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A CONTRIBUTION TO THE PATHOLOGY OF THE THYMUS GLAND.

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(Plates XIII.–XV.)

Development.

The thymus gland is developed from the hypoblastic lining of the pharynx. It takes origin as a tubular diverticulum from the dorsal portion of the pharyngeal aspect of the third visceral cleft on each side. This diverticulum has thick epithelial walls, and it grows by rapid proliferation of its cells. The two lobes of the organ are formed by extension downwards on the side of the trachea towards the pericardium, and by meeting the corresponding hypoblastic evagination of the opposite side.

The narrow upper part of the outgrowth remains for a time tubular, and connected with the pharyngeal cleft from which it originates. Ultimately this connection is broken through, and the expanded lower end sends out solid bud-like branches, after the manner of an acinous gland. Originally, therefore, the thymus is epithelial in structure; soon, however, it becomes invaded by connective and lymphoid tissue, so that it is ultimately transformed into a lymphoid organ. The concentric corpuscles of Hassall are the remnants of the epithelial structure of the gland (Cunningham).

It appears probable, from Beard's researches in elasmobranchs, which have been confirmed by other observers, that the leucocytes first make their appearance with the formation of the thymus. Beard is of opinion that they (leucocytes) are formed from the hypoblastic epithelium of the thymus rudiment (Schäfer).

The growth of the gland proceeds during the first two years of life, reaching the maximum period of development at the end of the second year. From this period the size of the gland remains somewhat stationary, until about puberty,[1] when the atrophy becomes much more rapid; but from my own experience and that of others, true gland tissue can be found even in adults of advanced age.

Anatomy.

The thymus gland in the new-born child is described by Professor Cunningham as being of pinkish colour and composed of two lateral lobes, generally

[1] I wish to draw attention to this fact, that although the weight of the gland does not decrease to any extent during this period, the histological changes are considerably altered.

of unequal size, separated by an intervening fissure. The main portion of the gland is situated within the thorax, but both lobes send prolongation upwards for a short distance into the neck, sometimes reaching to the level of the thyroid. The thoracic portion of the gland lies in the superior and anterior mediastina, and extends downwards as far as the level of the fourth costal cartilage, lying on the surface of the pericardium, and superficial to the innominate veins.

I have frequently noticed, in large and enlarged thymus glands, a small intermediate or third lobe, and other observers have had a similar experience. In the large majority of cases, however, such as one sees in the post-mortem room of a children's hospital, the thymus gland has either one or two lobes. According to Hektoen, "Small accessory thymic glands may occasionally be found about the periphery of the thymus body"; but I have never seen anything to justify the statement. It is also stated that the gland may be completely absent, but one would have to satisfy oneself by microscopical examination of the connective tissue from the normal thymic area before such a statement could be accepted as true. Sir John Simon remarks, "I have never noticed absence of the thymus except in cases of true acephalism."

The blood supply is derived from the inferior thyroid, internal mammary and possibly other arteries, and the gland is drained by the inferior thyroid, internal mammary, and both innominate veins.

The nerve supply, according to most authors, is derived from the vagus and sympathetic trunks. The cavity in the centre of each lobe is one of the most conspicuous features of large and enlarged thymus glands. The size of the cavity varies according to the freshness of the tissues. If we leave a thymus gland exposed to the air for some hours, we shall find at the end of that time that there is a large cavity in each lobe, filled with thick, yellow, often blood-stained fluid very similar to pus. The presence of this fluid has frequently given rise to various mistakes, more especially to the diagnosis of abscess formation. Sir Astley Cooper compared this fluid to chyle. If we squeeze a perfectly fresh and normal gland, this fluid wells up in all directions, but it apparently increases by the breaking down of the gland tissue, and will eventually give rise to a definite cavity in the centre of the lobe. I consider that this fluid arises from a liquefaction of the elements of the thymus, and it consists almost entirely of lymphocytes.

Histology.

Before considering the pathological changes, it may be well to refer to a few essential points of the normal histology of the gland.

The thymus gland is enveloped by a sheath of connective tissue, which sends off septa from its deep surface; these pass into the gland substance and separate the lobules from each other. Each lobule is composed of clusters of adenoid tissue with a small amount of connective tissue intervening.

A follicle consists of an outer cortical and an inner or medullary portion, but in the former the lymphoid cells are closely packed, whilst in the medulla of the gland they are much less numerous, and the retiform matrix is coarser.

The medulla contains the concentric corpuscles of Hassall. These bodies, which are first observed about the fourth month of fœtal life, are spherical in shape, and consist of flattened cells arranged concentrically around one or more central cells, and are frequently enclosed in a further group of flattened cells, *i.e.* they are compound.

I consider, however, that the central portion of Hassall's corpuscles has often undergone some form of degeneration.

These concentric bodies are remnants of the epithelial structures from which the gland was originally developed, and occur as islets owing to the

ingrowth of mesoblastic tissue. Large, pale-stained, somewhat granular nucleated cells form the chief constituents of this portion of the gland. Nucleated red blood corpuscles have been demonstrated in the medulla of the thymus by various observers, also polymorpho-nuclear neutrophile cells. Lastly, coarsely granular eosinophile cells are found throughout the gland, but more especially, from my own observations, along the line of the various septa. I will refer to this subject at a later period.

The blood vessels form a fine plexus around the various follicles, and from them capillaries penetrate into the medulla.

Weight of the Normal Gland.

It is doubtful whether we ought to give any exact normal weight for this gland. It appears to vary enormously, according to the health of the child and according to age. Anything and everything seem to produce some

Table I.—*Average Weight of the Thymus Gland according to various Authorities.*

Author.	Statement.
Testut	Weight at birth, 5 grms.
Arthur Robinson	,, ,, about ½ oz. = 14·285 grms.
Vierordt	,, ,, 24 grms. ,, at end of second year : 26 grms.
Robert Howden	,, at birth, about ½ oz.
Osler	,, ,, about 14 grms. ,, at 9 months, about 20 grms. ,, at end of second year : 25 to 30 grms.
Ziegler	,, at birth, 24 grms. ,, in a child aged 2 years, about 26 grms.
F. J. Roberts	,, at birth, ½ oz.
John Thomson	,, ,, about ½ oz. ,, about end of second year, 1½ to 2 oz.
Hugh Thursfield	,, of gland under the age of 2½ years is about 6 to 7 grms.
Jacobi	,, at birth, from 1 to 200 grains.
J. S. Fowler	,, of thymus gland, about ½ to 1 oz.
John Ruhrah	,, at birth, about 12 grms.
Friedleben	Intra-uterine life— 3 to 5 months, 0·3 grms. 6 ,, 7 ,, 2·3 ,, 8 ,, 5 ,, term 13·7 ,, After birth— 9 months, 19·8 grms. 9 months to 2 years, 26·2 grms. 3 years ,, 14 ,, 25·9 ,, 15 ,, ,, 25 ,, 21·0 ,, 26 ,, ,, 35 ,, 3 ,,

variation from the so-called "standard weight." I have come to the conclusion, from a careful analysis of my various tables, that the average weight of the gland, from birth up to the age of 2 years, is roughly about 7 to 10 grms. It is usually stated that there is very little alteration in the weight of the gland till puberty, when a rapid degeneration commences. It must be carefully noted that these remarks apply solely to the weight of the gland, not to any histological detail. If we examine a thymus from a child æt. 2 years and one from a case at puberty, although the weights may be similar, there is usually marked fibrosis in the latter. It is doubtful if any two glands taken from children of the same age will give the same result, and therefore I wish to emphasise that the weights which I have given as a standard are only roughly approximate, and not of any absolute value.

It is most obvious, if we are to judge by the literature, that there is a very great difference of opinion as to the normal weight of the thymus gland. Some observers give definite figures, but make no allowance for the variability in the weight of the gland. I think if the above remarks are expressed in a tabulated form they will best illustrate what has been previously stated.

Osler, in his text-book on medicine, agrees with Friedleben. The weight of the thymus gland, as given by both these authorities, is, to my mind, incorrect. A gland which weighs 25 to 30 grms. is considerably enlarged.

Hugh Thursfield, in a very able paper, based on his own observations which were made at the Great Ormond Street Hospital, came to almost identically the same conclusion as I have done. He says, in reference to the weight of the thymus gland as given by Osler, "This statement appears to be erroneous; the weight is enormously exaggerated." As I have already remarked, Thursfield considers that the weight of the gland varies between 6 to 7 grms. Testut, from an average of twenty cases, gives the average weight as 5 grms. Most other writers on this subject have followed in the footsteps of Friedleben. My own results are obtained from an examination of fœtal thymus glands, and from the glands of children who have died from acute diseases, *e.g.* broncho-pneumonia, etc. We must be careful, however, not to place too much stress on the weight of the thymus, because some glands which I have examined in children of six years or more, although about normal in weight, have consisted almost entirely of fibrous tissue.

Those who have made post-mortem examinations on children in whom the thymus gland has been found to weigh 20, 30, and 40 grms. or more, must be conscious of the striking disproportion between the weight of the child's body and the gland.

Fœtal Glands.

I have examined the thymus glands removed from ten fœtuses. The ages varied from the fourth month to term. I carefully examined the viscera in each case, but could not find any evidence of congenital syphilis, but as the fœtuses were obtained from the slums of Lambeth, syphilis could not be excluded. The largest thymus gland was obtained from an anencephalic fœtus which was an eighth-month child, and was very well nourished. The weight of the gland was found to be 22·2 grms. Sanné and others have already drawn attention to the fact that this type of monster has usually been found to have an enlarged thymus. The average weight of the thymus glands in the above cases, if we omit the anencephalic fœtus, is 4·575 grms., but if we include the monster, it is 6·053 grms. Thick fluid was found in the interior of all the normal and the enlarged thymus glands, and it was found to consist almost entirely of lymphocytes.

It was found impossible to differentiate cortex from medulla in the thymus

of the fourth-month fœtus, while in the gland of the fifth-month fœtus the differentiation was only slightly developed. The histological characteristics of every gland were otherwise normal. A large number of eosinophile cells were present in most of the thymus glands, but more especially in the thymus of the anencephalic fœtus. Hassall's corpuscles were normal in every case, but were usually much smaller than in children's glands. I consider, as I have already stated, that if a gland is atrophic, however slight this may be, these bodies are usually found to be enlarged; but the thymus was not atrophic in any of the fœtuses which I examined. Hæmorrhages were present in the thymus of a ninth-month fœtus, but I could not detect any inflammatory condition of the lungs to account for such hæmorrhages. Weber, however, has recorded hæmorrhages in the thymus at birth.

Technique.

The child was weighed in each case, as far as it was possible to do so, before the post-mortem examination was commenced. The relations of the thymus gland to surrounding structures and its appearances before removal from the body were carefully noted. The weight of the gland and its consistence were ascertained, and in most cases where we found enlarged or medium-sized glands, a bacteriological and histological examination of the thick fluid found in the interior of each lobe was made.

In a few cases fresh pieces of gland tissue were teased out in normal saline, but the result proved to be of little value.

The various fixing and hardening fluids employed were as follow:— Formalin (10 per cent.), gradually increasing strengths of alcohol, Müller's fluid, and lastly, Orth's bichromate formalin mixture. The last-mentioned fixative was found to give by far the best results. Paraffin was used for embedding in every case. Mayer's hæmalum and eosin proved to be the most satisfactory method for staining sections of the thymus, but Unna's polychrome methylene-blue, Mann's methyl-blue, Delafield's hæmatoxylin, and methyl-violet were also used. Lastly, sections from many of the glands were stained by van Gieson's method, in combination with either Mayer's hæmalum or Delafield's hæmatoxylin.

Films prepared from the fluid found in the interior of various thymus glands were either stained immediately by Leishman's or Jenner's methods, or fixed by heat and stained with alcoholic eosin and methylene-blue, or dilute carbol-fuchsin.

Histological Examination of the Fluid present in Normal and Enlarged Thymus Glands.

