The chest also has a spidery-like structure which is quite often interrupted (Fig. 64). The skin on the back has a peculiar appearance in parts - it seems to be drawn into a large number of small folds with crushing together of the papillae and epidermal cells. In these papillae, there is a large amount of fine plexus in which small fibres run into the papillae and seem to end by branching into several long thin fibrils running up towards the epidermal cells (Fig. 65). In other parts of the back the skin appears more like the skin of other regions, and the fine plexus has the structure shown in Fig. 66.

The palm and dorsum of the hand correspond to the sole and dorsum of the foot, except that there is not so much elastic plexus in the palm as in the dense parts of the sole.

The skin of the forearm is like that of the leg, as far as the fine elastic plexus is concerned. Figs. 67 and 68 show very characteristic parts, and Fig. 69 shows very pronounced degenerative change: in the latter connection, it should be remembered that this part of the body is often exposed to the weather, and changes in the main fibres are also pronounced in this region (see Fig. 30). Only a few separate fibrils are present in the skin behind the elbow (Fig. 70) although, as will be shown later, this part possesses a very copious layer of reticular fibres.

In the arm the skin is not nearly so thick as in the thigh, but the structure of the fine plexus is like that in the thigh on a smaller scale - groups of fibrils running out from small fibres which in the case of the arm are found more than half way up the papillae (Fig. 71). Fig. 72 shows an irregular, poorly developed plexus on the lateral side.

The fine elastic plexus becomes greatly enlarged and the fibres more numerous in connection with the origin of pilatory muscles. This is shown in Figs. 73 and 74. The fibrils extend up close to the epidermal cells and are spread out over a considerable area in relation to each hair muscle.

Thus, when the muscle contracts to erect the hair, it will also cause dimpling of the skin, as occurs to a marked degree on exposure to cold, presenting the well-known "goose-flesh" appearance.

2. Age Changes.

(a) 0-5 years. In striking contrast to the main elastic fibres which are present in large numbers in the infant's skin, there is almost complete absence of any fine fibrils immediately under the epidermis. This is very clearly seen in Figs. 75 and 76 illustrating parts of skin which in adults possess a very well-developed plexus of these fibrils. In Fig. 77 there are a few fine fibrils - as if they are beginning to appear about this age: again for this site, the number is far below what is found in the adult. The same condition is seen in other parts of the body in infants of about 1 year, i.e. the plexus of fine elastic fibrils under the epidermis is absent, or only commencing to appear.

(b) 15-23 years. In the skin of cases about 20 years of age a big change is found. There is now a fairly well-developed plexus, as seen in Figs. 78-80. This plexus consists of a few small fibres running horizontally, obliquely, and sometimes vertically a short distance below the epidermis, and from them a number of much finer fibrils spread out towards the epidermis - their number and arrangement varying from place to place on the body, and having more or less the same character for the same site on different bodies. The fine plexus can be greatly increased for special functions as has been shown above (p. 26) in dealing with pilatory muscles.

(c) 30-40 years. In this age group, the plexus is again seen to be well developed in Figs. 60, 62, 68 and 81. These four pictures show several of the many different forms it takes in normal conditions.

(d) Over 65 years. For the oldest age group, Figs. 82, 83, 61 and 63 show typical examples of the fine plexus. It can be seen that the small fibres are definitely thicker than those in younger subjects, and the fine fibrils are sometimes thicker, sometimes the same as in the other cases, but are sometimes completely absent.

The degenerative changes seen in old age can best be shown by comparison with what appears to be normal. Fig. 53 shows the normal appearances for the fine plexus in the sole of the foot in old age. The small fibres are only slightly thickened although there is slight irregularity at one side of the illustration. The fine fibrils are clear and well-formed, long and thin, reaching up close to the bases of the epidermal cells: there is also slight fragmentation of these fibrils at the right side of the section. In Fig. 84 the plexus again is normal for the age (35 years) and is a form commonly seen: there is an indefinite plexus with fine fibrils running close to the indented or digitate bases of the epidermal cells. In Figs. 52 and 86 it shows a slight degree of degenerative change. In Fig. 52 the fine plexus is seen to be concentrated in parts and forms rather irregular masses: and in Fig. 85 there is loss of fibrillar structure, and the small fibres have lost their individuality and form a broken-up, irregular mass filling a large part of the papillae. Premature degenerative changes are shown to an advanced degree in Figs. 86-90: the fine elastic tissue is completely absent in places and concentrated into dense masses in others, just under the epidermis: the fibrillar structure is seen to be lost, and the elastic tissue consists of irregular masses of tissue staining black with Weigert's stain.

Another kind of change is seen in Figs. 61 and 92. In Fig. 61 the small fibres which form the sub-epidermal plexus show slight thickening as is usual in an old subject's skin: the fibrils running from the plexus towards the epithelium are also thickened. In Fig. 91 the corresponding small fibres and fibrils are not thickened to any marked degree: but there are rounded, oval, or irregularly shaped balls with smooth edges, occurring separately at various intervals along the plexus, sometimes apparently attached to the other elements of the plexus, sometimes distinct from them. These masses stain dense black with Weigert's stain. This change is also seen in Fig.69. A peculiar feature about them is that while they occur in large numbers in the skin of old subjects, a few are sometimes found in young subjects (Fig. 92). Their significance is not understood.

Around the hair follicles, in their course through the dermis, the fine elastic plexus is found to follow the indentations of the epidermis which surround the sheath of the hair. This part of the plexus shows the same changes for the different ages as the part under the rest of the epidermis. It is not developed in infants (Figs. 6, 11 and 76): is best seen in youths and adults (Figs. 18, 19 and 37), and shows condensation and thickening in old subjects (Figs. 28 and 30).

It is interesting to speculate on the function of this fine plexus. Obviously its function or functions must differ from those of the main fibres since the distribution and age changes present such variations as have been illustrated. Its position so close under the epidermis and the presence of the fine fibrils stretching out towards the epidermis suggest that it plays a large part in binding the epidermis to the dermis. The connection between epidermis and dermis is very firm: if an attempt is made to separate them, the usual result is that the epidermis comes away along with the superficial layer of the dermis - the part containing the fine plexus. However, there must still be some tissue or substance between the bases of the epidermal cells and the fine fibrils of the elastic plexus, as, with Weigert's stain and sections cut thinly, there is always a distinct space between them. In a careful study of over 1,000 sections taken from different parts of the skins of normal subjects I have not been convinced that I have ever found these fine elastic fibrils actually entering the epidermis. In some parts of the body, especially the sole of the foot, and in rather thick sections, it sometimes appears to enter the epidermis, but this appearance can be explained by the section showing the edge of a papilla along with the bases of the epidermal cells:-

The existence of some tissue between the elastic plexus and the epidermal cells can be shown by Bielchowsky's silver impregnation method of staining for reticulum, and an appendix on the results obtained by this method is given below (p. 32).

Another possible function of this fine plexus may be suggested, although it is not proposed to offer any proof of it. The infant's skin has not the same power of regulating the temperature of the body as that of the adult. It may be that the fine plexus assists the retraction after dilatation of the capillaries in the papillae, and, in the superficial part of the dermis, the movement of hairs used in carrying out this function: the absence of the plexus in infants is a reason for the failure of the function: adaptation may come only with the development of the plexus.

E. RETICULUM: Junction between Dermis and Epidermis.

Opinion has changed in recent years as to the structure of the junction between the dermis and the epidermis. It used to be thought that there was a definite continuous eosinophil basement membrane on which the epidermis was placed, and that this membrane separated it completely from the dermis below. With the introduction of the silver impregnation methods for staining reticulum, however, numerous workers have shown that the basement membrane does not exist, that there is a close connection between the basal cells of the epidermis and the superficial part of the dermis, and that there is a network of reticular fibres between the two layers. A review of the literature on this subject is given by Manganotti (1930), and from his own work he concludes that "the layer of reticular connective tissue, the outermost part of the dermic mesenchyme, does not constitute a membrane in the sense of a rigid and clear formation apart from the two tissues (i.e. epidermis and dermis), but is probably merely a morphological appearance which the intercellular colloids assume in relation to the epidermal cells." Szodoray (1931) has described this reticular network in different parts of the skin and shown how the "lattice fibrils" interweave with the flabelliform processes at the bases of the epithelial cells.

In this work, I have already shown how the fine elastic fibres form a network in the papillary layer of the dermis, and yet never come into actual contact with the epidermal cells: there is always a distinct space separating them. Somewhere in this space is this layer of reticular fibres. Accordingly, the silver impregnation method of staining was used on sections from many of the blocks from which sections had already been stained by Weigert's method. One fairly simple method of staining (Foot, 1929) was employed throughout, to get uniform results. It was found that to get reasonable impregnation of the sub-epithelial fibres it was necessary to leave the sections rather longer in the silver bath than was necessary to show the reticulum in sections of other tissues, e.g. kidney, aorta, glands, etc., with the result that there is slight over-impregnation, staining brown or black the connective tissue fibres in the rest of the dermis. Various counterstains were used - acid fuchsin and phospho-molybdic acid (after Szodoray), or simply carmalum or saffranin.

In the sole of the foot, between the papillae, the reticular layer is shown typically in Fig. 93: it consists of numerous very small fibrils, varying in shape and size, set close up to the bases of the epithelial cells - apparently merely "filling up spaces" between the downward processes of these cells. But up in the papillae, the reticular fibres are much more distinctive. They are often seen very clearly in oblique sections of the tips of the papillae - see Figs. 94 and 95. Here there is a development of long wavy fibrils just below the epidermis, with short blunt ends reaching towards the basal cells, the so-called "Homma's bodies": it is very difficult to determine whether these structures enter the epidermal cells or not. Several of the larger ones appear to be artefacts formed in fixation, cutting and staining (Fig. 96), but the regular arrangement of the fibrils in the two previous illustrations points to there being some definite network. Whether it is an open meshwork spread round the tips of the papillae into the spaces of which the bases of the epithelial cells are fitted, or whether it is a series of fibrils running up to the cells and fixing them either by entering them or filling the spaces between their basal processes is difficult to determine. Fig. 97 shows a low power view of several of these papillae with the fibrils distinct at the tips. Fig. 98 shows these tips - the appearance here is of bundles of fibrils opening out slightly at the tips (apparently not merely filling spaces between processes) - a formation of definite fibrils. In all the above illustrations, there are a few larger reticular fibres towards the centre of the papillae connected to the fibrils at the edge, and sometimes connected with the reticular network round the papillary capillaries. In Figs. 99 and 100 the silver-stained tissue is condensed and consolidated into masses separated slightly from the bases of the epithelial cells - representing a quasi-hyaline degeneration, possibly due to old age.

While in this work the most distinctive appearances of this reticular layer have been found in the sole of the foot (as shown in the illustrations above), the study of other areas is also of considerable interest.

On the dorsum of the foot (Fig. 101) a few reticular fibres are seen, but they are not connected to the deeper structures, and the significance of these separated fibrils at right angles to the junction between dermis and epidermis is not easily understood. In Figs. 102 and 103 (both very densely impregnated), there is more of the appearance of the reticular fibres being interpolated between the bases of the epithelial cells than in other sections: here, the connective tissue fibres are also stained black and so deep connections are obscured. Fig. 104 shows a very characteristic hedgehog appearance: this section is cut parallel to the surface of the skin and so the hair follicles are cut transversely. Here, the reticulum is apparently arranged round the hair follicles in a radiate fashion, holding it in place, as it were. From the high power view (Fig. 105) the reticulum is condensed at the bases of the epithelial cells, and appears to be cementing their bases to the dermis.

Figs. 106-110 are a series of photographs from one section impregnated lightly to show how uniformly the reticulum is arranged, and how light staining picks up first the tips of the reticular fibres - the parts nearest the epidermis.

The skin of the posterior surface of the elbow was shown to have very little fine elastic plexus. With reticulum staining a very striking result was obtained (Figs. 111 and

112). The argyrophil tissue consists of a series of tall cylindrical rods arranged in pairs or small clumps, and fitting closely into the spaces between the epithelial cells at the tips of the papillae, with a thinner fibrillar layer between the papillae.

In the eyebrow (Fig. 113), there is seen to be a scattered light reticulum throughout the area which stains so densely black with Weigert's stain (Fig. 43), showing that the elastic tissue possesses a certain amount of reticulum.

A comparison of these photographs of skin stained for reticulum with those stained for elastic tissue given earlier will at once show that these two kinds of tissue have very different arrangements and distribution, and are quite distinct from each other. There is, as far as these methods of staining show, no continuation of the fine elastic fibrils as reticular fibrils up to the bases of the epithelial cells. Although the fine elastic tissue develops such characteristic forms as have been shown, close under the epidermis, it does not take part in the ultimate junction between the dermis and epidermis: the elastic tissue can play the part only of a reserve force in preventing separation. The elements concerned in the actual binding together of dermis and epidermis seem to be the reticular fibres with their striking arrangement and the bases of the epithelial cells. I agree with Manganotti that the reticular layer is probably a disposition of the intercellular colloids, with the additional observation that there is possibly some more definite formation in the parts where the fibrillar network is so well developed as in the tips of the papillae on the sole of the foot.

F. OEDEMA.

The histological changes in the skin were studied in 5 cases with oedema, including both recent and long-standing types. Even though there is a considerable amount of oedematous change throughout the cutis vera in sections of these subjects stained by haemalum and eosin, there is not very much difference in the amount and characteristics of the elastic tissue as shown by Weigert's stain. In cases with recent oedema the main fibres (Fig. 114) conform to the general appearance for a normal subject of corresponding age, though there is slight separation of the fibres. In long-standing oedema, the fibres are short and broken up, often to a marked degree. The fine plexus too is usually little altered in oedematous subjects. There is, however, one marked difference in it as compared with a normal case, viz. it lies deeper to the epithelium (Fig. 115). This finding is constant for all areas of the body, and shows that the loose areolar tissue immediately below the epidermis collects more fluid in oedema than the denser part with the main white and yellow fibres.

Silver impregnation in these cases also shows slight changes from the normal, as can be seen from Fig. 116 which is the same area of skin as that shown for elastic tissue in Fig. 114. The reticulum is seen to be still present at the junction of the dermis and epidermis - it is accordingly separated further from the fine elastic plexus than in normal cases. Also, the reticulum appears as arched structures surmounting oedematous areas in the dermis. With higher magnification (Fig. 117) there are fewer distinct fibrils than in normal cases, and their place is taken by loose strands and irregular masses surrounding oedematous blebs. This appearance gives striking confirmation to the view that the reticulum stained in this way is a physico-chemical condition of the intercellular colloids.

G. MYXOEDEMA.

Skin from a case of myxoedema was examined for its elastic and reticular tissue content. The block is believed to have been taken from the thigh. The structure varies considerably from the normal appearance (Figs. 118 and 119): the deep layers of the epidermis are very thin, whereas the stratum corneum is greatly increased in thickness, although very loose in structure. The dermal papillae cause sharp undulations in the whole thickness of the epidermis. Below the epidermis, there is a broad zone with few cells, and consisting of a pale-staining tissue. The fine elastic plexus lies below this and is well developed, with the fibres closely connected to each other: from it, long very delicate fibrils traverse the structureless area towards the epidermis. Deep to the fine plexus the main fibres show a normal arrangement.

With silver staining (Figs. 120, 121 and 122) the reticulum is confined to a narrow area immediately beneath the epidermis: in places definite rod-shaped fibrils are present, but elsewhere there is merely the appearance of argyrophil material fitting into the bases of the epithelial cells.

H. RÉSUMÉ OF HISTOLOGY.

The distribution of yellow elastic tissue in the skin is described and illustrated as a result of an investigation of 32 normal subjects, with additional observations from other subjects.

The elastic tissue is described in two parts:- first, large fibres in the deeper part of the dermis: secondly, a fine network of small fibres lying close under the epidermis.

Variations in the quantities and characteristics of these two parts are described and illustrated for

(1) skin from different situations of the body:
(2) skin from subjects of different ages.

The reticular fibres of the skin have been shown to be distinct from the elastic tissue.

A brief description is given of the changes in the elastic tissue and in the reticular fibres in subjects with oedema, and in one with myxoedema.

SECTION III: EXPERIMENTAL:

Experiments on Living Subjects.

Experiments on the Cadaver.

Interpretation of Results.

Results.

SECTION III: EXPERIMENTAL.

A. EXPERIMENTS ON LIVING SUBJECTS ON AMOUNT OF EXPANSION OF LIMB WITH EXERCISE.

When the limbs become swollen with exercise, the increase of fluid is partly in the muscles, partly in the vascular system, and partly in the connective, e.g. subcutaneous, tissues. The extent to which the limb swells varies considerably in different subjects and for different forms of exercise. The following graphs illustrate the latter point.

In Graph 1, the subject was at complete rest for one hour before the experiment; the exercise consisted of five-minute periods of running up and down stairs, with periods of rest in between. The blood pressure was noted before and after each period of exercise: the circumference of the thigh was measured at two levels, 10 cm. apart, at the same times, and from these measurements the area of the sector of the skin between was calculated: similarly, the area of a sector, 15 cm. in breadth, of the skin of the leg was found.

Area of surface of sector of cone = $\frac{h}{2}$ (C + c),

where h = length of sector,

C = circumference at one end of sector,

and c = circumference at other end of sector.

The graph shows that with the exercise the blood pressure rose considerably: the corresponding increase in the area of the skin, however, was very slight - in the thigh, there was only 1.75 per cent. difference, and in the leg only 2 per cent. difference between the highest and lowest readings. The significance of these small differences becomes evident only on consideration of other factors and will be discussed later.

In Graph 2, the measurements were taken during an evening while the subject was playing badminton, at the following sites:-

Circumference of forearms - 15 cm. above the ulnar styloid process.

Circumference of legs - 20 cm. above the medial malleolus.

Circumference of thighs - 20 cm. above the upper border of the patella.

The results as shown on the graph indicate considerable differences between the smallest and greatest readings for each part, from 5 per cent. in the right thigh to 17 per cent. in the right forearm. It is noteworthy that the swelling is most rapid in the right forearm and thigh, the parts most energetically used, and that later on in the evening it became more evenly distributed through all the limbs.

These experiments show that the skin can be stretched through a considerable range, and suggests that even small increases may be important. But they give no direct indication of the amount of the increased pressure below the skin which causes the stretching. No direct method of measuring this pressure on the living subject was available, and so the much less satisfactory, but still useful, method of comparison with the stretching of skin from the cadaver was attempted.

B. EXPERIMENTS ON THE CADAVER.

1. Stretching Strips of Skin.

The object of these experiments was to investigate the stretching of the skin under purely physical conditions: by correlating its behaviour under such circumstances with what has been shown in Graphs 1 and 2 it was hoped to be able to assess the pressures in the subcutaneous tissues. The first procedure adopted to find the force required to stretch the skin for small distances was that of measuring the extension caused by hanging weights to strips of skin. Ink marks, 10 cm. apart, were made on the skin, while still on the body, before any incisions had been made: a strip 12 cm. in length and 1 cm. in breadth was removed, extending for 1 cm. on each side of the 10 cm. marks: the strip was removed with as little subcutaneous tissue as possible, yet subjecting it to no stretching. It was suspended alongside a metre stick and the distance between the marks was noted: usually the strip had contracted, so that the marks were only about 9.5 cm. apart. A light cardboard pan was attached, and again the distance between the marks noted: weights were then placed on the pan and readings of the length of the strip taken. In this way were obtained the readings shown in Graph 3. The pan and threads used for holding the weights weighed only 10.8 gm., but this alone caused a considerable extension of the skin. Actually, the extensions of the skin measured in these experiments were found to be beyond the limits to which the skin would be stretched during life, and a finer method of measuring the skin expansion was seen to be required. Three points of value, however, were found from this procedure. First, while a strip marked 10 cm. on the body contracted to 9.5 cm. when removed from the body, if it were now cut into ten pieces, each 1 cm. in length as marked on the body, the parts laid together now measured only 8.3 cm. This points to the conclusion that each unit of the skin is continuously under some degree of tension, and this tension is released at any point by cutting the skin there. This is well seen in the retraction of the edges when an incision is made into the skin, e.g. at operation. Secondly, several attempts were made to stretch the strips as far as possible with the hands. In no case could it be stretched to more than 12 cm., and to less in older people, and in cases with oedema. The last point in this connection is that after stretching with considerable force (500 gm. weight), the skin did not return to its original length of 9.5 cm., but measured about 10 cm. It had lost some of its elasticity.

1. Stretching Circles of Skin.

(a) Method. It was then apparent that some instrument to measure very slight degrees of stretching of the skin was required, and further to show what magnitudes of change of pressure actually caused this stretching. The instrument described below was made to Professor J. Shaw Dunn's design by the Master of Works of Glasgow University, to both of whom I express my great indebtedness for supplying it to me. By means of it I have been enabled to test with a great degree of delicacy, the amount by which the skin stretched when exposed to small increases of pressure. The skin is here considered purely as a physical membrane: the whole thickness is taken but no deeper tissues, and so although the thickness varies considerably for different areas, it can be considered as a physiological unit being tested as to one of its physical properties, viz. its elasticity, or resistance.

The main part consists of a hollow brass cylinder or drum, into which there is one inlet opening (Figs. 125 and 126). Six screw bolts are fitted around the rim: fitting into the rim inside the bolts is a brass ring with seven sharp steel points projecting downwards to enter seven corresponding holes on the rim of the drum: over this ring another broader ring is placed with holes for the bolts. This latter can be clamped down firmly by nuts screwed down on the bolts, thus holding the smaller ring in position. The inner diameter of the first ring and that of the rim of the drum is 5 cm. On the second ring a lever is placed: this lever has two limbs, the shorter of which is angled and lies over the centre of the drum, and the longer has a pointer on it, giving readings on a curved scale on an upright stand. The longer limb is nine times the length of the shorter, and so an upward excursion of the short limb is magnified nine times, and can be measured on the scale as a downward excursion of the pointer. The inlet tube of the drum is connected to a water manometer and a movable reservoir of water.