Specimens of the fresh fluid were examined in normal saline solution, and stained films were prepared as already mentioned. The cells which were found in this fluid consisted almost entirely of lymphocytes; but large hyaline cells, connective tissue corpuscles, eosinophiles, and polymorpho-nuclear neutrophile cells were also present. In one case the cells were so degenerated that it was impossible to make a satisfactory examination of the fluid.

Examination of the Thymus Glands of various Animals.

There is little to be added on this subject to what has already been said about the normal human thymus. Perfectly typical specimens of eosinophile cells can be demonstrated in the thymus of a young rabbit, especially along the septal walls and in the connective tissue, but also among the lymphoid

corpuscles as in the human thymus. I have seen the transitional forms of eosinophile cells more often in the young rabbit's thymus than in specimens from any other source. The thymus in the cat, dog, rabbit, guinea-pig, rat, mouse, etc., is very small, but the glands from sheep and calves are large and bulky, and when perfectly fresh contain thick fluid similar to that which is met with in the normal or enlarged thymus of children. This fluid in animals is sterile, and consists of lymphocytes.

In some of the specimens Hassall's corpuscles were found to have undergone hyaline, granular, and calcareous degeneration. I have never seen in the thymus glands of animals any changes similar to those which occur in primary atrophy in the human subject.

The Adult Thymus.

The gland has been examined in adults of all ages up to 70. It usually appears to consist of little more than fibrous tissue intimately associated with the connective tissue in the neck, but sufficiently conspicuous to enable one to remove the gland at an autopsy even on old people. I did not weigh the gland in any of my cases, as it was so intermixed with the surrounding connective tissue that the results would have been valueless.

Invasion of the gland by adipose tissue appears to be the most common microscopical change in these cases. The adipose tissue separates islets of lymphoid corpuscles, in which there may be one, sometimes two, Hassall corpuscles, but rarely more. These bodies may be normal, or may show hyaline, granular, or calcareous degeneration. It is interesting to find that the islets of thymic tissue consist chiefly of lymphoid corpuscles, and not of endothelial cells, which we find so constantly in primary and secondary atrophy. I have never seen any eosinophile cells in these cases. In specimens of the glands such as I have described, stained with Sudan iii., or Scharlach, the relations of the adipose tissue to the rest of the gland tissue are shown better than by any other method. I have never failed to find the thymus gland either in children or in adults. It is sometimes so atrophied that it appears to be absent, but a careful search will always reveal thymic tissue in some of the "suspected pieces." The eldest case from which I obtained a specimen of the gland was that of a man aged 68.

Alexander Bruce examined six specimens of adult thymus glands up to the age of 40. His results are very similar to my own. His paper was of great value, as up to that time it was freely stated that the thymus gland was completely absent in adults. Now we know that those responsible for such statements could only have made a most superficial examination for the thymus gland at the autopsies.

Bacteriology.

On reference to Table VII., it will be noted that in seven out of eight cases examined, the glands were found to be sterile. The only

case (Table VII.) from which positive results were obtained is of great interest.

A child died quite suddenly, and at the post-mortem examination no organic lesions were found beyond an enlarged thymus and rickets. The right lobe of the thymus was larger and softer than the rest of the gland, and contained a large abscess cavity, which was surrounded by only a thin layer of gland tissue.

Broth and blood serum tubes were inoculated from the pus, which was thick and reddish-brown in colour. Film preparations were stained by Gram's method and weak carbol-fuchsin. Large numbers of capsulated cocci, diplococci, and short chains were seen which stained by Gram. Very small, delicate, transparent, and isolated colonies appeared on the surface of the blood serum, and a fine turbidity of the bouillon was noticed at the end of twenty-four hours. Films prepared from both of these media showed a coccus similar to the above, except that it was not capsulated. Sub-cultures were made on gelatin and blood agar. The organism grew well in the form of small isolated colonies on the latter media, and in a similar manner on jelly (24° C.), except that the rate of growth was much slower.

The pathogenicity of a broth culture was tested by inoculating 0·5 c.c. into the peritoneal cavity of a white mouse. Death occurred in about eighteen hours, and a similar organism was grown from the heart blood and spleen. Large numbers of cocci, diplococci, and streptococci were seen in film preparation made from a scraping of the spleen; these also stained by Gram's method.

The organism isolated from the thymic abscess in the above case may be described as the pneumococcus of Fränkel. Those who have had the opportunity of studying the relations of the various micro-organisms in children's diseases, are well aware of the variety of lesions which are produced by the all-important pneumococcus. I think this is, however, the first occasion on which this organism has been found in a case of suppuration in the thymus gland. It is a matter of considerable regret that a bacteriological examination of the heart blood was omitted in this case. There is no doubt that in many cases in which the pneumococcus has been isolated from a local lesion, the organism has also been present in the general blood stream.

Dr. Branson and myself have already referred to this subject, which is of great *practical* importance, especially in relation to prognosis. It is possibly owing to this fact that children and adults in whom the local lesion has been of a benign character, have yet succumbed, because such cases were examples of an unsuspected septicæmia.

All observers are agreed as to the rarity of acute inflammatory lesions of the thymus gland, but cases have been recorded following on acute pericarditis, pleurisy, and Ludwig's angina (Rolleston).

One has to be quite certain that the suspected abscess is not really a collection of thick fluid which is normally present in large and enlarged thymus glands. I should advise careful examination of the gland before and after its removal from the body, the preparations

of films from the fluid, and also that cultures should be made on artificial media.

Lastly, in tuberculosis of the thymus gland, Jacobi and others have demonstrated the presence of the tubercle bacillus in sections of the gland tissue.

Tuberculosis.

Tuberculosis of the thymus was found on four occasions. In three of the cases death occurred from general tuberculosis; in the last case the disease was practically limited to the thorax. In every case the thymus was almost entirely converted into a fibro-caseous mass, except for small areas of glandular tissue in one corner of the organ. There was little to be seen microscopically beyond areas of caseous tubercle and numerous giant cell systems. The capsule was apparently much thickened. In virulent forms of tuberculosis in children we not infrequently find almost every gland in the body converted into caseous material, and almost every organ similarly affected. In such cases a large group of tuberculous glands can usually be found in the superior mediastinum in the position of the thymus. We must be careful to isolate the thymus from these glands, as otherwise we are inclined to consider the whole mass as tuberculous lymphatic glands, or incorrectly to include the thymus with the tuberculous mass. In the early stages of general thoracic tuberculosis in children, these glands are small, but generally show evidence of tubercle; in the more severe cases, however, they are very much enlarged, and tend to adhere to all other neighbouring structures. I have not met with an example of either congenital or primary tuberculosis of the thymus, such as are recorded in the literature of this subject.

Demme has recorded a case which he considers an example of primary tubercle of the thymus.

A child born of non-tuberculous parents, whose weight at birth was found to be 2780 grms., was breast-fed for three weeks, and then fed on cow's milk. From this period the child gradually emaciated, but did not present any physical signs beyond some dulness over the manubrium sterni. Death occurred on the forty-second day of the illness. The thymus gland was found to be enlarged, and to contain three small but typical tubercles, in which tubercle bacilli were demonstrated. No other organ in the body was found to be tuberculous.

Congenital Syphilis.

Paul Dubois directed the attention of the profession to the relation between congenital syphilis and the thymus gland. It is doubtful if any statements ever rested on such an insecure basis. He considered that a thymus gland which contained what he incorrectly described as "pus," was evidence of congenital syphilis. When we refer to the literature of this subject, we find that other

observers followed in the same footsteps. Perhaps the greatest error which Dubois made was to consider the thick yellow fluid which he found in the thymus gland to be pus. I have already drawn attention to the fact that one of the most characteristic features of a normal or enlarged thymus is the thick fluid found in the interior of the gland. It certainly resembles pus to the naked eye, but is quite unlike it microscopically. There can be little doubt to my mind that the so-called "pus" in the thymus, which Dubois found in four cases of congenital syphilis, was really the fluid which is always present in a normal or enlarged thymus gland. I have never seen a specimen of a thymus gland which could be described as syphilitic. Four cases which, clinically, were examples of congenital syphilis, died of marasmus, but without any evidence of syphilis in the thymus.

Jacobi considers that an excess of connective tissue, whether the gland is large or small, is the most characteristic feature of a congenital syphilitic thymus. He also mentions that there is general thickening of the coats of the blood vessels in such cases. It does not require much evidence to prove that Jacobi's statement is incorrect.

We have it on the authority of Henoch, that he has twice seen multiple collections of pus, scarcely the size of a pea, in the thymus glands of infants. These children developed at the same time many pemphigus bullæ, especially on the palms and soles, and they died in the first week of life.

Ludwig Fürth, as a result of an examination of 200 autopsies on congenital syphilis, found syphilitic lesions in the thymus gland on seven occasions. It is claimed by some writers, as Dubois remarks, that the thymus gland is the earliest viscus to be attacked; it may be the only organ to show any evidence of syphilis.

Parrot, on the other hand, has never found a single example of syphilis affecting the thymus. J. A. Coutts discusses this syphilitic question at some length, and comes to this conclusion: "I feel justified in my belief that up to the present the involvement of the thymus in inherited syphilis is at least not proven." Personally, I think there is much to commend these remarks, for although there is no reason why the thymus gland should escape in congenital syphilis, yet we require much more evidence than Dubois, Diday, Jacobi, and others have brought forward of any special pathological lesion. In fact, if we relied on the evidence offered by Dubois for the recognition of a syphilitic thymus, we should find that it was extremely common, and much more frequent than congenital syphilis.

Atrophy.

I have classified atrophy of the thymus under two headings—Primary Atrophy and Secondary Atrophy.

Primary Atrophy.

I mean by this expression, an atrophy associated with "marasmus," whatever may be the cause, provided no true pathological changes are found at the autopsy which could have produced such a result. This condition, which may be produced by improper feeding, want of assimilation of food on the part of the child, and, lastly, the atrophy which we sometimes meet with as the only evidence of congenital syphilis.

Ruhrah has drawn attention to the fact that the most characteristic lesion of marasmus, beyond the wasting of fat and muscles, is atrophy of the thymus gland. There is no doubt that this observation is correct. Those who perform post-mortem examinations on infants must be struck by the extraordinary appearance of the gland in cases of marasmus. My own observations, drawn from an analysis of fifteen cases, are in accordance with what has been already stated. The thymus gland in some cases might be easily overlooked, as it appears to consist of little more than œdematous connective tissue. If we refer to Table II. we notice that the youngest of my cases was ten days old, while the age of the eldest child was two years. There was considerable loss of weight in every case, and in two cases the children were found to weigh about a third of the normal. One of the smallest glands I have ever seen (No. 2, Table II.) was found to weigh only 0·905 grm.; in three others the weight was under 2 grms., in five under 3 grms., in five under 4 grms., while in one case it was found to weigh 5 grms. The average weight was 2·680 grms.

If we refer to the condition of the thymus gland, we shall find that it was frequently described as "white, soft, and œdematous," and this is to my mind the most characteristic evidence of an atrophic thymus. These glands, however, usually cut with great resistance. I have never seen any thick fluid in an atrophic thymus, such as is invariably met with in large and enlarged glands. There is also complete absence of any lobular arrangement.

Ruhrah observed, from an analysis of eighteen cases of marasmus, that the lowest weight of the thymus gland was 1·2 grm., and the highest 7·5 grms., and that the average weight for sixteen of the cases was 2·2 grms. He states that, except for a terminal infection, the atrophy of the thymus was the only pathological lesion found. These results of the weight of the thymus glands are identical with my own.

Histological Changes.