The ring with the sharp points is laid on the area of skin to be tested, while still on the body: the sharp points are pressed into the skin. The ring is removed and the holes in the skin made by the points are all touched with Indian ink so that they can readily be found later. This area of skin with a small margin around is removed from the body, taking care that it is not stretched in the process and that no subcutaneous tissue is taken along with it: a very sharp scalpel or blunt-pointed scissors are useful for this procedure. The membrane of skin so obtained is then replaced on the ring, each sharp point being pushed through the mark it made on the skin while still on the body: the margin is cut to the outer edge of the ring. In this way the skin is replaced to exactly the same area, and presumably to the same tension as it has been at on the body. The drum is then filled to the rim with water and the level noted on the manometer, this being taken as zero. The ring with skin attached is placed on the drum in such a way that no air is imprisoned between the skin and the surface of the water: the second ring is put on and screwed tightly in position. The lever is placed in its stand with the short limb resting on the centre of the circle of skin. The water level in the manometer is readjusted to the zero if it has been altered in the latter manipulations, and the position of the pointer on the long limb noted on the scale as its zero.

The pressure of the water within the drum is increased by raising the reservoir, until half a centimetre rise is indicated by the manometer: after a few seconds (noting carefully that the half centimetre rise in pressure is maintained), the pointer became stationary and its level read. The pressure is raised by further half-centimetre increments, noting the level of the pointer after it has become stationary for each increase, up to a total increase of 5 cm. water pressure. Then increases of 1 cm. water pressure are noted up to a total increase of 10 cm. water pressure, and after that increases of 5 cm. up to a total of 35 cm. water pressure: at this last part the pressure is kept constant for 3 minutes before the level of the pointer is read, as it is found that the expansion of the skin is rather slow for such an increase of pressure to have immediate effects. The result of such an experiment is best shown as a graph, where the excursion of the pointer is plotted against the water pressure (e.g. Graph 4).

As a general rule the skin expands evenly, and its surface can be reckoned as a part of a sphere. But sometimes with high pressures the expansion is uneven - bulges form between tighter bands: this does not often occur, and never with pressures below 15 cm. water, and so in the subsequent calculations the surface of the skin is considered to be even and to form part of a sphere.

(b) Material Examined. The material examined by the above method consists chiefly of skin from cases upon which autopsies were performed in the Glasgow Royal Infirmary. The cases were chosen for suitability of age, and for condition of skin.

(i) Age periods were taken as follows:-

(1) About 15 years.
(2) About 25-30 years.
(3) About 45-50 years.
(4) About 65 years and over.

In children it was impossible to obtain areas of skin large enough for use with the instrument from narrowly-defined areas such as the medial side of the thigh, or leg, and difficulty was experienced in this way even for the period about 15 years.

(ii) Condition of skin. A representative number of cases in each group was obtained in which the skin was, as far as could be determined, 'normal.' Several of these cases died as the result of accidents, and in the others, death occurred after a relatively short illness - usually some form of acute sepsis.

Another series was taken in which there was oedema of varying degree in the lower limbs, sometimes also in the abdomen. These cases are relatively common in the older groups, but few young ones could be obtained. The youngest died from kidney disease, the older ones from heart conditions. Table II gives the numbers in each group.

Table II.

Age.	NORMALS			OEDEMA		
	Male	Female	Total	Male	Female	Total
15 years.	-	3	3	1	1	2
25-30 years.	5	-	5	-	1	1
45-50 years.	3	3	6	3	4	7
65 years and over.	2	1	3	3	-	3
Totals:	10	7	17	7	6	13

The numbers in the group of oldest cases could have been greatly increased from the material available, but as the results from all those examined were very similar, it was unnecessary for more examinations.

The areas of skin chiefly examined in these cases were the epigastrium, the medial and lateral sides of the thigh, and the medial and lateral sides of the leg. (In one case the medial and lateral sides of the arm were examined). They were not all investigated in every case, but sufficient were studied for each area in each group to show what can be taken as characteristic curves, and those given below in the results are all typical examples for the age and the area.

In a few cases, other membranes from the body were examined, viz. the fascia lata (in 7 cases), and the dura mater (2 cases). The fascia lata was exposed and all fat removed from the superficial surface: then the ring with the points was pushed in and held in position while the fascia was cut round it and ring and fascia removed together. The dura mater, however, was laid flat on a wooden bench and then the points of the ring pushed in.

On two occasions pieces of rubber from the back of thin rubber gloves were tested, and two graphs were made of the results of testing pieces of a sheet of pure rubber, obtained from the Natural Philosophy Department of the University. Difficulty was experienced in these cases in getting a true zero for the pointer, as the rubber became twisted and the surface uneven when the second ring was screwed into position. But the graphs given in the results are, as far as could be obtained, satisfactory representations of the stretching of the rubber.

An attempt was made to get some other 'elastic' tissue from the body - but unfortunately the human aorta is not large enough, at least in normal cases, to fit the ring of the instrument. A bullock's aorta was obtained and two areas of the arch, and two of the descending aorta were examined. In connection with these graphs, however, there is an experimental error to be noted. The aorta had very considerable thickness, whereas all the calculations are based on the assumption that the membrane has little or no thickness. This thickness will upset the results chiefly for small increases of pressure - and for this reason the smallest values are all liable to slight suspicion, chiefly in the skin of the epigastrium and lateral side of the thigh, which are always considerably thicker than the other areas tested. Also, in dealing with the aorta as compared with the skin, it should be remembered that the aorta does not usually function at such low pressures as are used here, whereas the skin functions normally at only the low pressures used, and on only rare occasions at 15 cm. water pressure and over.

C. INTERPRETATION OF RESULTS AND DEDUCTIONS DERIVED THEREFROM.

1. Graphs of Excursion of Pointer (Graph 4).

The first result to be noted from graphs obtained in this way is the rate and extent of the excursion of the pointer, as the pressure is increased. But the area of the skin for any given excursion of the pointer can be calculated from the formula:-

$$A = \frac{\pi}{4}\,(4x^2 + 25) \quad \text{(Taylor Jones)},$$

where A = area of expanded skin

and x = rise in level of the centre of the skin,

i.e. $\frac{1}{9}$ of the excursion of pointer.

The original area of the circle of skin is $\frac{\pi \times 25}{4}$

and so the change in area $= \pi x^2$

and the percentage change in area $= \dfrac{\pi x^2}{\frac{\pi \times 25}{4}} \times 100$

$= 16x^2$.

Using this formula and the readings of the excursion of the pointer as shown in Graph 4, the percentage increase in area can be plotted against the increase in pressure (Graph 5). It is more convenient, however, to retain the original graph of the pointer excursion and, when the increase in area is required, its approximate value can be found by consulting Table III, where the percentage changes in area are given for several readings of the pointer.

Table III.

Change in Area (per cent.)	Excursion of Pointer (cm.)
0.2	1.0
0.5	1.6
0.75	2.0
1.0	2.3
2.0	3.2
2.5	3.5
3.0	3.9
4.0	4.5
5.0	5.0
10.0	7.1
20.0	10.1

Thus, from Graph 4, a 5 per cent. increase in area will correspond to an excursion of 5.0 cm. of the pointer, and is obtained by increase of pressure of 2.75 cm. water. This means that if the skin is considered as a purely physical elastic membrane, an increase of 5 per cent. in the area of the skin of the medial side of the thigh would indicate that the pressure below that skin, i.e. in the subcutaneous tissues, had increased by 2.75 cm. water. Graphs of this character of skin from various parts of the body and from bodies of various ages are given, and the meaning of the differences discussed below.

2. Modulus Graphs.

Various physiological systems have been investigated as to their functional elasticity (J. H. Clark, 1932), and it seems reasonable to consider the elasticity of the skin from this point of view. The modulus, E, of elasticity may be expressed as $\frac{\text{change of pressure}}{\text{change of area}}$ and this was calculated for all specimens examined. It was assumed that the original pressure was zero as, probably being fairly small, it could not be accurately ascertained. As the results are to be interpreted only comparatively for the different sites and ages, and not absolutely, the assumption is justifiable as the inaccuracy applies in all instances. The values so obtained for E varied for the different pressures, but the form of the graphs obtained by plotting these values against the pressures is so consistently similar for all areas of skin examined, that some further consideration will be given to it, referring particularly to Graph 6.

For very small increase of pressure, the modulus is high but thereafter diminishes fairly rapidly. This rules out the suggestion that the skin is loose at the beginning and the large excursions of the pointer for the first few small increases of water pressure are merely 'taking up the loose.' In other words, the skin as removed from the body by the method described above is under a certain amount of tension.

After this descent, and between about 5 and 10 cm. water pressure, the modulus is independent of the pressure. This horizontal part of the curve indicates the range of 'perfect elasticity' of the skin. Professor Taylor Jones defines perfect elasticity as follows:-

> "A perfectly elastic substance is one which changes its size or shape under the influence of forces, and in which the change of size or form is proportional to the force, and in which the deformation disappears entirely when the force is removed."

Above 10 cm. water pressure, the modulus increases linearly with the pressure. This means that there is less increase of area for a corresponding increase of pressure, i.e. there is increasing resistance to stretching. It is a striking feature that for all the experiments performed on skin with this instrument, this part of the modulus curve always turned out to be a straight line. It seems that there must be some further significance in this point which is not at present appreciated.

This modulus curve can also be read as a measure of the 'resistance' of the membrane used. The lower the value obtained for E for a given pressure, the greater must have been the change of area for that pressure - i.e. the less resistant was the skin. This is seen especially where different areas of skin from one body were tested - certain areas were always less resistant than others (to be discussed below).

3. Tension Curves.

Another aspect of this problem arises on consideration of the tension in the skin for the various pressures to which it was subjected. The tension, T, is obtained from the formula.

$$T = \frac{\text{Pressure Area}}{4\pi x} \quad \text{(Taylor Jones)},$$

$$\text{where} \quad x = \text{rise in level of centre of skin},$$

$$\text{i.e.} \quad = \frac{1}{9} \text{ of the excursion of pointer}.$$

The graph obtained by plotting the values so obtained for T against the corresponding pressures, as seen in Graph 7, is typical of all the graphs of T. It shows that the tension increases in direct proportion to the increase of pressure - to an almost perfect degree (all the graphs are not quite so uniformly straight, but suggest that that is the normal result).

Certain very striking points are raised by this graph. In the first place it suggests that where the line would cut the Y axis - i.e. when the pressure is that at which it was on the body - there is present a tension of

5×10^3 dynes/cm. So far the tension of the skin on the living body has not been measured. Can the values thus obtained on the dead body be assumed to approximate to those of the living? And again, if this graph is produced backwards, it will cut the X axis at minus 4.0 cm. water pressure. The consistency of the curves for all the results calculated out makes it seem justifiable to assume that the information so obtained could be applied thus:- If the pressure is zero when the tension is zero, then the pressure present under the skin when it was removed from the body was 4 cm. water.

(This immediately raises possibilities in connection with the problem of tissue tension, and I will endeavour to show that the conclusions drawn from these results corroborate the results obtained in a very different way - viz. by workers with plethysmographs).

4. Work Done.

The amount of work done in stretching the skin for small increases of pressure was calculated from the formula:-

$$W = \frac{1}{6} k \pi^2 r^2 x^3 + \frac{1\ k}{10} \pi^2 x^5 \qquad \text{(Taylor Jones),}$$

where $k = \dfrac{pr.}{\text{increase of area}}$ and is constant (taken to be so for small values - where the modulus curve is horizontal).

r = radius of drum,

and x = elevation at centre ($\frac{1}{9}$ of the excursion of pointer).

The graph obtained for pressure values up to 6 cm. water is shown for the subject 15836 (Graph 8). To appreciate the full significance of the amount of work done against the resistance of skin and so reversely by the skin, it would be necessary to measure changes of area of the skin over a whole limb, or even the whole body, for a given time.

D. RESULTS.

1. Normal Subjects.

The graphs of four of the subjects mentioned in Table II are shown in detail: each of these cases is typical of its age group and the others of the group confirm all the points brought out in these graphs. A few details of these four subjects are given:-

16081 was a girl of 14 years, who died from meningitis secondary to otitis media. The otitis media had been present for some months, but the symptoms of meningitis had been present for only 10 days before her death. It was noted at the time of autopsy that her skin was normal.

15836 was a young man, 25 years of age: he died from appendicitis and peritonitis and was slightly dehydrated at death: his skin was very tough.

16089 was a foundry worker, of 47 years, who died of meningitis following otitis media. The skin of the abdomen was of very good texture: that of the thighs was slightly dry, and that of the legs dry and scaly.

16023 was a man of 65 years, an engineer: the cause of his death was cerebral thrombosis with bronchopneumonia. His skin appeared to be normal.

The following "series graphs" show the results obtained in these subjects by stretching the skin from (1) the epigastrium, (2) the medial, and (3) lateral sides of the thighs, (4) the medial, and (5) the lateral sides of the legs.

(a) Consideration of the series of graphs of Excursion of Pointer against Pressure (Series Graph 9) shows two very striking features.

First, taking each case separately, the pointer is seen to expand more, for any given increase of pressure, for skin of the medial side of the thigh than for the lateral, and similarly for the medial more than for the lateral side of the leg. Also, there is more expansion in the thigh than in the leg, for any stated pressure. This order was strikingly constant in all cases examined. The skin of the epigastrium varied, but was always fairly loose, and from special examination of the female cases was found to have no relation to the occurrence of previous pregnancies.

Secondly, the older the skin the more quickly the expansion occurs in all areas. This is shown by the more rapid rise in the graph for small pressures in the skin of the oldest subject, and to a less extent in the middle-aged one than in the two younger subjects. Actually, the highest expansions shown on the graphs do not vary greatly for any one area, in the different ages, although the way in which the final expansion is reached varies greatly.

These features and their importance can well be shown by taking certain values from the graphs, as is done in the following tables, and considering them.

Table IV.

Pressures Required for 2 per cent. increase in area
(≡ 3.2 cm. excursion of pointer):

	Epigastrium	Thigh, Med.	Thigh, Lat.	Leg, Med.	Leg, Lat.
16081	> 1	1.5	< 3	2	2.5
15836	-	1.5	2.5	>2.5	3
16089	>1	< 1.5	> 1.5	1.5	2
16023	> 5	> 0.5	< 1	1	-
Pressures Required for 5 per cent. increase in area (≡ 5.0 cm. excursion of pointer):					
16081	2	>2.5	5	< 4	<4.5
15836	-	< 3	4.5	5	6.5
16089	2	2.5	3.5	3	3.5
16023	> 1	> 1	1.5	> 2	-
Pressures Required for 10 per cent. increase in area (≡ 7.1 cm. excursion of pointer):					
16081	3	< 4.5	9.5	7	9
15836	-	5	> 8	11	12.5
16089	3.5	< 4.5	> 6	6.5	9
16023	2.5	2	2.5	6	-

Pressures measured in cm. of water.

It will be seen that to produce a 2 per cent. increase in area in the skin of the thigh of an old subject, a pressure increase of less than 1 cm. H_2O would be sufficient - the skin, as is well known, in old subjects is remarkably lax. But for the same increase in area for a young person, double the pressure would be required. Similarly for the leg, where, for example, to produce a 5 per cent. increase in area more than twice the pressure would be required in the younger person than for an older person.

Table V.

	Epigastrium	Thigh, Med.	Thigh, Lat.	Leg, Med.	Leg, Lat.
Percentage Increase in Area resulting from 1 cm. increase pr.					
16081	2	>1	<0.5	>0.5	0.5
15836	-	1	<0.5	<0.5	0.3
16089	>1	1	0.75	1	0.75
16023	4	4	3	2	-
Percentage Increase in Area resulting from 3 cm. increase pr.					
16081	10	7	2.5	3.75	3
15836	-	5.25	3.25	2.5	2
16089	8	6.5	4.75	5	3.75
16023	10	13	10	6	-
Percentage Increase in Area resulting from 5 cm. increase pr.					
16081	13	11	5	7	6
15836	-	10	6	5	4
16089	13	12	8	8	7.5
16023	12	19	13	10	-

From Table V, if an increase of 1 cm. water pressure occurred in the subcutaneous tissues all over the body in a young adult, the skin of the legs would be stretched by less than ½ per cent., and of the thighs by about 1 per cent.: but, in both cases there would be more expansion on the medial side - and thus more fluid would collect at the medial side, an important point in the consideration of the flow of lymph. In an old person, even for such a small increase of pressure the skin would expand very considerably as there is not the same resistance to change of pressure, the skin being functionally less active. For a 3 cm. increase of pressure these increases of area are even more marked and the importance of small increases of pressure under the skin in relation to the development of oedema can be seen. Even for this slight pressure variation the change in area of the old subjects' skin comes near the limit of oedema formation - Drury and Jones (1927) quote Mende as showing that palpable oedema forms when the limb volume increases by 8 per cent. of the original volume. In younger subjects, even with an increase of 5 cm. water pressure, the increase in area of the skin of the limbs is still within the limits reached during normal life.

To summarise these results, the skin in the old subject expands greatly for the first small increases of pressure, but does not expand much after that for any increase of pressure: whereas young skin expands relatively slightly for small pressures and goes on expanding, though to a less degree, for greater pressures.

(b) The differences in the reactions of the skin from different areas, and at the various age periods are well shown by the graphs of the Elasticity Modulus against the Pressure (Series Graph 10). It was explained above how the part of the curve which is practically horizontal represents the limits for which the skin is truly 'elastic' in the physical sense of the term. It will be seen from these graphs that it is only in the younger subjects that there is such a part in the curve: in the oldest subjects the curve rises sharply, after the initial fall, from pressures as low as 2 cm. water or less, in some cases with no horizontal part at all. But in the two youngest cases, the rise does not become definite until a pressure of about 10 cm. water has been reached in almost all parts: and even above these values, the rise is not so sharp as in the older cases - a feature seen for each area tested.

It was also shown above how the actual value of E, at any given pressure, could be taken as an indication of the resistance of the skin to that pressure. Thus it is clear that in each case, the skin of the legs is more resistant than that of the thighs, and the lateral side is more resistant than the medial. Also, the lowest values of E in younger skins are considerably higher than the lowest values in older skins - in other words, the younger skin is much more resistant than the older.

(c) It is from the results shown by graphs of Tension against Pressure (Series Graph 11) that the most interesting speculative possibilities arise. From these graphs it is seen that the tension in the skin increases proportionally to the increase in pressure. In several of the cases, the values for ½ cm. and sometimes 1 cm. increase of pressure do not correspond well with the other values, but it should be remembered that the method and instrument used are very delicate, and the first adjustment is difficult - probably the non-correspondence of these values is due to experimental error. Apart from that, it will be seen that the proportional increase varies - the slope of the graph increases with old age, for each part, and, in each case the slope is sharper for the lateral than for the medial sides of the legs and thighs. These facts, of course, correspond with the differences in the other sets of graphs.

Consider the tension values when the graphs cut the Y axis, i.e. when the skin is at the pressure it was at before being removed from the body: these values are then the tension at which the skin was, on the cadaver (Table VI).

Table VI.

Case No.	Age in yrs.	Epi-gastrium	Thigh, Medial	Thigh, Lateral	Leg, Medial	Leg, Lateral
16081	14	2.5×10^3	2.5×10^3	6×10^3	5×10^3	6×10^3
15836	25		4×10^3	6×10^3	7.5×10^3	8×10^3
16089	47	3×10^3	1.5×10^3	4×10^3	1.5×10^3	4×10^3
16023	65	1×10^3	1.5×10^3	1.5×10	2.5×10^2	

dynes/cm.

From the table it is obvious that this original tension varies considerably - and in the same way as the resistance - for age and site. When one considers the area of skin on the body, one realises that there must be a very considerable amount of energy distributed throughout this tissue.

Now, suppose the graphs are all continued back to where they would cut the X axis, these negative values (Table 7) would be the positive pressure under the skin when it was removed from the body - i.e. the so-called "tissue tension" (of course, after death): as the graphs are not always perfectly straight, in producing them backwards it was decided that for the sake of uniformity the line would be taken as an average through the largest number of points in one straight line.

Table VII.

Case No.	Age in yrs.	Epigastrium	Thigh, Medial	Thigh, Lateral	Leg, Medial	Leg, Lateral
16081	14	1.5	2.0	4.0	3.5	4.0
15836	25	-	3.5	4.5	4.0	4.5
16089	47	1.5	2.0	2.5	2.0	2.5
16023	65	0.5	1.0	1.0	1.5	-

cm. H_2O

This table shows that, in each subject, except the first, all areas have approximately the same value for "tissue tension" - as is only to be expected, as any differences during life would tend to become equalised after death, when other factors causing variation, such as muscular movement and erect posture, are removed and the tension in the skin allowed unopposed play. But where there are differences in the tension, the higher values are in the legs rather than epigastrium and thighs, and in the lateral sides rather than the medial sides.

> In the first subject, the "tissue tension" values under the epigastrium and medial side of thigh are exceptions in that the tissue tension in them is much lower than in the skin of the other areas in that case. No reason can be offered for this, beyond noting that in very few cases was the tension in the epigastrium over 2.0 cm. water.

A very striking feature brought out by this table is that in the two younger subjects the average "tissue tension" was about 4 cm. water; in the middle-aged cases it was down to 2 cm., and in the old case, to $\frac{1}{2}$ or 1 cm. Thus the lack of resistance in the old subject's skin is compensated to a certain extent by its being at a lower original tension: and a rise in pressure under the skin will be met by a greater increase in expansion, thus reaching a similar tension to a younger person's tension for a smaller expansion.

2. Subjects with Oedema.

In normal subjects, although each individual one gave slightly different values, yet in each age group the graphs shown correspond closely with the others of the group. In the cases with oedema, however, there is little or no correspondence with age, and very often noteworthy variations for the different areas of skin in each subject: each subject thus presents features of its own. But the main points wherein these differ from the normals and from each other can be shown from the graphs of the five subjects given (Series Graphs 12, 13 and 14). The findings in these cases will be discussed separately.