An increase of the fibrous stroma was noted in every case. This tissue spreads irregularly throughout the gland, and divides it into numerous alveoli. In five of the glands the fibrosis was very

marked. In most cases there was some thickening of the outer coat of the arteries, but more especially in the five cases in which the fibrosis was most marked. Van Gieson's stain was found to be most useful for the demonstration of this change in the coats of the arteries. In eleven cases the differentiation of cortex and medulla was most imperfect, generally impossible. In one case (No. 4) the divisions of the gland were obvious. Perhaps the most characteristic change present in an atrophic thymus is the replacement of the lymphoid corpuscles by cells with spindle-shaped nuclei and endothelial cells. The amount of lymphoid tissue is very sparse when compared with a normal gland. Giant cells, some with three or four nuclei, others with only two nuclei, are usually numerous. These cells resemble the small giant cells which are met with in the lymphatic glands in lymphadenoma. Hassall's corpuscles appear to be much more numerous, but this is probably due to the marked atrophy of the glandular tissue while the corpuscles remain, and thus appear to be out of all proportion to the rest of the gland. I have also found that they are generally much larger than normal. Calcification of these corpuscles was found in many cases. It is not uncommon to find that half a Hassall corpuscle is calcified, while the remainder is granular or homogeneous in appearance, and may be surrounded by a few flattened cells. Hæmorrhages have been noted in two cases. I will refer to the significance of this fact below. On two occasions the gland substance was replaced by adipose tissue. It is frequently found that a clear space, surrounded by flattened cells, appears to be the only evidence of a Hassall corpuscle. I have found that the concentric corpuscles stain bright-red with eosin, and generally yellow, sometimes deep orange, but never red with van Gieson's stain. This last statement is of interest, as Professors Ruhrah, Stokes, and Rohrer have observed that these corpuscles in marasmic glands usually stain bright rose-red by van Gieson's method, although sometimes they stain an orange colour. They suggested that these changes might be due to a chemical alteration in the epithelium of the cell bodies from a kerato-hyalin into true hyalin. A large number of specimens of epitheliomata of the skin were stained with this picro-fuchsin stain for comparison. The epithelial concentric bodies of epitheliomata, which are regarded as kerato-hyalin, stained an orange-yellow colour, but a moderate number of these pearls contained globular bodies which stained a rose-red colour, and this was considered as evidence of true hyalin. I consider these statements erroneous. I have never been able to stain Hassall's corpuscles in any of my marasmic thymus glands rose-red, but nearly always bright yellow, and occasionally deep orange colour. Secondly, although there is an exceptional opportunity for the study of squamous-celled carcinomata in the Clinical Laboratory of St. Thomas's Hospital, I have never succeeded in staining any portion of the concentric bodies rose-red, but

have always found that they stain yellow or at the most deep orange colour.[1]

Von Recklinghausen considered that one of the special characteristics of hyaline material was due to the property which it possessed of staining deeply with such acid dyes as acid fuchsin, or eosin. Ernst considers that true hyaline material stains a deep red colour with van Gieson, while colloid stains an orange or a yellowish-brown colour, but also that hyaline material, which is formed in connective tissue, is stained deep red by fuchsin, while that which is derived from epithelial cells stains orange-yellow. Von Kahlden considers that Ernst's statements are not justifiable because true colloid often stains a deep red.

If we compare the brief summary which I have given above of the work of Professor Ernst on hyaline and other forms of degeneration, we shall see that my observations on Hassall's corpuscles and "cell nests" are similar to his, and in direct opposition to those of Professor Ruhrah.

Secondary Atrophy.

I have included under this division such causes as tuberculosis and chronic non-tuberculous affections, *e.g.* chronic empyema, etc., some of the most important factors in the etiology of the wasting diseases in children.

1. *Wasting due to tubercle.*—From an analysis of twenty-six cases (Table III. includes twenty-eight cases, but the weight of the thymus gland in two cases was unfortunately omitted), the average weight was found to be 3·065 grms. The smallest gland I have ever seen is included in this list. It was found to weigh 0·345 grm. The largest specimen weighed 9·310 grms.

2. *Wasting due to chronic non-tuberculous affections.*—The results are calculated from an analysis of twelve cases. The average weight of the thymus gland was found to be 2·605 grms. I have omitted one case (No. 9) from this record, because the thymus gland was inseparable from the fibrous mediastinitis, the result of inflammation, and could only be weighed in conjunction with this tissue. These results are almost identical with the marasmic record, namely, 2·680 grms. The smallest gland in this series weighed 1·280 grm., while the largest gland weighed 4·400 grms.

Naked-Eye Changes of the Thymus Gland in Secondary Atrophy.

The gland was frequently described as soft, white, and œdematous;

[1] Mr. Shattock has suggested that these discrepancies may be due to the van Gieson's stain, which is of a different strength, and used in different manner by various workers. I can only say, however, that I have used several samples of van Gieson's stain, but have only been able to obtain results similar to those obtained by Professor Ruhrah on one occasion.

but while these changes are so characteristic in primary atrophy, in secondary atrophy they have not the same significance. If we find the thymus corresponds to the above description in a case of marasmus, we are fairly confident that it will present marked microscopical changes; but in the form of atrophy now under discussion, we may find that a thymus gland which has been described as "soft, white, and œdematous" may not reveal any microscopical alteration of structure.

In some cases the gland has been found to be hard and nodular, owing to tuberculous caseation, surrounded by dense fibrous tissue. Secondary atrophy teaches us above everything else that we cannot accurately judge the condition of the thymus gland until a microscopical examination has been made.

Microscopical Histology.

The capsule of the gland is frequently thickened, and fibrous bands may be seen passing in all directions throughout the gland tissue. The complete alteration in the structure of the thymus gland, which has already been described under marasmus, is also found in this form of atrophy, although not so frequently.

Fibrosis of the gland is the commonest microscopical change which we meet with in secondary atrophy. Sometimes it is of a slight degree, and only present along the "septa," while in the most severe case the gland consists of little more than fibrous tissue and thickened blood vessels. The Hassall corpuscles appear to undergo forms of degeneration similar to those met with in marasmic glands, but calcareous degeneration was found in a larger percentage of the cases of secondary atrophy, and might be described as fairly common. We occasionally find that one-half of a Hassall's corpuscle has undergone calcareous degeneration, while the other half is granular.

Endothelial cells and connective tissue corpuscles are usually found in the most atrophic glands, as in marasmus, to have replaced the normal glandular structure, namely, lymphoid corpuscles. Various varieties of "giant cells" are also met with. Eosinophile cells are either absent or very scarce. We must always remember that these glands which have lost all definite outline, and which appear to have undergone severe degenerative changes, may fail on miscroscopical examination to show more than a slight fibrosis.

Mettenheimer arrived at similar conclusions from an analysis of thirty-seven cases of secondary atrophy of the thymus gland.

Conclusions Derived from the Study of Fifteen Cases of Primary Atrophy and Forty-one Cases of Secondary Atrophy.

1. Atrophy of the thymus gland is the most characteristic morbid lesion found in cases of marasmus.

2. In all wasting diseases of children we meet with a similar condition.

3. Atrophy of the thymus gland in children and wasting of the tissues are usually found to go hand in hand.[1]

4. We never find thick fluid in the interior of the gland in these cases. It is usually impossible to differentiate the cortex from the medulla.

5. The most characteristic alterations in the histology of the thymus gland in cases of marasmus are as follow:—Fibrosis, which is usually well marked and often accompanied by thickening of the outer coat of the blood vessels; atrophy of the lymphoid corpuscles, which are replaced by endothelial cells, connective tissue corpuscles, and small "giant cells"; all varieties of degeneration are found to occur in Hassall's corpuscles.

6. In secondary atrophy we may meet with similar changes in the thymus gland as are met with in marasmus, although less frequently.

7. We are able to judge, with some degree of certainty, the state of nutrition of a child, by a macroscopical and microscopical examination of the thymus gland.

[1] Friedleben arrived at a similar conclusion many years ago.

TABLE II.—*Marasmus.*

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
1[1]	10 weeks.	10½ lb.	6 lb.	3·440 grms.	White, soft, and œdematous; no evidence of any syphilitic lesion.	Increase of fibrous tissue; lymphoid cells predominate; many Hassall's corpuscles seen.	None.
2[1]	16 days.	7½ ,,	4½ ,,	0·905 ,,	Soft, white, and œdematous; no evidence of any syphilitic lesion.	Very marked fibrosis; very few lymphoid cells; many Hassall's corpuscles seen; thickening of blood vessels.	Acute bronchopneumonia.
3[1]	7 months.	16½ ,,	10½ ,,	3·555 ,,	Very hard; no evidence of any syphilitic lesion.	Fibrosis; fewer lymphoid cells; many eosins and Hassall's corpuscles.	Acute lobar and lobular pneumonia.
4	14 weeks.	13 ,,	6¼ ,,	5·150 ,,	Red and firm.	Cortex and medulla can be differentiated; marked increase of fibrous tissue; lymphoid cells predominate; many giant cells and no eosins.	None.

[1] These cases were diagnosed clinically as examples of marasmus due to congenital syphilis.

TABLE II.—*Marasmus*—continued.

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
5	8 months.	18 lb.	8 lb.	1·900 grms.	Small, white, and œdematous.	Fibrosis; very few lymphoid corpuscles; many Hassall's corpuscles seen.	Acute broncho-pneumonia.
6	3 ,,	11 ,,	5½ ,,	2·140 ,,	Red, soft, and small.	Very marked fibrosis; only small islets of lymphoid tissue to be seen; adipose tissue has invaded gland.	None.
7	8 ,,	18 ,,	9 ,,	3·0 ,,	Small, red, and firm.	Calcification of some of Hassall's corpuscles, which are increased; many eosins; fibrosis.	None.
8	4 ,,	13 ,,	4½ ,,	1·150 ,,	Red and soft.	Fibrosis; calcification of some of the Hassall corpuscles; lymphoid cells very few.	None.
9[1]	10 days.	10½ ,,	3½ ,,	1·0 ,,	Small, red, and soft; no evidence of any syphilitic lesion.	Well-marked fibrosis; eosins numerous; many hæmorrhages; lymphoid cells replaced by spindle cells and endothelial cells.	None.
10	7 months.	17 ,,	7½ ,,	2·82 ,,	White, soft, and œdematous.	Extreme fibrosis, &c.	Acute broncho-pneumonia.
11	6 ,,	16 ,,	8¾ ,,	2·77 ,,	White, soft, and œdematous.	Marked fibrosis; great diminution of lymphoid corpuscles; many giant cells; thickened blood vessels.	Acute broncho-pneumonia.
12	2 years.	26 ,,	14 ,,	2·560 ,,	Very small.	Marked fibrosis; thickening of blood vessels; numerous spindle cells and endothelial cells replacing lymphoid corpuscles.	Extensive general thrombosis of veins; adrenal hæmorrhage.
13	1 ,,	20 ,,	8½ ,,	3·800 ,,	Small and firm.	Marked fibrosis.	Acute broncho-pneumonia.
14	10 months.	18½ ,,	10½ ,,	3·470 ,,	Soft, white, and œdematous.	Marked fibrosis; large numbers of Hassall's corpuscles; atrophy of lymphoid tissue.	Acute broncho-pneumonia.
15	1¼ years.	..	..	2·560 ,,	Soft, white, and œdematous.	Enormous increase of fibrous tissue; marked atrophy of gland tissue; great thickening of blood vessels.	Acute broncho-pneumonia.

[1] This case was diagnosed clinically as example of marasmus due to congenital syphilis.