16163, a girl of 13 years, died of subacute glomerulonephritis: there was definite emaciation. The feet and ankles showed a moderate degree of oedema, but, on incision, all subcutaneous tissues in the body were found to be waterlogged. The skin from the epigastrium and from the lateral side of the thigh was easily replaced on the instrument after removal from the body, but that from the medial side of the thigh had contracted greatly and was replaced on the same marks only with difficulty.

The Pointer Excursion graphs (Series 12, top row) show that in this subject there is not much difference in the expansion of the skin from the epigastrium and from the lateral side of the thigh and that of skin from similar areas in a normal subject: they show only slightly increased expansion in the epigastrium, and in the lateral side of the thigh, the expansion is slightly slower at first. But the skin from the medial side of the thigh expands considerably less in the oedematous case than in the normal of the same age. Similarly the modulus curves (Series 13, top row) show the same values for the epigastrium and lateral side of the thigh in the oedematous and normal cases: but those for the medial side of the thigh in the oedematous case have risen, it should be noticed, almost to those for the lateral side of the thigh. The tension curves (Series 14, top row) are rather irregular compared to those for normal cases, and this irregularity is found chiefly in the three cases of younger ages shown here - 16163 (female, 13 years), 16014 (female, 28 years, Series 14, second row);and 16145 (male, 50 years, Series 14, fourth row): in these cases it will be noted that the curve is (within the limits of experimental error), a straight line (as in all other cases) for the higher pressures, but tends to be raised above this line for the lower pressures.

It might be suggested that this phenomenon was due to a lack of precision in the instrument, which might be caused in two ways - one, the difficulty of setting the zero level accurately and so having a slight error in the lower values: two, the neglect in the calculation of the thickness and weight of the skin, which also would be more obvious in the lower values. Both of these explanations, however, seem very unlikely, as this deviation is present to a pronounced degree only in certain types of cases - viz. younger cases with oedema. This deviation must be accepted as a feature in this condition and it has considerable importance in the following way: it implies that the tension in the skin is higher for low pressures than would be expected from its behaviour towards high pressures - actually, the pressure under the skin must be higher than the pressures calculated in the same way as for the normal skin: a satisfactory method of finding the estimated Tissue Tensions in these oedematous cases could not be found.

In 16014, a female of 28 years, who died of rheumatic endocarditis with auricular fibrillation, there was oedema of the legs and thighs, especially on the medial side. The expansion of the epigastrium, always a very variable feature, should not be affected in such a case and nothing in the graphs show any departure from normal. But in the medial side of the thigh it will be noticed that there is very marked expansion, a very low curve of modulus values and low tension values - the skin has lost its resistance even more completely than it would with old age in a normal subject; Whereas the skin of the lateral side of the thigh has maintained normal characteristics.

15868, female 59 years, suffered from a carcinoma of the cervix which involved both ureters, causing anuria. When she died, there was fairly marked generalised oedema. On the whole, the skin really corresponds with that of normal old subjects - an early rapid increase of area followed by little further increase, a modulus curve falling rapidly to an early minimum with no horizontal part but rising fairly quickly in a straight line, and a tension curve starting low and rising straight and quickly. The most obvious variation in this subject is the slight expansion of the skin of the epigastrium, with its very rapidly rising modulus and tension curves. There is slightly more expansion in the lateral side of the thigh than in the medial, and as this is one of the very few cases in which the usual order of resistance is varied, it is worthy of further consideration.

Here, the oedema is of rapid onset and there has been no time for the skin to become accustomed to the new conditions, as in 16014. In 16163, also a fairly acute case of oedema, the curves for the medial thigh approximate closely to those for the lateral thigh, but have not passed them, as in this third case. The explanation of this unusual result seems to be as follows: with the increased accumulation of this oedema fluid in the subcutaneous tissues, there is a consequent rise of tissue tension - the skin is stretched more than usual, and in the natural order of things the looser parts, e.g. medial side of thigh, stretch further than the tighter parts, e.g. lateral side of thigh: thus there is increased flow of fluid to these parts: in this case, there seems to have been a slight overbalance - this explanation seems more probable than that in this case there was an actual difference in the nature of the skins of these areas. This reasoning conforms, in a pathological degree, to what will be suggested later as the normal method of flow in lymphatics.

16145, a male of 50 years, had well-marked, firm oedema - he suffered from exophthalmic goitre and auricular fibrillation. In this case, it must be admitted that there is not much difference in the expansions from that in normal cases. The modulus curves, however, show that there is less of a horizontal phase than in the normal - less range of true elasticity, and the values thereafter rise more rapidly - the skin is then more resistant. Similarly, the tension curves rise slightly more rapidly. It should be remembered that in this case there is the irregularity mentioned in dealing with the first case with oedema - the tension values for low pressures are above the straight line formed by the values at high pressures: this is also present, but to only a very slight degree, in the normal case at the corresponding age - 47 years (16089).

16140, male of 70 years, was a case with hypertension and gradual heart failure: there was very marked, generalised oedema. All areas of the skin showed greater resistance than normal, and estimated "tissue tensions" were all above normal - all indicating that the skin was more on the stretch than usual, as if the "tissue tension" during life was also above usual.

3. Materials other than Skin.

Brief mention of the results obtained with these (Series Graph 15) will suffice. Dura mater and fascia lata acted in a similar way to each other: the first few centimetres' increase of pressure caused great expansion, and there was little further for higher pressures. The modulus curve in each case rose rapidly from zero - a point of difference from all the skin tested; there is no question of these membranes having any true elasticity and there is no original resistance in them. Similarly with the tension curves - they rise rapidly from zero.

Fascia lata in oedema may react as in normal cases or it may show a variation from the normal as in 16134. This patient was a man of 76 years who died from coronary thrombosis: there was very slight apparent oedema of the ankles only. On cutting the fascia lata, however, a considerable quantity of fluid came out from the deep tissues, and it was noted that the fascia had been under considerable tension. The results obtained by stretching it further on the instrument in the ordinary way, emphasised the original condition: there was only gradual further increase of area, the modulus curve commenced at a very high level and showed marked decrease up to a pressure of 15 cm. water, after which it remained level, and the tension was high to begin with, and increased greatly as compared with the normal one.

The Pure Rubber gave an unexpected result: for the first few centimetres' water pressure, it increased greatly in area, then increased more gradually for further values. The modulus showed values increasing greatly at first, but gradually less for higher pressures: it is not truly 'elastic,' in that it did not increase in area proportionally to the increase in pressure. The tension curve does not look as if it would ever be a straight line - it commences at zero (its edges do not retract when cut, as with a substance under tension) - and increases with decreasing increments.

The Bullock's aorta is unique - but that may be partly due to experimental error. The thickness and weight of the material were much greater than in any other substance used, and this may have caused the first readings to be lower than perhaps they should have been, theoretically.

SECTION IV: DISCUSSION.

Correlation of Histology and Experiments.
Tissue Tension, Tissue Fluid and Lymph.
Physiological Phenomena.
Tissue Tension and Oedema.
Conclusions.

SECTION IV: DISCUSSION.

The results of these various experiments raise several points for discussion. First, there is the question of correlating the histological pictures of the different thicknesses of the skin and the quantities of elastic tissue and white connective tissue found in various areas with the 'resistance,' as shown by the macroscopic experiments on the same areas.

Another point is the theoretical consideration of the part played by this elastic membrane, the skin, in the maintenance of tissue tension, with the associated problems of increase and decrease of tissue fluid, the formation of lymph, and the flow in lymphatics. Further points are practical applications of these theories to various physiological and pathological phenomena.

A. CORRELATION OF HISTOLOGICAL AND EXPERIMENTAL OBSERVATIONS.

In the correlation of the histological pictures and the 'resistance' of the skin, there are two main lines of approach. One is the consideration of the changes found in the elastic tissue and in the resistance of the skin at different ages. The other is the more detailed comparison of the thickness of the skin and of its proportion of elastic tissue at the different sites with the resistance of those sites.

The findings connected with the first point are straightforward. In the young adult skin, the elastic fibres are well formed and regular, and distributed fairly evenly throughout the skin: at this age, the resistance of the skin is greatest and there is nearly always a range of perfect elasticity reached after stretching by the first few centimetres of water pressure. With advancing age, the elastic fibres become irregular and fragmented, and their distribution becomes irregular: now the skin is lax, with little resistance and with no range of perfect elasticity.

The second point is rather more involved. In the epigastrium, the skin is usually very thick but contains few and short elastic fibres: its resistance is at first easily overcome, but asserts itself fairly soon and expands little afterwards. In the lateral side of the thigh, the skin is nearly as thick as in the epigastrium, but it contains a large proportion of long, well-formed fibres: its resistance is great at first, yet it goes on increasing in area for pressures much greater than those which cause further increase in area in skin of the epigastrium. The skin of the medial side of the thigh is thinner than that of the preceding areas, but contains a proportion of elastic fibres much greater than the epigastrium and only slightly less than the lateral side of the thigh: its resistance for small pressures is less than that of the lateral side, and more than that of the epigastrium, yet it goes on expanding for greater pressures much more like the skin of the lateral side of the thigh than that of the epigastrium.

In the leg, the skin is very much thinner than in the thigh, but its elastic tissue is as great in proportion to the thickness: the resistance is much greater than the thigh skin - the total increase in area for any given pressure is considerably less, but the fairly gradual increase in rate of the expansion is similar to that of the thigh. The observations on this point can be summarised in tabular form as follows:-

Part.	Thickness.	Elastic Fibres.	Resistance.
Epigastrium	Greatest here.	Few and short.	Slight at first (cf. other areas): marked later.
Thigh, Lateral	Not quite so thick.	Very numerous and long.	Considerable at first: fairly well marked later.
Thigh, Medial.	Of medium thickness.	Many and long.	Always slightly less than Thigh, Lateral.
Leg, Lateral.	Thinner.	Considerable number: fairly long.	Very great at first: increases later.
Leg, Medial.	Thinnest.	Slightly fewer: fairly long.	Slightly less than Leg, Lateral.

These two points will now be considered together. The chief elements in the skin which are probably concerned in causing the resistance are the yellow elastic fibres and the white connective tissue fibres: they are always present together, but in varying proportions. In the skin of the thighs of younger subjects (e.g. 16081 and 15836, medial and lateral) there are large numbers of well-formed yellow fibres. In the modulus graphs of these skins, there are longer horizontal parts of the curve (between approx. 5 and 10 cm. water pressure) than in any other of the graphs from other ages. In the epigastrium, where there is the largest proportion of white fibres and in all areas of skin of older subjects in whom the yellow fibres are histologically altered, there is a shorter horizontal part in the graphs and the curve commences its steady rise sooner. The inference is that the white fibres act physically like rubber as far as expansion is concerned, with a gradually increasing modulus of elasticity, whereas the well-formed yellow fibres in younger subjects in conjunction with the white fibres form a truly 'elastic' membrane with a constant elasticity modulus, within limits. That is to say that in young and healthy adult skin the expansion occurs at first by stretching of the combined yellow and white fibrous tissue in a truly elastic manner (i.e. it returns to normal when the stretching force is removed), but, beyond certain limits (or possibly after continued stretching within these limits), the expansion occurs at the expense of the white fibres in a non-elastic manner. In the skin of old subjects, the elastic tissue plays little part and expansion occurs by stretching of the white fibres. After such expansion, return to normal is not so rapid, or so complete as after expansion of skin containing normal yellow fibres.