TABLE III.—*Tuberculous Cases.*

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
1	16 months.	21 lb.	14½ lb.	3·55 grms.	White, œdematous, and soft.	Gland appears to be normal.	General tuberculosis.
2	6 years.	45 ,,	19½ ,,	..	Very small and œdematous. (I could not identify the entire gland.)	Extreme fibrosis.	General tuberculosis; subdiaphragmatic abscess.
3	6 months.	16 ,,	9¾ ,,	2·160 ,,	White, œdematous, and small.	Only a few areas of thymus tissue left; extreme fibrosis, and invasion with adipose tissue.	General tuberculosis; glands most affected.
4	5½ years.	44 ,,	..	4·20 ,,	White, œdematous, and very soft.	Very extensive calcification of Hassall's corpuscles; gland otherwise normal.	Tuberculous meningitis.
5	1½ ,,	22 ,,	15½ ,,	1·400 ,,	White, œdematous, and soft.	Large areas of caseation; giant cells numerous.	General tuberculosis.
6	11 months	20 ,,	16¾ ,,	5·800 ,,	Red and firm.	Calcification of many of Hassall's corpuscles; gland otherwise appears to be normal.	Tuberculous meningitis, &c.
7	3½ years.	33 ,,	19½ ,,	1·870 ,,	White, œdematous, and soft.	Fibrosis; atrophy of lymphoid tissue; adipose tissue invading gland.	General tuberculosis.
8	5 months.	15 ,,	7¾ ,,	1·570 ,,	White and soft.	Large numbers of Hassall corpuscles; fibrosis; lymphoid corpuscles replaced by endothelial cells.	General tuberculosis.
9	2½ years.	28 ,,	21 ,,	5·740 ,,	Red and firm.	Gland appears to be normal; large numbers of eosins.	Acute miliary tuberculosis.
10	6 ,,	Child was fairly well nourished.	..	2·370 ,,	Small, red, and firm.	Well-marked fibrosis.	Large cerebellar tumour; tuberculous meningitis, &c.
11	2½ ,,	28 lb.	14½ ,,	2·630 ,,	White and soft.	Well-marked fibrosis; atrophy of lymphoid corpuscles; calcification of Hassall's corpuscles.	Tuberculous peritonitis.
12	7 ,,	Large child, but rather wasted.	..	5·820 ,,	Large, red, and firm.	Some increase of fibrous tissue; gland otherwise normal.	General tuberculosis.

TABLE III.—*Tuberculous Cases*—continued.

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
13	4 years.	35 lb.	18½ lb.	4·350 grms.	The lower extremity of the gland was attached to the pericardium, and appeared to be fairly normal. The whole of the body was composed of fibro-caseous material, surrounded by dense connective tissue. No cavity formation.	Gland tissue almost entirely converted into caseous material; numerous giant cells.	General tuberculosis.
14	10 months.	18½ ,,	7 ,,	2·370 ,,	Small and soft.	Well-marked fibrosis.	Thrombosis of the middle meningeal artery; general tuberculosis.
15	2½ years.	28 ,,	14 ,,	2·500 ,,	Small and soft.	Slight atrophy of gland tissue.	Chronic thoracic tuberculosis.
16	2 ,,	26 ,,	20 ,,	1·230 ,,	Small, red, and firm.	Considerable atrophy of gland tissue; fibrosis.	General tuberculosis.
17	$1\frac{8}{12}$,,	24 ,,	14½ ,,	2·950 ,,	Small, œdematous, and white.	Considerable atrophy of gland tissue.	General tuberculosis.
18	3 ,,	31 ,,	14½ ,,	0·950 ,,	Extremly atrophied, white, and œdematous.	Extreme fibrosis; very little glandular tissue left.	Chronic abdominal tuberculosis.
19	$1\frac{6}{12}$,,	22 ,,	15¼ ,,	2·000 ,,	Red, firm, and small.	Well-marked fibrosis.	General tuberculosis.
20	..	Great wasting.	..	..	Gland was not weighed, as it could not be separated from the tuberculous glands which surrounded it. It, however, appeared to be much atrophied.	Atrophy of gland tissue; increase of fibrous tissue and invasion with adipose tissue; no evidence of tubercle.	General tuberculosis.
21	$1\frac{7}{12}$,,	22½ lb.	12½ ,,	1·720 ,,	Red, firm, and small.	Gland tissue almost entirely converted into caseous material; numerous giant cell systems.	General tuberculosis.
22	8 ,,	Wasted.	..	9·310 ,,	Large, red, and soft.	Some fibrosis, otherwise normal.	General tuberculosis.
23	$1\frac{11}{12}$,,	25 lb.	18 ,,	5·000 ,,	Red and soft.	Invasion of gland with adipose tissue; well-marked fibrosis.	General tuberculosis.
24	6 months.	16 ,,	12½ ,,	0·345 ,,	Very small and soft.	Extreme fibrosis; lymphoid corpuscles replaced by spindle cells and endothelial cells.	Chronic glandular tuberculosis.

TABLE III.—*Tuberculous Cases*—continued.

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
25	$3\frac{6}{12}$ years.	33 lb.	18 lb.	0·600 grms.	Small, soft, and white.	Fibrosis; atrophy of gland tissue; Hassall corpuscles show degenerative changes.	General tuberculosis.
26	9 months.	18 ,,	12 ,,	0·922 ,,	Small and white.	Well-marked fibrosis; no evidence of tubercle.	General tuberculosis.
27	$1\frac{11}{12}$ years.	24 ,,	14 ,,	3·559 ,,	Small and firm.	Large number of hæmorrhages; increase of fibrous tissue; calcification of some of the Hassall corpuscles.	Tuberculous ulceration of intestine; caseous mesenteric glands; gangrenous varicella; adrenal hæmorrhage.
28	2 ,,	26 ,,	$14\frac{1}{2}$,,	4·700 ,,	Œdematous and very hard.	Large areas of caseation; giant cell formation.	Tuberculous broncho-pneumonia.

TABLE IV.—*Chronic Non-Tuberculous Cases.*

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
1	9 months.	18 lb.	8 lb.	1·600 grms.	White, soft, and œdematous.	Marked fibrosis, and invasion of the gland with adipose tissue.	Internal hydrocephalus; acute ependymitis.
2	$1\frac{1}{2}$ years.	22 ,,	$12\frac{3}{4}$,,	2·270 ,,	White, soft, and œdematous.	Marked fibrosis, so that the gland was divided into numerous alveoli; large numbers of eosins; lymphoid cells much diminished.	Chronic empyema.
3	10 months.	19 ,,	$12\frac{1}{2}$,,	2·770 ,,	Small, red, and firm.	Marked fibrosis; scattered hæmorrhages; no alteration in the lymphoid tissue.	Chronic bronchitis.
4	1 year.	Emaciated.	..	2·60 ,,	Soft and œdematous.	Atrophy of lymphoid tissue which is replaced by endothelial cells, &c.; very few eosins.	Chronic meningitis; internal hydrocephalus.
5	..	20 lb.	$10\frac{3}{4}$,,	2·420 ,,	Soft, white, and œdematous.	Marked fibrosis.	Chronic broncho-pneumonia; rickets.

TABLE IV.—*Chronic Non-Tuberculous Cases*—continued.

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
6	1 year.	20 lb.	12½ lb.	1·880 grms.	Soft, white, and firm.	Marked fibrosis; atrophy of lymphoid tissue.	Chronic non-tuberculous meningitis.
7	1½ ,,	25 ,,	14½ ,,	4·150 ,,	Large; soft and flabby in some places, hard in others.	Gland appears to be normal.	Chronic empyema.
8	11 months.	20 ,,	6½ ,,	3·340 ,,	White and œdematous.	Fibrosis of gland; lymphoid tissue appears to be normal.	Congenital cardiac disease.
9	1½ years.	25 ,,	15 ,,	9·800 ,, (This record is of no value; *see* details.)	Large, white, and very hard.	Enormous increase of fibrous tissue; large numbers of spindle cells; no eosins seen.	Chronic mediastinitis; adherent pericardium; chronic broncho-pneumonia; small loculated empyema. The thymus gland was embedded in the firm fibrous adhesions which had spread in all directions in the mediastina, and it was, therefore, impossible to isolate the gland.
10	2 months.	9 ,,	5½ ,,	2·200 grms.	Small, red, and firm.	Some increase of fibrous tissue; gland otherwise appears to be normal.	Congenital cardiac disease; recto-vaginal fistula.
11	2½ years.	..	Very marked wasting.	1·280 ,,	Small, white, and hard.	Well-marked fibrosis; invasion of gland with adipose tissue; atrophy of lymphoid cells.	Post-basal meningitis; chronic hydrocephalus.
12	2½ ,,	28 ,,	14½ lb.	2·960 ,,	Small and white.	Replacement of lymphoid corpuscles by endothelial cells; no eosinophile cells seen in gland.	Very large spleen; subcutaneous hæmorrhages of all the serous membranes and in the mucous membranes.
13	8 months.	18 ,,	9½ ,,	4·400 ,,	Small and firm.	Marked fibrosis; numerous hæmorrhages.	Chronic empyema; acute broncho-pneumonia.

TABLE V.—*Fœtal Glands.*

Number.	Age.	Average Weight of Children of Corresponding Ages.	Weight of Children in the Recorded Cases.	Weight of the Thymus Gland.	Naked-Eye Changes in the Thymus Gland.	Microscopical Histology.	Results of Post-Mortem Examination.
1	8 months.	..	Not stated; very large and fat.	22·200 grms.	Large, red, and firm; thick, yellowish-white fluid in the interior of the gland.	Normal gland; large number of eosinophile cells.	Very large adrenal glands. Anencephalic fœtus.
2	9 ,,	..	Well nourished.	5·900 ,,	Red and firm.	Normal gland; very large number of eosins.	None.
3	5 ,,	..	..	0·600 ,,	Small, red, and soft.	Differentiation of cortex and medulla poorly marked; large number of eosinophile cells present; lymphoid cells appear to be normal.	None.
4	9 ,,	..	Well nourished.	3·600 ,,	Red and soft.	Gland appears to be normal.	None.
5[1]	8 ,,	4½ lb.	3 lb. 3 oz.	7·5 ,,	Large, red, and soft; thick fluid in the interior of gland.	Normal gland; large number of eosinophile cells present.	None.
6[1]	8 ,,	4½ ,,	3 lb. 1 oz.	6·0 ,,	Large, red, and soft; thick fluid in the interior of gland.	Normal gland; large number of eosinophile cells present.	None.
7	9 ,,	7½ ,,	7 lb.	9·500 ,,	Large, red, and firm; thick fluid in the interior of gland.	Large number of hæmorrhages; gland normal; numerous eosinophile cells.	None.
8	6 ,,	1 lb. 8 oz.	1 lb. 2 oz.	2·500 ,,	Small, red, and soft.	Gland normal; large number of eosins seen.	None.
9	8 ,,	4½ lb.	3¾ lb.	6·0 ,,	Large, red, and soft; thick, yellowish-white fluid in the interior of the gland.	Gland normal.	None.
10	4 ,,	..	..	About the size of a pea.	Lobules of gland were very well marked.	Cortex and medulla not differentiated; no eosinophile cells seen; numerous Hassall's corpuscles.	None.

[1] Twins.

Acute Diseases.

I have collected thirty-three cases of children of all ages from seven days up to fourteen years who had succumbed to the various acute maladies.

Weight of the Glands.

The average weight of the glands in these cases was found to be 5·440 grms. The largest gland weighed 14·070 grms. and the smallest gland weighed 1·250 grm. The average weight of the thymus in acute diseases is less than normal; but if we refer to Table VI. we shall see that the children also lost weight, some considerably, from the acute diseases from which they had suffered. We should expect, therefore, some diminution in the weight of the thymus—an expectation which is realised.

Cause of Death.

The common cause of death was generally found to be some pneumococcic infection, either broncho-pneumonia, lobar pneumonia, empyema, etc. It is impossible to overestimate the importance of the pneumococcus in children's diseases.

Histology.

Hæmorrhages in the substance of the thymus were found in something like 95 per cent. of the deaths from broncho- and lobar pneumonia. They are also often present in deaths from empyema; but we must remember that acute broncho-pneumonia is by no means a rare cause of death in this disease.

Hæmorrhages have also been described in the thymus gland of the new-born, and in deaths from convulsions, whooping-cough, asphyxia, etc. We found in a microscopical section of the thymus gland, obtained from a case of broncho-pneumonia, enlargement of the blood vessels and scattered hæmorrhages throughout both the glandular and connective tissues. In some cases the gland was normal; in others, nothing abnormal was found beyond the hæmorrhages.

Fibrosis was present in a few cases, but was never accompanied by the various changes in the cellular tissues of the thymus which we meet with in marasmus and advanced "secondary atrophy."

Hassall's corpuscles were frequently found to have undergone calcification.

There is little to be found in the literature, as regards the thymus in acute diseases. Peculiar alterations in the histology of the glands have been described in diphtheria, but of these I know nothing.

Dyke Acland has recorded some observations which he made on the thymus in a case of hæmophilia, and in one of "purpura."

There were spherical masses in the thymus, so large as to be readily visible to the naked eye. They were bounded by a layer of flattened elongated cells with well-defined nuclei, and contained many epithelioid cells, some of which had a faint indication of a nucleus. The fibrous stroma of the glands was much increased.

I examined the thymus of two or three children who had purpura among other symptoms, but I never found any changes similar to those described by Acland. Dr. Acland informed me in a private communication that he was not sure of the nature of the bodies which he described.

TABLE VI.—*Acute Diseases.*

Number.	Age.	Average Weight of Children at the various Ages in Lbs.	Weight of my Cases in Lbs.	Weight of Thymus Glands in Grms. and Mgrms.	Appearance of the Thymus Glands at the Autopsies.	Microscopical Examination of the Glands.	Cause of Death. Changes found at the Autopsies.
1	2 years.	26	20¼	6·480	Red and firm.	Scattered hæmorrhages; otherwise normal.	Acute emypyema; acute meningitis.
2	2 ,,	26	18½	5·700	Red and firm.	Calcification of some of Hassall's corpuscles; increase of fibrous tissue; lymphoid corpuscles normal.	Confluent broncho-pneumonia.
3	1 5/12 ,,	20	12½	3·510	White, soft, and œdematous.	Gland appears to be absolutely normal except for hæmorrhages.	Acute broncho-pneumonia.
4	4 ,,	..	Well nourished.	2·920	Firm gland.	Increase of fibrous tissue dividing gland into pseudo-acini; numerous eosins.	Acute pneumococcic meningitis.
5	2½ years.	..	Well nourished.	5·720	Very œdematous; white and soft.	Increase of fibrous tissue which is very œdematous and infiltrated with leucocytes; lymphoid tissue normal.	General pneumococcic infection.
6	5 months.	15	15	9·420	Large, red, and firm; thick fluid in interior of gland.	Normal; very large number of eosins.	Acute broncho-pneumonia.
7	1 year.	20	12	2·720	Red, soft, and small.	Hæmorrhages present; increase of fibrous tissue which is œdematous.	Acute broncho-pneumonia.
8	7 years.	..	Well-developed boy.	6·240	Large, red, and firm.	Gland normal; numerous eosins.	Pyæmia; acute osteo-periostitis.
9	1 1/2 ,,	21	11½	3·660	Red, small, and firm.	Numerous hæmorrhages; slight fibrosis.	Acute broncho-pneumonia.

TABLE VI.—*Acute Diseases*—continued.

Number.	Age.	Average Weight of Children at the various Ages in Lbs.	Weight of my Cases in Lbs.	Weight of Thymus Glands in Grms. and Mgrms.	Appearance of the Thymus Glands at the Autopsies.	Microscopical Examination of the Glands.	Cause of Death. Changes found at the Autopsies.
10	5 months.	15	8½	1·250	Very small and firm.	Marked fibrosis; many eosins.	Pneumococcic arthritis; pneumococcic septicæmia.
11	5 ,,	15	8½	2·200	Red, firm, and small.	Gland normal.	Epidemic diarrhœa; no morbid lesions.
12	14 weeks.	13	7¾	6·255	Large, red, and firm.	Gland normal; numerous hæmorrhages.	Acute broncho-pneumonia; diarrhœa and vomiting.
13	9 months.	18	10½	4·250	Soft, white, and œdematous.	Well-marked fibrosis; many eosins.	Pneumococcic arthritis; pneumococcic septicæmia.
14	6 weeks.	9½	6½	4·620	Red and firm.	Numerous hæmorrhages; slight calcification of many of Hassall's bodies; large numbers of eosins.	Acute broncho-pneumonia.
15	10 months.	18½	12½	4·270	Red and firm.	Gland normal; no hæmorrhages seen; many eosins.	Acute broncho-pneumonia; empyema.
16	6 ,,	..	Very fat child.	8·060	Large, red, and firm.	Gland normal; many eosins.	Acute broncho-pneumonia; rickets.
17	11 ,,	19	14½	4·040	Soft, white, and œdematous.	Gland normal; many eosins.	Lobar and lobular pneumonia.
18	10 ,,	18½	13	5·545	Red and firm.	Gland normal, except for numerous hæmorrhages; many eosinophiles.	Acute broncho-pneumonia; fatty liver.
19	8 ,,	17	14	7·100	Red and firm.	Slight fibrosis; calcification of some of Hassall's bodies; many eosins.	Empyema.
20	5 weeks.	9	6½	3·250	Red and firm.	Gland normal; many eosins.	No morbid lesions; acute diarrhœa.
21	1 ½ years.	21	12½	..	Soft, white, and œdematous.	Well-marked fibrosis; many spindle-shaped connective tissue cells infiltrating gland.	Acute broncho-pneumonia; acute empyema.
22	..	..	12½	2·500	Small, red, and firm.	Many hæmorrhages.	Gangrenous varicella; acute broncho-pneumonia.

TABLE VI.—*Acute Diseases*—continued.

Number.	Age.	Average Weight of Children at the various Ages in Lbs.	Weight of my Cases in Lbs.	Weight of Thymus Glands in Grms. and Mgrms.	Appearance of the Thymus Glands at the Autopsies.	Microscopical Examination of the Glands.	Cause of Death. Changes found at the Autopsies.
23	4 months.	13	9½	3·050	Small, red, and firm.	Slight fibrosis; many hæmorrhages; otherwise normal gland.	Acute broncho-pneumonia.
24	6 ,,	16	13	9·200	Large, red, and firm.	Many eosins; some of Hassall's corpuscles calcified; gland otherwise normal.	Retro-pharyngeal abscess.
25	2 years.	26	20	6·300	White and soft.	Normal; many eosins.	Lobar and lobular pneumonia.
26	1 5/12 ,,	20½	17½	1·600	White and soft.	Numerous hæmorrhages; gland infiltrated with adipose tissue; marked fibrosis.	Acute broncho-pneumonia; adrenal hæmorrhage.
27	13 days.	7½	7½	1·800	Red and soft.	Numerous hæmorrhages; well-marked fibrosis; very few eosins; Hassall's bodies normal.	Acute general pemphigus.
28	1 week.	7	9	7·850	Large, red, and soft.	Gland normal; numerous eosins.	Tetanus neonatorum.
29	6 years.	..	Well-nourished girl.	14·070	Large, red, and firm.	Gland invaded with adipose tissue; some increase of fibrous tissue; some of Hassall's bodies calcified.	Acute rheumatism.
30	7 ,,	..	Well nourished.	10·000	Large, red, and firm.	Many of the Hassall bodies were calcified; gland otherwise normal.	Appendicitis; acute general peritonitis.
31	5 weeks.	..	Well-nourished child.	4·350	Red and soft.	Numerous eosins; gland otherwise normal.	Extreme pallor of all organs; œdema of brain; acute diarrhœa.
32	11 years.	..	Well-developed girl and well nourished.	8·770	Large and firm.	Gland normal.	Acute rheumatic fever; adherent pericardium; chronic mitral disease.
33	14 ,,	..	do.	7·420	Large, red, and firm.	Gland normal.	Acute pericarditis; malignant endocarditis; acute pleuritis, and chronic endocarditis.

Graves' Disease.

I obtained a specimen of an enlarged thymus from a case of Graves' disease through the kindness of my friend Dr. Seligmann.

The gland appeared to be almost normal. Connective tissue corpuscles and endothelial cells were, however, more numerous in places throughout the gland tissue than are met with under normal conditions. Some of Hassall's corpuscles showed well-marked calcification, while others stained in a homogeneous manner with acid dyes. I did not observe anything like the numbers of eosinophile cells as are present in the enlarged thymus glands in children. The alteration in the structure of Hassall's corpuscles which were observed in this case are, of course, quite consistent with those present in a normal thymus.

Hector Mackenzie and Walter Edmunds examined two enlarged thymus glands obtained from cases of Graves' disease. They did not consider that the structure of the gland differed in many respects from the normal, but they thought that the concentric corpuscles did not appear to undergo degeneration so readily as in the thymus glands of healthy people.

The relation which the thymus gland bears to Graves' disease has been under discussion for some years. Sir Astley Cooper refers to a most interesting case in his monograph on the thymus.

A young girl had suffered from severe dyspnœa for a short period, for which he could give no relief. There had been a "swelling" in the neck for some years, but it had increased considerably of late. Deglutition was also affected to some extent. At the autopsy, he found a large thyroid and a very large thymus. It seems to me that this case may have been one of Graves' disease; and if so, it would be the first recorded case in which enlargement of the thymus was observed.

Cases of "Sudden Death" and "Found Dead." "Lymphatism."

I have been able to collect sixteen of these cases. All occurred in children under two years of age, except one case, which occurred in a man aged nineteen, who died from tetanus.

The Thymus Gland.

The average weight of the thymus gland in my cases was found to be 25·11 grms. The largest gland weighed 47·050 grms., and the smallest gland 7·770 grms. Hæmorrhages were seen on the surface of the gland in one case only. Thick fluid, which resembled "pus" to the naked eye, but which consisted almost entirely of lymphocytes, was present in the interior of the gland in every case. I have already dealt fully with the characters of this fluid.

A bacteriological examination of the fluid was made in eight

cases, but in seven it was found to be sterile; in one case I found the pneumococcus. This case has already been described under the bacteriological section.

Microscopical Histology.

The structure of the thymus gland in these cases was found to be normal, except for one point, which is of considerable interest. Eosinophile cells have been described in the thymus, but only the variety which occurs in the blood, and also in very small numbers. I have found in the large or enlarged thymus glands very large numbers of eosinophile cells, which are of four varieties—

1. Large cells, with a single, darkly stained, granular and round or oval nucleus, which is generally situated at the periphery of the cell. Large numbers of coarse eosinophile granules are arranged in an irregular manner around the nucleus.

2. Similar cells, but with a pale, delicately stained non-granular nucleus.

3. Cells with a transitional nucleus.

4. Lastly, the true polymorpho-nuclear eosinophile cells of the blood.

These cells are found scattered throughout the gland tissue, occasionally in clumps, where they form 20, 30, 40, or even 50 per cent. of the cells. We find large numbers along the septa and in the connective tissue, and it is undoubtedly in such situation that these cells are most common. The first and second varieties of eosinophile cells are about equally common, and form at least 95 per cent. of the coarsely granular oxyphil cells in the thymus. The polymorpho-nuclear cells are rarely met with. I found in the thymus of a young rabbit large numbers of the transitional type, which are so common in the bone marrow. The eosinophile cell of the thymus differs from the eosinophile of the blood in two ways—(1) the nucleus, as already stated, is nearly always single, and frequently situated at the periphery of the cell; (2) the granules are generally smaller than those in the true eosinophile cell of the blood.

In some specimens of thymus glands large numbers of eosinophile cells may be seen in the interior of the small blood vessels, which are present in most microscopical sections. Differential counts have shown that the eosinophile cells may form 10 per cent. of the whole. In such situations, however, the polymorpho-nuclear type of eosinophile cells predominate, although a few of the tissue eosinophile cells are also present.

Although these cells are found chiefly along the septa and in the connective tissue, we must remember that in the atrophic thymus in which the connective tissue is generally in considerable excess, the eosinophile cells are usually few in number, and sometimes even absent.

It is also interesting to find that the "tissue eosinophile cell"[1] and the polymorpho-nuclear eosinophile cell may both be present in the interior of small blood vessels. I cannot at present give any exact information as regards the relation which exists between tissue eosinophile cells and those of the blood, if any.