Attention may be drawn to the similarity of the modulus graphs for rubber, fascia lata, dura mater and the latter parts of the graphs for skin as supporting the suggestion that the white fibres when alone act in a similar way to rubber *qua* expansion.

Thus it appears that the yellow fibres are truly named 'elastic,' as compared with the plastic white fibres. The resistance of the skin is due first to the resistance of the combined yellow and white connective tissue fibres; later to the white fibres alone. When the skin expands, it does so first by stretching of the combined fibres, and later by stretching of the white fibres. The two types of fibres seem to be distributed in such a way that where more expansion is required (i.e. in the limbs), there is a larger proportion of the yellow fibres, but on the trunk where there is not much necessity for expansion, the yellow fibres are few in number. It would be interesting to observe if there is an increase in the number of yellow fibres in the abdomen in connection with pregnancy. Lindholm (1931) has already noted the existence of more elastic fibres in the abdomen of adult females than in the thorax, whereas the opposite occurred in males. The point is worth fuller investigation.

While these investigations support the views of Riehl and Kyrle (quoted by Sternberg, 1925) that the elasticity depends on the arrangements of tissues which make it up, the yellow fibres forming a support for the softer white fibres, they also tend to show that the elastic property resides chiefly in the yellow fibres. It is very improbable that the different kinds of fibres act entirely by themselves when the combination of both is present, but the specific property of true elasticity depends almost entirely on the presence of a large proportion of the yellow fibres among the white connective tissue fibres.

B. THE SKIN AND TISSUE TENSION, TISSUE FLUID AND LYMPH.

The results given above at first glance seem to indicate that the resistance or elasticity of the skin is of such small magnitude as to be of little importance in the body mechanism: in a young adult, an increase in area of 5 per cent. could be produced in the skin of the leg by increasing the pressure below the skin by only 5 cm. water - surely a very considerable increase in area for a very slight rise of subcutaneous pressure. But these small pressures are of great significance when considered in relation to the forces at work in capillary filtration and reabsorption, in view of recent experiments in the study of these subjects, and in the formation of oedema. Since Starling (1896) showed that the collosmotic pressure of the blood serum was the principal force causing reabsorption of crystalloids from the tissue spaces to the blood stream, many attempts have been made to measure the collosmotic pressure of the serum, the blood pressure in the capillaries, arterioles, and venules, and to introduce other factors at work in the process of filtration and reabsorption.

Collosmotic Pressure.

Starling himself measured this pressure and found it to be about 30-40 mm. mercury. Recently Krogh (1929) gives the results of collosmotic determinations by various earlier investigators as ranging from 30-50 cm. water and says that he favours the higher ones. Later, Krogh, Landis and Turner (1932) give the value as 35 cm. water: Govaerts (1932) gives 35-40 cm. water: and Wells, Youmans and Miller (1935) give the average as 30-35 cm. water. From the fairly uniform results obtained by these and other workers, it can be taken that this pressure usually ranges between 30 and 40 cm. water.

Capillary Pressure.

There is much more variation in results here owing to the difficulty of applying direct methods to its measurements. Indirect methods have been tried - chiefly by the use of capsules (see Appendix to Krogh, 1929) - but they are not satisfactory. Direct micro-cannulation has been carried out in a wonderful manner by Landis (1930, 1934) and his results are the standard ones - but it should be remembered that by this method it is the lateral pressure that is being measured, not the full head of pressure in the capillary lumen: it is this lateral pressure, however, that is concerned in the filtration and reabsorption process. In a capillary loop, he finds the pressure at the arteriolar end to be about 45 cm. water, in the loop about 28 cm., and at the venous end about 17 cm. water.

Thus recent measurements of these two forces lend support to Starling's explanation as applied to filtration and reabsorption of fluid between capillaries and tissue spaces (see Diagram 1). But other factors are also concerned, though to a minor degree: some of them act by modifying directly the two main factors - e.g. starvation and plasmapheresis lower the collosmotic pressure, increased venous pressure raises the capillary pressure; while others act more independently - e.g. tissue tension, collosmotic pressure of interstitial tissue fluid, and lymph flow.

Lewis and Grant (1925) study the mechanism by which tissues deprived of blood supply become repossessed: in the course of their experiments, which involved the cutting off of the blood supply to a limb for varying times, and the use of a plethysmograph, they find that the volume of the limb increased by 3 per cent. at 41°C. after arterial occlusion for two minutes: also, if the venous pressure in the limb was raised, the limb volume increased, and after a certain time equilibrium was established as follows:-

Venous pressure of 35 cm. water → 1 % increase in volume
" " 55 cm. " → 2 % " "
" " 95 cm. " → 5-6 % " "

This establishing of equilibrium suggests that some other mechanism or mechanisms had come into play to assist the collosmotic pressure in dealing with the increased venous and capillary pressure.

Drury and Jones (1927) also use a plethysmograph to study the rate at which oedema forms on congestion of the veins: these authors calculate the filtration in c.c. per minute per 100 c.c. of limb, and find that a rise in venous pressure causes a rise in rate of filtration - there is twice as much filtration when venous pressure is doubled. Also the temperature is concerned - it has most effect in causing increased flow from 26-36°C. They describe another feature which later workers have gone into more fully - they show that the transudation rate declines in time and when the experiment is repeated in a short time - i.e. that the amount of fluid originally present in the limb is important.

Lewis (1927) introduces an important point when he shows that the capillary blood pressure can be increased to 34 cm. water before there is increase in the volume of the arm. Also, Krogh, Landis and Turner (1932) find that filtration commences when venous pressure is raised to about 17 cm. water (measured by capsule), and thereafter is proportional to the further increase of venous pressure. These writers also point out that the removal of the excess fluid depends on the amount of fluid present in the tissues - i.e. on the volume of the tissues. They used an elaborate "pressure plethysmograph." Landis and Gibbon (1933) extend these studies to show that temperature has an effect, and they write - "It seems probable that fluid accumulating in the tissue spaces develops a tissue pressure which retards filtration and reduces further loss of fluid from the blood stream." This force diminishes the power of increased venous pressure, or venous congestion, to filter out fluid, as they can exclude any change in capillary permeability: lymphatic drainage can not have much, if any, effect in their series of experiments. Krogh (1929) has already written - "Oedema, of course, causes distension of the elastic skin and rise in pressure, counteracting the further increase of oedema." This is the only suggestion which I have been able to discover in the literature that the elastic property of the skin plays a part in the causation of tissue tension - and the point is not elaborated further.

Weech, Snelling, and Goettsch (1933) try to sum up the factors concerned by stating that -

> the collosmotic pressure of the blood serum minus the osmotic pressure of the interstitial tissue fluid is equal to the capillary blood pressure minus the elastic tension,

with the acknowledgment that lymph flow is an additional agent.

Youmans, Wells, etc. (1934), again, find increased tissue pressure very important in the maintenance of equilibrium of the forces observed when a subject stands for one hour. They find that there is an increase of 30-65 per cent. in collosmotic pressure, and of 4 per cent. in limb volume in their experiment, but no oedema develops in normal subjects: the normal venous pressure, standing, in the ankles is 100 cm. water: the blood becomes concentrated by 13 per cent. in the arms, by 25 per cent. in the feet. It is unfortunate that it is so difficult to measure the flow of lymph as that seems to be the chief factor not considered in their experiment.

Attention may be drawn to the point that in all the above references where there is mention of increased tissue tension, there is also increase in volume, and Krogh realises that there has been an extra call upon the elasticity of the skin.

It is proposed here to discuss more fully the connection between the development of tissue tension with the stretching of the skin.

The skin of the subject No. 15836 (a representative case for discussion, as he was a healthy man of 25 years) was under tension when removed from the body: this tension varied for the area of skin from 5 x 10^3 dynes/cm. on the medial side of the thigh to 10 x 10^3 dynes/cm. on the lateral side of the leg. The existence of this tension for each centimetre of skin throughout the whole of the area is shown by the fact that when a cut is made the edges become curled to a greater or lesser extent: also, for skin in general, by the result given above of the experiment where a strip of 10 cm. length was cut into ten equal parts and the parts laid together measured now only 8.3 cm. This tension can thus not be communicated to a distance, but exerts its influence only in its own centimetre, as it were. This force is always present, and it continually works towards reduction in the area of the skin - and that means towards reduction in volume of the limb. There must be a force continually acting against this tendency - a force tending to increase the volume of the limb. It is well known that the volume of a limb is never constant: there is a small increase and decrease with each beat of the pulse, and with the phases of respiration. The actual amount of the increase is very small, but its presence indicates the delicacy of adjustment of the forces concerned. The heart is the origin of the outgoing pulse wave: the blood forced into the limb at each beat possesses a certain amount of energy: it is measured as a force with pressure of 110-115 mm. mercury in the brachial artery: in the smaller arteries, the pressure becomes divided up, and some of the energy is taken up by the resilience of the arterial walls: but there is still a considerable amount of pressure in the arteriolar ends of the capillaries and it decreases towards the venous end. The tension of the skin is the only force which is able to bring about the decrease in the limb volume after each arterial pulsation: the increase in volume stretches the skin slightly, thus increasing the skin tension, and when the force of the pulse wave has passed this increased tension is sufficient to cause contraction, until met by another pulse wave. But the amount of tension in the skin is very small compared to the force of the pulse beat in the large arteries: and its action is accordingly comparable to the fine adjustment of a microscope: the coarse adjustment is represented by the grosser changes in limb volume resulting from the balance of capillary pressure versus collosmotic pressure. In the capillaries the pulse wave is no longer felt - the capillary blood pressure is practically constant: similarly, the collosmotic pressure is a fairly constant quantity. Working on Starling's conception, these two forces are normally well balanced: Landis shows that on the average the pressure at the arteriolar end of the capillary loop is above, and at the venous end is below the collosmotic pressure (see Diagram 1).

While these forces are balanced there is no gross change in limb volume, and only the finer changes with pulse and respiration are found. Whenever the capillary blood pressure reaches 34 cm. water (Lewis, 1927), or the venous pressure 17 cm. (Krogh, Landis and Turner, 1932), there is a gross change in the limb volume: the pressure inside the capillaries forcing fluid out is now greater than the force (collosmotic pressure) drawing it in again, throughout the length of capillary available for the interchange. The excess fluid forced out collects as interstitial fluid, and stretches the skin. The skin resists such increases and the result is an increase of tissue tension - along with an increase in volume of the limb. As soon as the increase of tissue tension is sufficient to enable the collosmotic pressure of the serum to reabsorb any further fluid pressed out of the capillaries by the increased blood pressure within them, a new equilibrium is obtained with the limb increased in volume. Obviously, only a slight increase of tissue tension will be required at first to set up the new equilibrium, and only slight stretching of the skin is required. Or while the increase in pressure within the capillaries may be considerable in amount, it may not be maintained for long enough to necessitate the establishing of a new equilibrium.