An examination of the blood in cases of enlarged thymus, etc., has rarely been attempted, simply because of the extreme difficulty of making the diagnosis. A case was recorded by James Ewing of a child, æt. 5 years, who died quite suddenly under chloroform. An examination of the blood before death gave the following result:—76 per cent. lymphocytes out of a count of 500 cells, and only 2 per cent. of eosinophile cells. I have examined the blood in one or two "suspected cases," but have not found any eosinophile cells. In rickets, which is so often accompanied by enlargement of the thymus, eosinophilia has been described by Hock (20 per cent.) and Weiss (16 per cent.). Morse found in his cases that the average number of eosinophile cells was 3 per cent., and the highest count was 7 per cent. We should also expect to find that an increase of these cells in the blood of children, as compared with adults, is physiological, if the eosinophile cells found in a normal thymus are in any way related to the eosinophile cells in the blood. Cabot states: "In infancy the percentage of eosinophiles is very often higher than in adults, so that in them eosinophilia may be considered physiological." Ewing appears to arrive at a similar conclusion, namely: "In children a relatively high proportion of eosinophile cells is the rule, and the variation in numbers is slightly greater. The average appears to be about 1·2 per cent. greater than in adults." If all these statements could be accepted without discussion, we might be able to trace some connection between the thymus gland and the eosinophile cells in the blood, but unfortunately this is not possible. First, we must always remember the frequency with which children suffer from the various forms of parasites; even the common thread-worm may produce an eosinophilia of 7 per cent., while the other varieties generally produce a much larger increase in this type of leucocyte. Secondly, we frequently find it stated that the eosinophile cells amounted in a certain case to, *e.g.*, 10 per cent. If, however, we study the literature more carefully, we shall find that only 100 leucocytes were counted. There is not the least doubt that we cannot obtain reliable information unless we make a differential count of 500 leucocytes. I have frequently found that the eosinophile cells amounted to 8 per cent. in the first 100, but when 500 cells were counted they

[1] Eugene Opie has drawn attention to some interesting points in connection with the life-history of the eosinophile cell. He mentions that these cells are found in most glands in the body, but does not include the thymus, and also states that the eosinophile cells are most numerous along the course of the blood vessels in the serous membranes. He makes the most unfortunate observation, however, that the large mononuclear eosinophile cell only occurs in the bone marrow.

only reached about 2 per cent. This observation, of course, applies to all varieties of leucocytes, but more especially to those which are normally few in number, namely, mast cells and eosinophile cells. It is, of course, also most important to know the total number of leucocytes in the blood. If we follow on these lines, we shall find that much of the literature is valueless. Lastly, I have not found that an eosinophilia is so common in children as Cabot and Ewing have claimed. I think, therefore, that although the thymus gland may be one of the seats of origin of the eosinophile cells, there is not yet sufficient evidence for this statement to stand without any fear of contradiction.

I have never seen eosinophile cells in the thymus glands of old people or in old animals. It is in the active glands of healthy children, or in the enlarged glands associated with "sudden death," etc., that we find such enormous numbers. An exactly similar result was obtained from an examination of the thymus glands of young animals. I do not consider that these cells are connective tissue cells with eosinophilic granules, but, on the other hand, I am unable to bring forward any evidence, as yet, as to their true origin.

Results of the Autopsies on my Cases.

I have already referred to the thymus gland as found at the autopsies on cases of "sudden death," "lymphatism," and "found dead." Hypertrophy of the lymphoid tissue throughout the body was present in seven cases. This refers especially to the tonsils, adenoid tissue of the pharynx, and lymphatic glands (especially mesenteric, pharyngeal, and thoracic). I never found enlargement of the papillæ of the back of the tongue to any appreciable extent. The thyroid gland was enlarged in only one case. The solitary follicles of the intestine and Peyer's patches were distinctly enlarged in four cases. We must be very careful before we place much weight on this observation, as the lymphoid tissue in these situations in children is usually very prominent. In the recorded cases, however, definite enlargement was very obvious. Rickets was definitely present in eight cases. Of the remaining cases, death occurred from tetanus in a boy æt. 19, so that it is unlikely that rickets was present; and it was stated that in the last seven cases there was no evidence of rickets. In three cases, however, the children were rather young for rickets. It is quite certain that rickets is very often accompanied by enlargement of the thymus and by hypertrophy of the lymphoid tissue generally, especially that of the pharynx. Jackson Clarke is reported to have said that "hyperplasia of the adenoid tissue in the naso-pharynx and throughout the body was as characteristic of rickets as the hyperplasia of the epiphyses." Some people consider that rickets is secondary to the lymphatic hyperplasia in certain cases. I never observed hypoplasia

of the heart and aorta as described by some observers. The spleen was moderately enlarged in seven cases. Hæmorrhages on the serous membranes was a fairly common lesion in my cases. I never found subcutaneous hæmorrhages. The blood in the right heart was sometimes fluid, at other times clotted, but the heart itself was never overdistended with blood. I always failed to find any thrombosis of veins or arteries in any part of the body, although a careful search was made in each case.

A lymphoid condition of the bone marrow has been recorded in a few cases (Osler).

A summary of the common changes found in these cases is as follows:—Enlargement of the thymus gland; hypertrophy of the adenoid tissue of the pharynx; enlargement of the lymphatic glands throughout the body, but especially the pharyngeal, thoracic, and mesenteric glands; hypertrophy of the solitary follicles and Peyer's patches of the intestine; enlargement of the spleen; and, lastly and very commonly, rickets.

Causes of Enlargement of the Thymus Gland.

(1) Lymphatism, (2) rickets (?), (3) exophthalmic goitre, (4) myxœdema, (5) cretinism, (6) acromegaly, (7) lymphatic leukæmia, (8) lymphadenoma, (9) myasthenia gravis, (10) Addison's disease, (11) scurvy, (12) epilepsy, (13) anæmia, (14) anencephalic fœtus, (15) new growths,[1] (16) lastly, but not least, enlargement from unknown causes.

What Relation does the Thymus Gland bear to "Sudden Death," Lymphatism, and "Found Dead"?

The knowledge which we possess of this subject is almost entirely due to the energy of a few writers, more especially Grawitz, Friedleben, Paltauf, Ewing, Jacobi, and Osler.

Etiology of "Sudden Death."

1. *Suffocation from pressure exerted by enlargement of the thymus.*—The great supporter of this theory is Professor Jacobi. He considers, as the space between the manubrium sterni and the vertebral column is little more than 2 cms. across in young children, and as this space is occupied by the œsophagus, trachea, blood vessels, nerves, connective tissue, etc., that with enlargement of the thymus, if "congestion" should occur for a few seconds, the space is so narrowed that suffocation takes place. Jacobi also considers that pressure on the

[1] Dr. T. D. Savill makes a most unfortunate error in reference to this question. He says ("Enlargement of the Thymus"): "A certain degree of enlargement is normal to childhood, and this may give rise to dulness over the manubrium. In the rare cases, enlargement is met with in after life; it is generally due to carcinoma, and it may be a primary deposit."

recurrent laryngeal and other nerves may have an important bearing on the cause of death in these cases.

2. *Death is due to intravascular clotting.*—It is thought that some substance is secreted by the thymus which produces the above condition.

3. *A specific micro-organism!*

4. *Adenoids.*

5. *Toxæmia.*

6. *Reflex.*

The views of Jacobi have produced more discussion than perhaps any other in relation to the thymus gland. There are both strong supporters and opponents of this theory.

Brouardel considers that the thymus gland does compress the trachea, and that this compression gives rise to a slight degree of spasm, which rapidly causes the child's death. He also refers to a most important point, namely, that as the trachea and bronchi are very elastic in children, they are able to resume their normal states directly the sternum is removed. We cannot, therefore, draw accurate deductions at the autopsy as to whether the trachea has been compressed or otherwise. Grawitz, however, who called the attention of the profession to the relation of the thymus gland to sudden death in 1888, considered that death was not due to compression of the trachea and bronchi, because the calibre of the air passages was not reduced in size in any of the autopsies in his cases.

Siegel, quoted by Osler, mentions the following case:—A boy, æt. 2½ years, had had for two and a half weeks cough and dyspnœa, the latter of which was worse at night. Tracheotomy was performed without relief, but at a subsequent operation the anterior mediastinum was opened from above. A piece of the thymus gland appeared at the site of the operation, and therefore the gland was stitched to the fascia over the sternum. The child made a complete recovery. König, also quoted by Osler, removed a portion of the thymus gland, with a similar result. Caillé reported a case of sudden death in a child, æt. 6 months, due, in his opinion, to compression of the large blood vessels by an enlarged thymus. Putnam referred to a similar case in a child under his care. The thymus gland at the autopsy was found to weigh 6 oz. All these observers and many others agree in the main with Jacobi.[1] Some physicians consider that weakness of the head and neck muscles is a possible factor as a cause of death in cases of enlarged thymus. Trousseau, on the other hand, one of the most able physicians who ever lived, considered that death in these cases was due to spasm of the glottis. Paltauf believed that capillary bronchitis was the cause of death in

[1] Dr. Frederick Taylor has recorded a case of lymphatic leukæmia associated with enormous enlargement of the thymus, but unaccompanied by any dyspnœa.

many of these cases. He stated that this disease was often difficult to diagnose in young infants unless the smaller bronchi were carefully slit up with fine scissors, and that, therefore, many deaths which were incorrectly ascribed to the thymus were really due to broncho-pneumonia. Thursfield, in the paper quoted above, describes in detail four cases of sudden death which he collected at the Great Ormond Street Hospital. He favours the view that death is due to a "toxæmia," chiefly from the fact that one of his cases developed hyperpyrexia before death. Blumer, as a result of an analysis of nine cases, has elaborated a similar theory. There are some who hold that vascular thrombosis is the cause of death in most of these cases. W. G. Spencer gives his support both to this theory and to the pressure theory. He contends that even though there is no evidence of pressure on the trachea in the post-mortem room, we must not say that such a condition does not exist; the relations are quite different in the living subject. There is not, however, to my mind, the slightest evidence in favour of the view of intravascular clotting. I obtained only negative evidence from post-mortem observations on my own cases of enlarged thymus. Thursfield and many others have arrived at a similar conclusion.

Thymic Asthma, or Millar's Asthma, or Laryngismus Stridulus.

Thymic asthma has been described as a very severe dyspnœa which occurs in infants and very young children, and is due to an enlargement of the thymus gland which obstructs respiration by pressure on the trachea. Many German physicians considered that the laryngismus stridulus of English writers was really thymic or Millar's asthma. I will briefly refer to the opinions which have been expressed by the most eminent physicians in Europe and America as to whether such a disease as thymic asthma really does exist.

Strümpell writes as follows:—

"The old name of thymic asthma arose from the idea that the attacks were due to an increase in the size of the thymus gland, but this opinion is wholly unfounded."

Henoch is, if possible, still more emphatic on this question—

"Anything else that has been written on the etiology of laryngeal spasm is either hypothetical or positively incorrect; particularly the view that the disease arises from enlargement of the thymus gland (asthma thymicum); which view still has its supporters."

Osler has written by far the most exact summary on this important subject. I will refer to a few of the chief points to which he has drawn attention:—

"There can be, I think, no question that the ordinary laryngismus seen in rickety children is a convulsive affection, and is *not* the result *of compression*." "But a very greatly enlarged thymus may seriously hamper the structures within the thorax."

He then mentions Siegel's and König's cases, to which I have already referred.

Friedleben, whose name is so closely associated with the thymus gland, was the first to oppose strongly the view that the enlargement of the thymus gland was the cause of such dyspnœa. Osler completes his account of thymic asthma, after referring to Siegel's and König's cases, as follows:—

"These are cases that go far to disprove Friedleben's dictum—*Es giebt kein asthma thymicum.*"

Herard, in 1847, published a monograph on spasms of the glottis. He considered that the thymus gland bore no relation to sudden death.

There is no doubt that those German physicians who considered that thymic asthma and laryngismus stridulus were synonymous terms were incorrect; but if we give our full attention to the subject, we shall observe that both "symptoms" are very commonly associated with one group of pathological phenomena, generally known as the lymphatic constitution.

One of my cases (No. 1, Table VII.) died quite suddenly.

The child, æt. 16 months, was seen sitting up in bed playing with her toys, about two minutes afterwards she was found to be dead. Many suggestions were made at the time as to the cause of death, such as laryngismus stridulus, enlarged thymus, etc.

I found, at the autopsy, well-marked evidence of rickets and hypertrophy of the lymphoid tissue throughout the body. There was no evidence of intravascular clotting, and no distension of the right side of the heart with blood. The thymus gland was found to be absolutely normal.

I doubt if any physician could accurately ascribe a cause for death in this case. The point, however, to which I wish to draw attention is that rickets, and with it hypertrophy of the lymphoid tissue throughout the body, is frequently associated with cases of sudden death. Enlarged thymus is often found in such cases, although in the case in question the gland was normal. The relation which laryngismus stridulus bears to rickets has long been recognised. John Thomson writes:—

"Laryngismus occasionally occurs . . ., but in the great majority of cases it is met with in rickety children. . . ."

Lymphatism.

The attention of the profession has been drawn to this important disease especially by the work of Paltauf. It occurs chiefly in children and young adults. It has been found that subjects of this affection die quite suddenly, or during the administration of an anæsthetic, slight operation, or while bathing. The sad death of Professor Langerhans' son, as soon as his father had given him a preventative dose of anti-diphtheritic serum, was considered to be due to lym-

phatism. Osler relates one case of death under anæsthesia for adenoids. Some physicians consider that deaths during convalescence from infectious fevers are due to this condition. Sometimes children are noticed to be unwell by their parents for a short time before "sudden death" occurs. They have either refused food or will not play with other children, or have suffered from slight sickness or diarrhœa. Occasionally these children have had one or more convulsions before death. In four of my cases convulsions are known to have occurred. In one case there was one convulsion; in two cases the convulsions lasted for some few minutes; in the fourth case the child had one fit after another for a few hours, and was quite unconscious between each fit, till the fatal termination occurred.

The great objection to the diagnosis of lymphatism is the fact that it has been made a "refuge for the destitute." There are some people who, as one observer remarks, "know more about lymphatism than they do about consolidation of the lungs." In fact, the lymphatic constitution is found to be almost a matter of everyday experience, similar to so-called thymic abscess; but even in face of these facts there is no doubt that lymphatism is a most important disease.

We now come to the large group of cases known as "found dead." There is no doubt that many of these cases are examples of overlaying. Mr. Wynn Westcott and other coroners have done much to prove that this view is correct. On the other hand, most of these children,—certainly in my cases,—were found to have well-marked enlargement of the thymus. One of the most perfect examples of lymphatism recorded was No. 9, Table VII., of my series.

I strongly oppose the view that all cases of "found dead" in infants are examples of lymphatism, but I must say I think that some of these cases are undoubtedly due to this affection. There is no need to discuss this question any further, as no one but the mothers of these babies can supply the true facts required, and they generally prefer not to do so.

Graves' Disease and Lymphatism.[1]

Sudden death is known to occur in Graves' disease. Hale White has recorded two examples of this calamity. At a discussion, at the Clinical Society of London, on 120 cases of Graves' disease brought forward by Professor Murray, Dr. Hale White stated that he had found enlargement of Peyer's patches and of the lymphoid follicles of the intestine in certain cases of exophthalmic goitre.

In Seligmann's case, from which I obtained the thymus gland, it was proved at the autopsy that there was enlargement of the spleen, lymphatic glands throughout the body, lymphoid follicles, and Peyer's patches of the intestine, thymus and thyroid glands. The patient was killed in a street accident.

[1] The relation of the thymus gland to Graves' disease has already been referred to.

TABLE VII.—"*Sudden Death*," "*Found Dead.*"

Number	Age.	Average Weight of Body.	Weight of Body.	Weight of Thymus Gland.	Condition of Thymus Gland at Autopsy.	Microscopical Examination of Thymus Gland.	Result of Autopsy.	Cause of Death, etc.
1	$1\frac{4}{12}$ years.	20 lb.	15½ lb.	7·770 grms.	Large, red, and firm.	Normal gland.	Rickets. Hypertrophy of the lymphoid tissue throughout the body.	Child died suddenly while in bed playing with her toys.
2	$1\frac{7}{12}$,,	22 ,,	14½ ,,	22·106 ,,	Large, red, and firm, except the right lobe, which contained a large abscess cavity in which was thick reddish-brown fluid, from which was obtained a pure culture of the pneumococcus (*see* text for particulars).	Gland appeared to be normal.	Rickets. Overdistended stomach (contained large quantity of potato-skins); hypertrophy of the lymphatic tissue throughout the body.	Child taken ill quite suddenly with a sort of convulsion and fell back dead.
3	3 ,,	11 ,,	$9\frac{5}{12}$,,	28·060 ,,	Large, red, and firm.	Gland normal; large numbers of eosins.	..	Found dead in bed.
4	8 ,,	18 ,,	13½ ,,	29·030 ,,	Large, red, and firm; cultures from cavity in thymus gland were sterile.	Gland normal; numerous eosinophiles.	..	Found dead in bed.
5	6 ,,	16 ,,	13½ ,,	18·037 ,,	Large, red, and firm.	Normal gland; enormous numbers of eosinophiles.	Rickets; general lymphatic hypertrophy.	Death in convulsions.
6	1 year.	20 ,,	14½ ,,	34·00 ,,	Large, red, and firm; cultures from glands were sterile.	Normal gland; numerous eosins.	Rickets; general lymphatic hypertrophy.	Sudden death.
7	10 months.	18½ ,,	17 ,,	22·050 ,,	Large, red, and firm.	Gland normal; numerous eosins.	..	Found dead in bed.
8	9 ,,	18 ,,	$14\frac{7}{12}$,,	31·050 ,,	Large, red, and firm; cultures from gland sterile.	Large numbers of hæmorrhages, otherwise normal gland; eosins plentiful.	..	Found dead in bed.
9	5 ,,	15 ,,	$10\frac{13}{12}$,,	47·050 ,,	Large, red, and firm.	Gland normal; numerous eosins.	Rickets; general glandular hypertrophy; enlargement of spleen and thyroid, etc.; some blood clot on right side of heart, but not overdistended; no intravascular clot discovered; hæmorrhages on both pleuræ.	Found dead in bed.

TABLE VII.—"*Sudden Death*," "*Found Dead*"—continued.

Number.	Age.	Average Weight of Body.	Weight of Body.	Weight of Thymus Gland.	Condition of Thymus Gland at Autopsy.	Microscopical Examination of Thymus Gland.	Result of Autopsy.	Cause of Death, etc.
10	19 years.	Full-sized man; body well nourished.	..	17·250 grms.	Large, red, and firm.	Calcification of Hassall's corpuscles; gland otherwise normal; no eosins seen.	None.	Death from tetanus.
11	11 weeks.	12 lb.	$9\frac{7}{16}$ lb.	46·500 ,,	Large, red, and firm.	Gland normal; large numbers of eosins.	None.	Sudden death.
12	1½ year.	22 ,,	12½ ,,	10·820 ,,	Large, red, and firm.	Gland normal; numerous eosins.	Rickets; acute bronchitis; general enlargement of the lymphatic glands; enlarged spleen; enlargement of the solitary follicle of the intestine and Peyer's patches; tonsillar hypertrophy.	..
13	8 months.	Well nourished.	..	35·070 ,,	Large, red, and firm; no hæmorrhages seen on surface of gland.	Normal gland; numerous eosinophile cells.	Rickets; enlarged mesenteric glands, Peyer's patches, and solitary follicles of intestine; enlargement of the spleen; general lymphatic enlargement; thyroid not enlarged.	No cause for death; sudden onset of convulsions, terminated fatally in a few hours.
14	5 ,,	15 lb.	12¾ ,,	20·400 ,,	Large, red, and firm. A culture from fluid in interior of gland was found to be sterile.	Normal gland; numerous eosins.	Rickets.	Convulsion; death occurred in a few minutes.
15	9 ,,	18 ,,	$15\frac{7}{16}$,,	20·00 ,,	Large, red, and firm; cultures sterile.	Normal gland; eosinophile cells numerous.	None.	Found dead in bed.
16	4 ,,	14 ,,	$9\frac{7}{16}$,,	11·00 ,,	Large, red, and firm; cultures sterile.	Normal gland; large numbers of eosins.	None.	Found dead in bed.

We might, therefore, describe this case as an example of lymphatism occurring in Graves' disease in an adult male. Sections of the spleen, which were examined in this case, showed prominent Malpighian bodies, many of which had undergone hyaline degeneration. It appears, therefore, that certain cases of Graves' disease

have pathological phenomena similar to those that are known to occur in lymphatism.

Conversely, it has long been known that in some cases of lymphatism, enlargement of the thyroid has been present.

TABLE VIII.—*Showing Average Weights of the Thymus Gland obtained from various Sources.*

No.	Source.	Number of Cases.	Average Weight of Gland.
1	Primary atrophy	15	2·680 grms.
2	Secondary atrophy (tuberculous)	26	3·065 ,,
3	,, ,, (non-tuberculous)	12	2·605 ,,
4	Acute diseases	32	5·440 ,,
5	Fœtal specimens	10	6·53 (1)[1] ,, or 4·575 (2) ,,
6	"Sudden death." "Found dead"	16	25·011 ,,

[1] This result is probably incorrect, as I have included the large thymus of the anencephalic fœtus. The second average is, therefore, more likely to be correct.

It will remain for pathologists in the future to trace the connection between all these various links, and to establish the condition known as "sudden death" on a pathological basis, instead of the hypothetical basis on which it now rests.

In conclusion, I wish to offer my best thanks to Mr. Shattock for the great interest which he has taken in this monograph, and for much valuable help.

To the Staff of the East London Hospital for Children, with whom I was closely associated as pathologist, I have to express my gratitude for the full use of pathological material; to Dr. Coutts, Physician to the Shadwell Hospital, for many valuable suggestions, and for the great interest which he has always taken in this work; lastly, to Dr. Rose, to whom I am indebted for some of the most valuable pathological material, derived from the East End of London.

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DESCRIPTION OF PLATES XIII.–XV.

PLATE XIII.

FIG. 1.—Normal thymus gland of a child, æt. 2 years. (× 225 diameters.)

FIG. 2.—This specimen of a thymus gland shows a coarse cellular structure, which is due to large endothelial cells which have replaced to some extent the normal lymphoid tissue. (× 225 diameters.)

FIG. 3.—A section of a thymus gland from a case of marasmus. Observe the large size of, and the numerous Hassall corpuscles; two of which, to the left of the figure, have undergone hyaline degeneration. (× 450 diameters.)

FIG. 4.—Atrophied thymus gland removed from a case of broncho-pneumonia. The darkly coloured areas represent hæmorrhages. (× 225 diameters.)

FIG. 5.—Atrophied thymus gland from a case of secondary atrophy of glandular tissue largely replaced by adipose tissue. (× 225 diameters.)

PLATE XIV.

FIG. 6.—An isolated area of thymus gland from an old man, lying in a mass of adipose tissue. A Hassall corpuscle can be seen in the upper part of the figure. (× 225 diameters.)

FIG. 7.—Same Hassall corpuscle as shown in Fig. 6, but more highly magnified. (× 450 diameters.)

FIG. 8.—Hassall corpuscle which has undergone calcification. (× 450 diameters.)

FIG. 9.—A section of an atrophic thymus which shows large areas of fibrous tissue. (× 225 diameters.)

FIG. 10.—A specimen of an enlarged thymus gland which shows an enormous number of eosinophile cells. (× 450 diameters.)

PLATE XV.

FIG. 11.—Same specimen as Fig. 10, but much more highly magnified. ($\frac{1}{12}$ oil imm.).

FIG. 12.—Specimen of an enlarged thymus gland removed from a case of sudden death in an infant. Weight of gland, 34 grms. (Nat. size.)