Under normal conditions of life, capillary and venous pressures vary considerably within short periods of time depending on the amount of work being done, the changing of posture, etc. Few direct experiments have been made on the former, but from analogy with arterial pressure it is possible that it may rise to almost double its resting value when active exercise is taken. Thus in the first experiment quoted (Graph 1) where the subject ran up and down stairs during periods of five minutes the arterial pressure rose quickly to very high levels, but also fell fairly rapidly: probably the capillary pressure behaved in the same way. But the high values were not maintained for long: there was no establishing of equilibrium and so the limb volume did not increase greatly: there may have been only a very small increase of tissue fluid, most of the increase being due to increased amount of blood present. In the second experiment (Graph 2) when the measurements of limb circumference were taken during an evening's badminton, the exercise was over longer periods and, at first, with short rests: it is noteworthy that the increases here are much greater at first and tend to become balanced later. In these instances, the capillary pressure presumably rises far above the collosmotic pressure and filtration is predominant: but several forces are available to assist in the removal of the extra tissue fluid. The flow of lymph is known to become a prominent feature in limbs that are exercised: muscular movement is stated to assist in the flow in both lymphatics and veins: and the tissue tension is raised, by the increased resistance of the skin. Similarly, when venous pressure is raised by congestion or standing, or by back pressure from a weak heart, the capillary pressure must rise above the collosmotic pressure. Several examples of carefully controlled experiments on these aspects are recounted in the literature, e.g. Youmans, Wells, etc. (1934). Landis and Gibbon (1933) use a pressure plethysmograph and increased venous pressures to investigate the effect of tissue pressure on movement of fluid through the capillary wall. Their method of estimating or measuring tissue pressure is by raising the venous pressure to increase the limb volume, and then finding how much excess fluid is present. Thus they find that 1.5 c.c. fluid per 100 c.c. tissue abolish further filtration at a venous pressure of 20 cm. water. Unfortunately, their result is from experiments on the forearm: I was not able to obtain sufficient areas of skin from that part and often had difficulty in subjects of normal size in obtaining sufficient from the legs. But if the results of stretching the skin in subject 15836 for the lateral and medial sides of the legs are averaged and compared with Landis and Gibbon's findings, the following conclusion is reached:-

1.5 per cent. increase in area of the skin is represented by 2.8 cm. excursion of the pointer: i.e. is represented by 2.5 cm. increase of pressure in both medial and lateral sides of the leg. If the venous pressure is 20 cm. water (Landis and Gibbon) it is now 3 cm. above the value at which increase in limb volume commences and it seems reasonable to assume that the capillary pressure has risen by a slightly smaller amount, i.e. 2.5 cm. This implies that the increased tension of the skin is sufficient to balance the rise of pressure under it, viz. the increase in tissue tension.

Further, Landis and Gibbon find that an increase of 4 c.c. fluid per 100 c.c. tissue abolishes further filtration at a venous pressure of 40 cm. water. Now,

$$\frac{\text{volume of cylinder}}{\text{surface area of cylinder}} = \frac{\pi r^3 h}{\pi r^2 h} = \frac{r}{1},$$

where r stands for the radius of the end of the cylinder: r does not increase in these experiments in appreciable proportion to the other measurements and can be neglected: i.e. for 4 per cent. increase in volume of the limb, the error will not be appreciable, if the surface is considered as having increased by 4 per cent. also. Four per cent. increase in area of the skin is represented by 4.5 cm. excursion of the pointer, corresponding to an increased pressure of 4 cm. water in the medial side of the leg, and 5 cm. in the lateral side - an average of 4.5 cm. water pressure.

With the rise of venous pressure to 40 cm. water, the capillary blood pressure will rise to a certain extent: but it would scarcely be reasonable to assume that it was also doubled - in fact, it seems likely that it will not be much above the normal venous pressure: and if it is about 40 cm. water, then it has risen just about the 4.5 cm. that the skin expansion suggests (see Diagram 2).

Thus, in experiments where lymphatic drainage is probably not a factor of any importance, it can be shown fairly definitely, that the increased tissue tension developing in a limb swollen from venous congestion can be attributed to the resistance of the skin, due to stretching.

Where lymphatic drainage is not cut off, the tension of the skin is found to be quite incomplete in balancing the forces when the equilibrium between capillary pressure and collosmotic pressure is upset. Thus Lewis and Grant (1925) find that, with a simple plethysmograph, a venous pressure of 35 cm. water gives only a 1 per cent. increase in volume, 50-55 cm. gives 2 per cent. increase in volume, and so on. Obviously the increased tensions in the skin corresponding to increases of the order of 1 per cent., 2 per cent., etc. are quite inadequate to deal with increases of pressure under it in any way comparable to venous pressures of 35 cm., 50-55 cm., etc. Another mechanism must be introduced here, viz. lymphatic drainage. In the normal resting condition, it is stated that there is little or no flow in the lymphatic vessels. But Drinker and Field (1933) show that lymph is probably the same as tissue fluid, perhaps slightly concentrated at times. It is only to be expected that if the forces causing reabsorption into the blood vessels at least equal the forces causing filtration, no tissue fluid will be left over to go via the lymphatics. When the filtration forces are higher than the reabsorption ones, the excess tissue fluid must be disposed of in some other way: and so the lymphatics are utilised.

Anatomists are agreed at the present time that the lymphatic system is closed with a lining endothelium as permeable as the capillary blood vessels (Hudack and McMaster, 1932). Further, it has been known since the time of Hunter that at least the large lymphatics are valved in a continuous fashion. Based on these facts and on Starling's defence (1894) of Ludwig's theory of the formation of lymph by filtration, the following theory is offered as an explanation of lymphatic drainage in the limbs. The lymphatic capillaries are not patent while the tissues are at physiological rest, i.e. while filtration is completely balanced by reabsorption. Whenever the part becomes active, there is increased capillary pressure, increased filtration, increased tissue fluid, and consequent increase of volume: the circulation of tissue fluid becomes temporarily slowed down, and some of the fluid enters the lymphatic capillaries: at this stage, the fluid can as easily escape from the lymphatics and be reabsorbed by venous capillaries: but if the latter have more fluid than they can cope with, some is left in the lymphatics. Meanwhile, with the increase in volume of the part, the tissue tension is increasing steadily, in addition to the slight increase and decrease with each pulse beat. This increased tension is small, but quite sufficient to force the fluid from the smallest lymphatics into larger ones: in these larger ones, as the walls become thicker and less permeable, escape for the fluid becomes increasingly more difficult. And when the valved vessels are reached, back flow is no longer possible and the fluid is now lymph: a little water may have escaped during its journey in the small lymphatics, but the fluid is essentially the excess of interstitial fluid which the capillaries could not reabsorb. Even when the valved vessels are reached the force required to drive on the lymph is still very small and is still supplied by the tissue tension, which results from the resistance of the skin maintaining the normal volume of the part. Force is required to drive the lymph only to the next valve, such force being available from the increased tension due to each cardiac systole. It is as if the limb were divided into a large number of transverse planes corresponding to the valves in the lymphatics: between the pulse beats the skin tension is constant, the tissue tension is constant, the arteries are empty, and there is fluid in the lymphatics. During systole the arteries become filled and the tissues distended, and the skin resists sufficiently to cause a temporary increase in the tissue tension. This temporary increase must in its turn do some work - the lymphatics provide the only outlet for it: the lymph cannot be pushed backwards because of the valves: but the force available is sufficient to push the lymph forwards into the next higher plane. The process is then repeated in this next plane. In the larger lymphatics another factor plays a large part, and is also concerned with the flow in veins. When two or more small lymphatic vessels join to form a larger channel, the cross-sectional area of the latter is smaller than that of the total of the areas of the tributaries: the result is that the lymph must flow more quickly, to allow of the same volume being dealt with by the same amount of force. As the number of lymphatic tributaries increase, a corresponding increase of flow results and a considerable head of pressure develops in the larger lymphatics. This will explain the transmission of fluid in vessels where slight increases of tissue tension could hardly be expected to have much effect on the flow on account of the thickness of the vessel walls: this factor may play a very considerable part, as Hudack and McMaster (1932) have shown that the lymphatic radicles, at least in the ear of the mouse, are comparatively wide vessels, while the proximal collecting vessels are fairly narrow. How does this theory apply to such facts as we have mentioned in relation to limb volume with increased venous pressure, and in connection with the problem of the nondevelopment of oedema on standing, and similar problems? Lewis and Grant (1925) show that limb volume increases, with increased venous pressure, to the following extent:-

Venous pressure.	Increase in volume of forearm.
35 cm. water.	1 per cent.
55 "	2 "
80 "	4 "
95 "	5-6 "

To be considered also are the findings of Landis, Jones, Angevine and Erb (1932) who, when they raised the venous pressure and then took blood from the veins and compared the content, with regard to protein, cells, haemoglobin, and made haematocrit estimations, obtained the following results:-

Venous pressure.	Loss of fluid from blood (cf. control limb).
25 cm. water.	0-2 c.c. per 100 c.c. blood.
55 "	2-5 " " "
80 "	7-9 " " "
110 "	12-19 " " "

On combining the figures obtained by these two sets of observers and taking into consideration the obvious fact that, with increased venous pressure there will be engorgement of the veins and so more blood in the limb, it is clear that at 55 cm. venous pressure, the blood becomes concentrated by two to five per cent. and the whole limb volume also increases by 2 per cent. - which means that there must be a considerable increase of interstitial fluid - i.e. potential lymph: this fluid cannot be returned to the blood stream in the limb, and the only other exit is by the lymphatics. It must return to the blood stream fairly rapidly or results of the control limb (Landis, Jones, etc.) would not remain as constant as they do. The only force known to have changed is the pressure of the skin, and this has increased quite considerably and so caused increased tissue tension.

The same points are brought out, even more clearly, by Youmans, Wells, Donley, Miller, and Frank (1934) who noted the following in subjects who stood motionless for about one hour:-

Venous pressure in foot - approx. equals 100 cm. water.
Increased volume in leg - " " 4 c.c. per 100 c.c. tissue - i.e. 4 %
Concentration of blood in foot - " " 25 % (re serum Protein).
Concentration of blood in arms - " " 13 % (re serum Protein).

Increase of serum protein equals 18-40 % .

And increase of collosmotic pressure equals 29-65 % .

If the venous pressure rises from about 8-10 cm. water or less (at heart level) to 100 cm. water in feet on standing, there must be a corresponding increase of the opposing forces or mechanisms: the chief one - the collosmotic pressure - rises to about 50 cm. water - and that leaves a large amount still to be accounted for. But equilibrium is not established so far as the blood itself is concerned: it loses 25 per cent. of its fluid to the interstitial tissues: this fluid stretches the skin and calls into play its increased tension, both to assist in the capillary balance and to promote the extravascular circulation. Muscular contraction as a factor in the circulation is practically eliminated in this series of experiments. The increase of tension in the skin is considerable, for an increased volume of approximately 4 per cent. - it is doubled. The blood of the arms is concentrated by 13 per cent. and that is a fair sample of the total blood of the body: the excess fluid must be in the lower limbs, accounting for some of the 4 per cent. increase. But the blood of the legs is concentrated by 25 per cent. - another 12 per cent. of fluid is therefore lost as it circulates through these limbs: and presumably a corresponding amount must be returned to the circulation in the lymphatics as quickly as it is lost from the blood: this means that the lymphatic flow must be considerable in amount (see Diagram 4). The first volume of interstitial fluid will be utilised in the lower limbs to develop the increased tissue tension required for the ordinary filtration-reabsorption processes. These authors also find that oedematous patients behaved much as normal ones.