FIG. 13.—(*a*) Specimen of a thymus gland removed from a case of sudden death in an infant. Weight of gland was 46·5 grms. (*b*) Thymus gland obtained from a case of marasmus. Weight of gland was found to be only 0·905 grms. (*c*) Thymus gland which was obtained from a case of secondary atrophy and found to weigh only 0·345 grms. (Nat. size.)

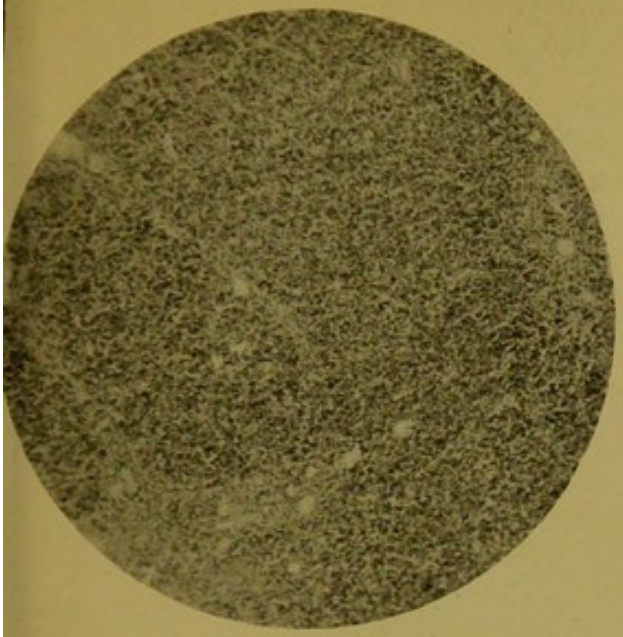

Fig. 1.

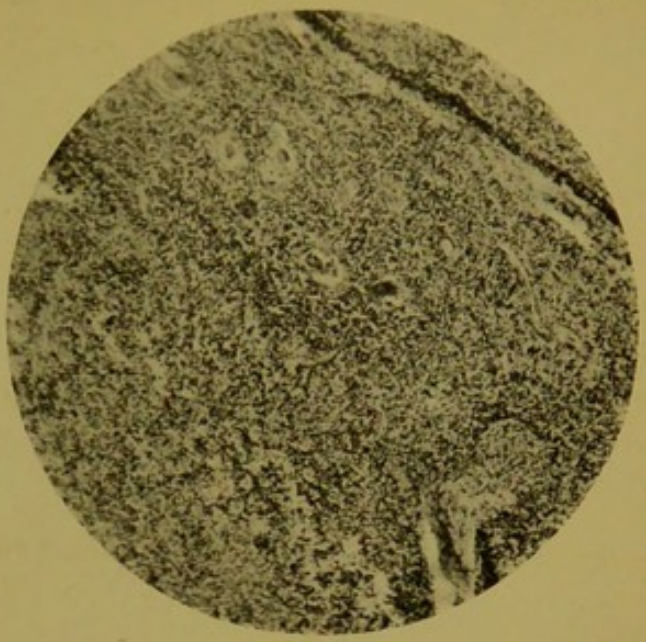

Fig. 2.

Fig. 3.

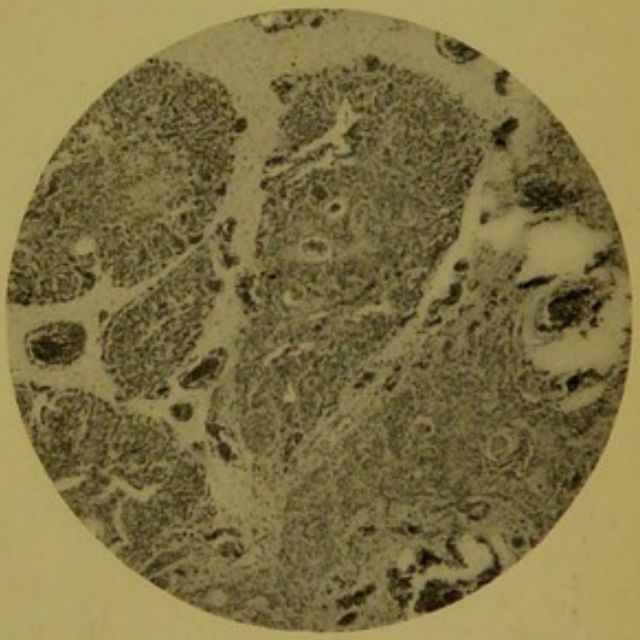

Fig. 4.

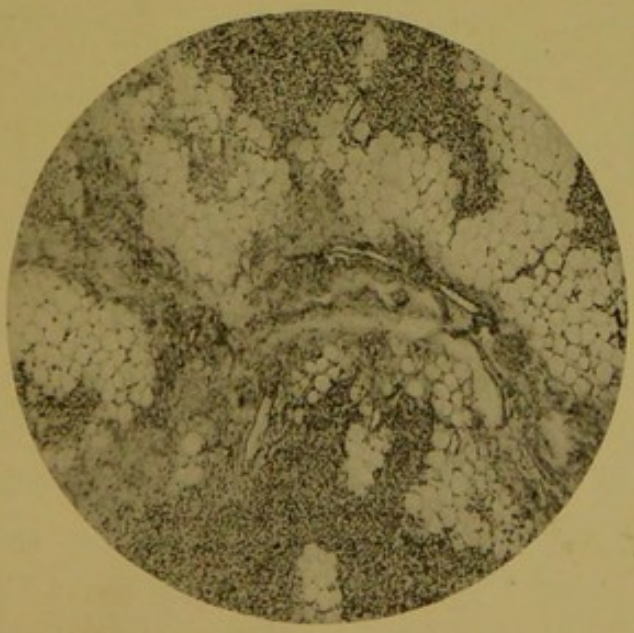

Fig. 5.


ROYAL COLLEGE OF SURGEONS OF ENGLAND
LIBRARY

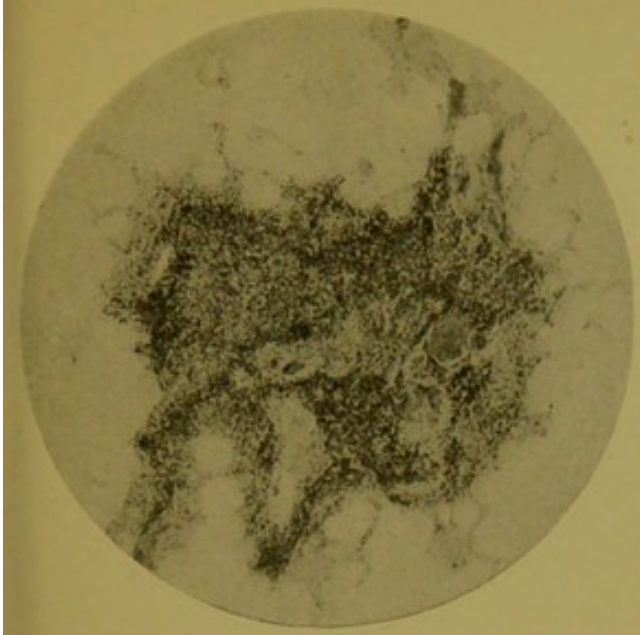

FIG. 6.

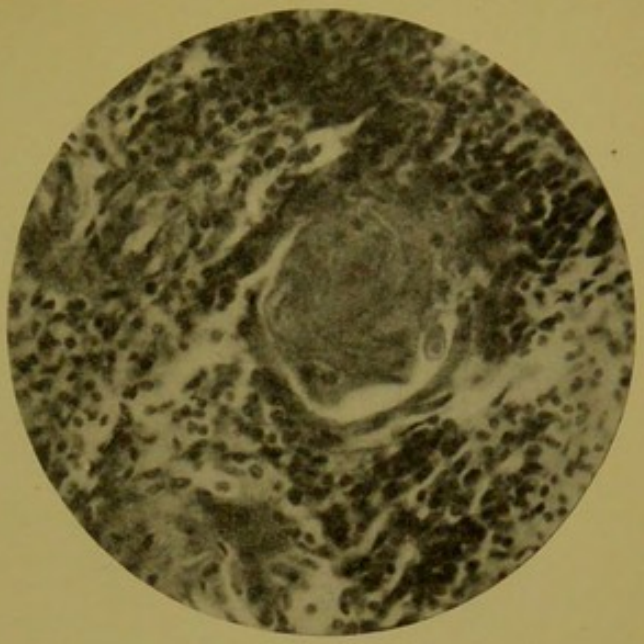

FIG. 7.

FIG. 8.

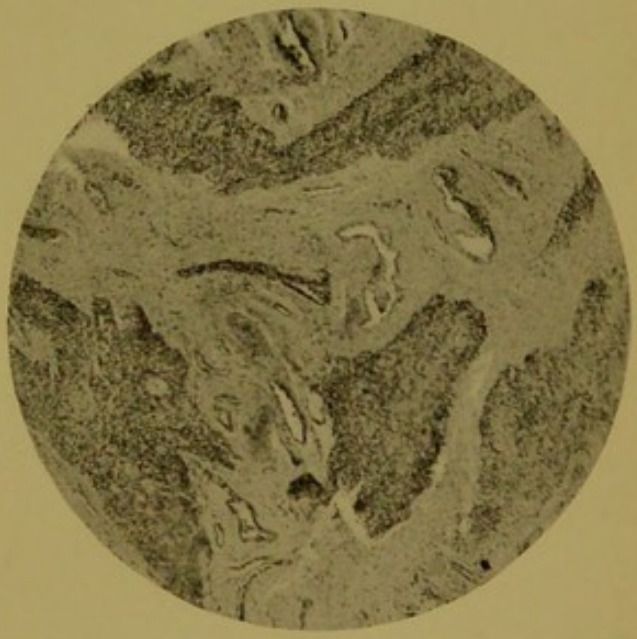

FIG. 9.

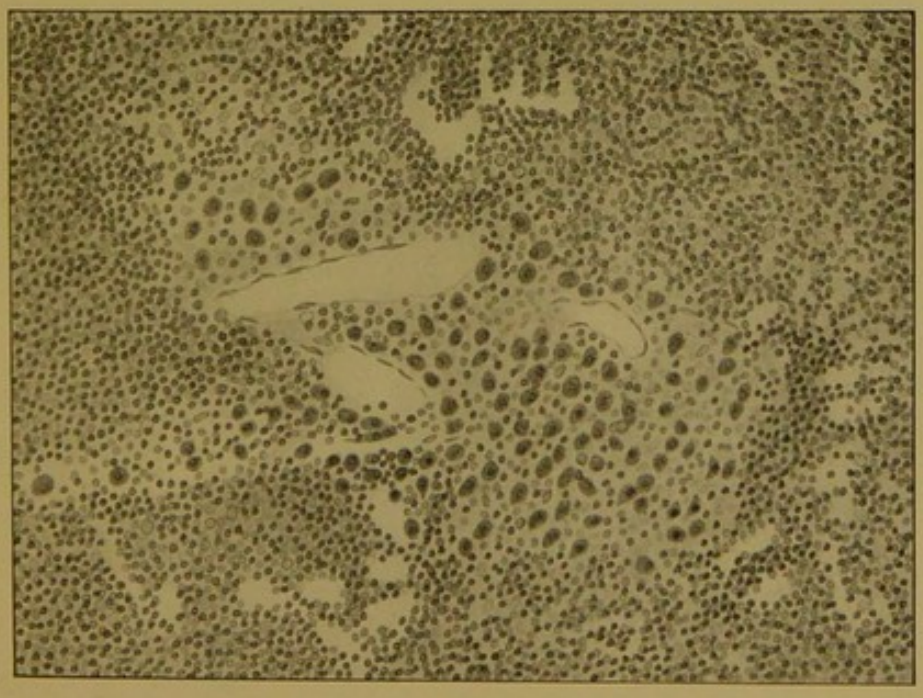

FIG. 10.