From recent experiments of intradermal injections of dyes, McMaster (1937) states that in spite of increased lymph formation, there is no upward flow in the superficial lymphatics of a dependent limb: but also, there is no backflow, which he ascribes as due to the valvular function. But White, Field and Drinker (quoted by McMaster in above reference) have shown that there is an increased flow of lymph from a cannulated vessel when the limb is dependent. McMaster assumes that the difference in his results and those of White *et al* is due to the operative interference by the latter. If that were the case, he is also assuming that the valves above the site of operation have become incompetent and are now permitting back flow - an assumption which I do not think is justified. This question, however, requires further investigation.

The result of the badminton experiment can be explained in more detail by considering the effect of increased tissue tension along with lymph flow, and the distribution of fluid in all the limbs. The parts most active show the greatest initial increase in size, i.e. in the right forearm and thigh. The legs were probably already somewhat swollen from standing and some walking just previously and so would not show any immediate increase: the left leg actually shows a slight decrease at first, probably in response to immediate demand for more fluid for the whole circulation. Then, as all the limbs demand an increased circulation, some fluid is taken from the ones which received the great original increase, and there is a tendency for a constant volume to be reached for each limb. Now the tension in the skin of the legs is higher than that in the skin of the thighs: also, the increase in tension for any given increase of pressure is much greater in the leg skin - or, the increase in area of the skin (and therefore the circumference of the part) for any given increase of pressure is less in the leg skin: it seems likely, then, from the greater increase in circumference of the thighs than of the legs, that the pressure under the skin - the tissue pressure - has increased by the same amount in each part: i.e. a new equilibrium has been reached (see Diagram 5). But it must involve lymph flow as well as tissue tension, for still the tissue pressure has not risen nearly sufficiently to balance the probable increase in capillary blood pressure caused by such pressure (cf. experiment of running upstairs).

In general, then, the capillary blood pressure and the collosmotic pressure are kept in delicate equilibrium by fine changes of tissue tension changing with each pulse beat: the force or source of energy for the tissue tension is the elastic capacity of the skin. When the equilibrium is grossly upset by increase of capillary blood pressure, e.g. by exercise or posture, the limb swells, the skin tension is considerably increased and now initiates or grossly increases the lymphatic circulation, as well as causing higher tissue tension, and a balance is once again obtained.

C. TISSUE TENSION IN CONNECTION WITH PHYSIOLOGICAL PHENOMENA.

It is obvious from common experience and from the results given above that the elasticity of the skin is not the same all over the body. There are areas of the skin modified to perform other functions, and in them the elastic property is subservient to these other functions. Thus, there is little or no elastic tissue in the skin of the palms of the hands and the soles of the feet: here, the skin is firmly adherent to the deeper tissues. The same is the case with the skin of the palmar aspects of the fingers and toes. Now, the skin of the backs of these areas is at first glance fairly loose: but on further investigation it is loose within only a short range - it is firmly fixed to the deeper tissues at the sides of the hand, at the knuckles, and over the interphalangeal joints. When the balance is upset between the intracapillary pressure and the collosmotic pressure, the whole hand and fingers increase or decrease in volume: the change affects first the dorsal subcutaneous tissues and soon influences all the tissues. Thus we get the great thickening and "podginess" of the hands and fingers in hot atmospheres: for an increase of temperature causes dilatation of the superficial blood vessels, with consequent increase of pressure in them: this causes an increase in the volume of fluid filtered to the tissues (Landis and Gibbon, 1933: Youmans, Akeroyd, and Frank, 1935).

The eyebrows and the scrotum are other areas where the skin contains practically no elastic tissue. But these areas are also peculiar in that in addition to the lack of elastic tissue there is no firm connection to firm deeper tissues to compensate for the lack. This means that in a generalised upset of balance between collosmotic and capillary pressures, if the latter is increased there will be excess filtration all over the body, but it will be resisted at first at all parts except in the eyelids and scrotum - a fact well seen in acute nephritis. For the oedema will show first, here, in spite of any other subsidiary factors such as posture.

The skin of the limbs and trunk forms far the greatest proportion of the total area of skin. It possesses the elasticity described above and the variations in its degree at the different parts of the lower limb have been pointed out and their consequences suggested already. To recapitulate, they are as follows:-

1. The skin of the leg is more resistant than that of the thigh: accordingly, the leg skin can deal with greater changes of tissue tension within smaller limits of expansion than the skin of the thigh. The greater power of expansion of the thigh skin is probably a mechanism provided to allow it to deal with larger volumes of fluid, as it must pass on

fluids to and from the leg, in addition to dealing with the fluid of the thigh itself.

2. The skin of the medial sides of the leg and thigh is less resistant than that of the lateral sides of the corresponding parts. In consequence of this, when there is any increase of tissue fluid in the subcutaneous tissues, more will collect at the medial sides. Is this a reason for the lymphatics and largest superficial veins running up the medial sides of the limbs?

It was not possible with the instrument available to test the skin of the forearm and arm in the same way, but I think the results would have been similar.

3. In the abdomen, there is not the same need for a mechanism to deal with large variations of tissue tension, as the variations in capillary pressure are never so large, owing to posture changes, as in the limbs. It is not surprising, therefore, to find that the skin tension is usually fairly low and the expansion of the skin for small increases of pressure is large. There is no need for more complicated mechanism for that area.

The variations in the elasticity noted for different ages can be briefly summed up by saying that with advancing age, the skin expands more quickly for small pressures, and then more slowly for higher pressures under it. That is, if the balance of filtration forces is slightly upset, there will be greater changes in an old person's skin than in a young person's. But, if the loss of balance becomes greater, there is still the same power of adjustment in the old person - but it would not stand up to the strain as long as in a young person. Thus, in old persons there is a loss of adaptive power in the extra-vascular circulatory system, as there is also in the intra-vascular system.

D. TISSUE TENSION AND OEDEMA.

The results of the cases with oedema in which the skin acted in a way similar to skin from normal cases, though commencing at different initial levels, and the observation of Youmans, Wells, etc. (1934) that oedematous patients behaved such as normal ones, suggest the conclusion that the deposition of fluid in the tissues (even to the extent of causing oedema) is a purely physical adaptation, in which a physiological mechanism is stretched beyond normal.

This conclusion is widely accepted for cardiac oedema, where the venous pressure is obviously increased and there is no other mechanism to compensate for it after the elasticity of the skin has been overcome by continued stretching.

In cases with heart failure, the capillary blood pressure is falling below the level to which the tissue exchange is accustomed and the venous pressure becomes increased. As a result of this change the pressure is considerably raised at the venous end of the capillary loops chiefly in the dependent parts so that less and less of the capillary endothelium is available for reabsorption purposes: this process is progressive as times goes on. When the time is reached that the normal safety margin is passed, the collosmotic pressure can no longer reabsorb the tissue fluid even with the assistance of increased tissue tension and lymphatic drainage, and oedema appears, first in the lower limbs, and thence spreading upwards. Gravity, it is well known, plays a prominent part in this type of oedema.

In renal oedema, mention is often made of abnormality in the capillary endothelium of the general circulation as a primary cause, but no satisfactory proof is offered. With the more recent accounts of the functional disturbances in the kidneys in nephritis (Shaw Dunn, 1933, 1935), however, the oedema can be understood as an attempt by the body to keep the blood composition as normal as possible, in spite of the abnormal filtration and reabsorption of water and salts by the kidneys, or because of the excessive loss of albumen leading to a diminished serum protein. The findings in the cases with oedema, both those quoted from the literature and the original ones given above, show that the development of the oedema is merely an extension of the normal swelling of the limb. There is at first no alteration in the elasticity of the skin and it still behaves in the usual way to alterations of tissue tension, and these alterations, as explained above, account for the differences in the results from the normal.

In acute nephritis, there is damage to the endothelium of the glomerular capillaries with lessened filtration and oliguria. With diminished circulation through the glomerular capillaries and therefore diminished excretion of water, yet continued ingestion, there is a consequent tendency to hydraemia. But the body is always very careful to preserve the composition of the blood as constant as possible, and possesses several mechanisms to compensate for tendencies to change in it. In this case, the mechanism utilised is that of depositing the excess fluid in the interstitial tissues. Shaw Dunn (1935) quotes Kaliebe (1917) as having found an increase in body weight in early cases of war nephritis, and H. McLean (1919) as recording considerable falls in weight to a constant normal in recovery from acute nephritis. But there is no necessity for assuming damage to the capillary endothelium of the general circulation to bring this retention about. For with the tendency to hydraemia, there will be excess filtration from the arterial ends of the capillaries and diminished reabsorption (because of the lower collosmotic pressure due to the hydraemia) at the venous ends until a new balance is again established - thus leaving an increased volume as tissue fluid, and causing increased flow in lymphatics. Now, gravity will not have so much effect in this condition, as the lack of balance is of a very slight degree and applies (equally) to all areas of capillary interchange except in the glomeruli. The excess will collect and appear at first where there is little opportunity of resistance to it - i.e. where the tissue tension can increase least - in the eyelids and scrotum, where there is practically no elasticity in the skin, and later throughout the body. McMaster (1937) shows that there is greatly increased flow in the lymphatics in renal oedema, and this is further support for the mechanisms outlined above.

In subacute glomerulonephritis, the process of adaptation at work in the acute stage becomes modified chiefly by the factors of time and subsequent changes in the blood and in the kidney. For the initial glomerular damage is usually not as severe as in acute nephritis, and the early loss of regulating power for fluids in the glomerular capillaries may be slight and may not produce such obvious changes in other tissues of the body as in the acute stage. But the defence mechanism used in the early stages becomes further called upon as the percentage protein in the blood diminishes owing to the albuminuria, which is so marked a feature of the disease.

E. CONCLUSIONS.

The tension in the skin, due to its elastic tissue content, plays an important part, although it is of small magnitude, in the maintenance of tissue tension, and also of equilibrium in the filtration and reabsorption process in the subcutaneous capillary blood vessels. When this equilibrium is upset by changes of posture, taking of exercise, etc., the elasticity of the skin is capable of raising the tension below it and thus increasing the tissue tension and flow of lymph in order to establish a new equilibrium.
When the upset is due to pathological changes in the blood or circulatory system, the same mechanism is brought into play, but is not always sufficient to enable a new equilibrium to be established without the pathological condition of oedema developing.

SUMMARY.

1. The histology of the elastic tissue in the skin is described.
2. A method is described for determining the elasticity of the skin after death.
3. The importance of the skin as a physical "elastic membrane," possessing a certain amount of tension, is discussed with relation to tissue tension and the extravascular circulation of fluid in the limbs.
4. A short account is given of the part played by the skin, by reason of its elasticity and its effect on tissue tension, in the development of oedema.

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The research work described above, and the composition of this Thesis is my own work.

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