

PROGRESS IN PEDIATRICS

A REVIEW OF SOME RECENT PUBLICATIONS ON ANATOMY AND PATHOLOGY

G. M. SMITH
ST. LOUIS

THE AURICULOVENTRICULAR BUNDLE IN DIPHTHERIA

Ever since Mönckeberg's¹ investigation of the myocardium and bundle of His in connection with cases of death in diphtheria, it has been known that the effect of diphtheria toxin on the auriculoventricular bundle has not been a selective one, and that this special structure of the heart tissue undergoes pathologic changes in this disease quite similar in character to that of the rest of the myocardium. These and other investigations of the heart in diphtheria have often been conducted on patients dying of the disease, who during life did not necessarily show symptoms typical of cardiac failure or of heart-block. Tanaka² examined fifteen hearts of children dying during the course of or after diphtheria. He found that the acute cardiac weakness was due to general myocardial changes without involvement of the auriculoventricular bundle, and he concludes that the changes in the latter tissue can seldom be regarded as the cause of death. Fatty degeneration and a "waxy-like" degeneration of the muscle fibers consisting of loss of cross striations with a partial or complete loss of nuclear staining, were found as the chief changes in the His bundle.

Rohmer,³ in particular, has taken up recently the study of heart disease in children with special reference to the involvement of the auriculoventricular bundle. His investigations clinically were supported with observations on the heart by means of the electrocardiogram, and for this reason the anatomical findings in cases of heart-block described by him as appearing between two and three days before death, are important and a distinct contribution to this subject. The His bundle from Tawara's node to a point beyond the division into the right and the

1. Mönckeberg, J. G.: Untersuchungen über des Atrioventricularbündel im menschliche Herzen. Jena, 1908.

2. Tanaka, T.: Ueber die veränderungen der Herzmuskulature, vor allem des Atrioventricularbündels bei Diphtherie. Virchows Arch. f. path. Anat. 1912, Bd., cxcvii, Part 1.

3. Rohmer, P.: Neuere Untersuchungen über den Diphtherieherztod. Jahrb. f. Kinderh., 1912, lxxvii, Part 4, p. 391.

left branches was examined in serial section. Rohmer found that, although the myocardium in general gave striking evidence of fatty and inflammatory changes, the bundle of His, in sharp contrast, was only slightly affected and that, too, only in a few scattered places. In both cases the left branch of the auriculoventricular bundle gave evidence in places of a waxy degeneration associated with interstitial changes, but in no region was this more extensive than one-half the diameter of bundle tract. Rohmer supplemented his clinical observations experimentally with the injection of rabbits with sublethal and lethal doses of diphtheria toxin, without being able to produce histologic evidence of injury to the conducting bundle. Rohmer concludes that in diphtheria, pathologic changes in the auriculoventricular bundle are, to a certain degree, independent of changes in other parts of the myocardium, and that the conducting tissue may or may not be affected. At all events, no specific selective action exists on the part of diphtheria toxin for the tissues composing the His bundle. Diphtheria toxins may, however, so affect the conducting bundle from a functional stand-point that a heart-block can be produced without demonstrable anatomical lesions.

THE LESIONS IN THE LUNGS CAUSED BY THE INFLUENZA BACILLUS

Davis⁴ points out that during epidemics of influenza, pneumonia is found in 5 per cent. of cases with a mortality that varies between 15 and 50 per cent. Davis has had occasion to study the pneumonic lesion in connection with five cases of influenza meningitis which occurred in children during the first two years of life. The bronchopneumonia developed early in the course of the disease, making its appearance at times even before the development of symptoms indicating an involvement of the meninges. The lungs in all five cases were affected in much the same manner, the lower lobes on both sides showing the principal areas of consolidation. Although a delicate layer of fibrin covered the visceral pleura over the regions of consolidation in the lung, in no case were adhesions formed, nor was there fluid exudate in the pleural cavities. The pneumonia was found to be lobular in character, and morphologically resembled the bronchopneumonia seen as a complication of many other infectious diseases. The author found in these cases histologic evidence of fibrin in the pulmonary alveoli, but this was not abundant. The smaller bronchi appeared to be the site of severest infection. The influenza bacilli were found in the bronchial exudate but associated with other microorganisms. Complications such as hemorrhage, necrosis, abscess, gangrene, or bronchiectasia were not noted in this series of cases.

4. Davis, D. J.: The Changes in Influenzal Pneumonia. *Jour. Infect. Dis.*, 1912, x, 259.

BRONCHIOLITIS OBLITERANS

In 1901 Lange⁵ described first in adults two cases of disease of the bronchi which he designated as "bronchiolitis obliterans," in which, as the name implies, an obliterating process occurred involving the smaller bronchioles. Since his publication, there have appeared at intervals, descriptions of other cases of quite similar nature affecting both adults and children. In some of these cases the etiologic factor was found in severe irritation of the bronchi, as by inhalation of irritant gases or foreign bodies; in other instances the etiology has been very obscure. Wegelin's⁶ case appeared in a child of 3½ years in whose trachea a plum stone had become lodged. The smaller bronchioles and lung alveoli, even at a distance from the primary source of irritation, showed the characteristic lesions at the death of the child seven weeks after the accident. Dunin-Karwika⁷ has observed another case occurring in a girl of 16 years. The patient died on the eleventh day of her illness after exhibiting prostration, rapid pulse and respiration, a moderate temperature, and coarse râles over both lungs. The appearance of both lungs was edematous, and the cut surface of the lung showed numerous small prominent whitish nodules suggesting miliary tuberculosis. The microscopic sections, in brief, showed that most of the finer bronchioles were more or less filled with a round, polyp-like, newly-formed tissue continuous at a constricted basal portion with a much thickened and infiltrated peribronchial connective tissue. The alveoli of the lung, also, in places were compressed by thick fibrous septa that were continuous with the peribronchial tissue. In some regions there was noted in the alveolar spaces an actual ingrowth of connective tissue similar to that which so typically affected the bronchioles. Dunin-Karwicka believes that the intrabronchial connective tissue masses have their origin from the connective tissue around the bronchioles, and the latter condition represents an inflammatory reaction of the peribronchial lymphatics induced by gaseous, mechanical, or bacterial irritation. Other observers have thought that an injury to the bronchial epithelium is the earliest lesion; and that the fibrinopurulent exudate in the lumen of the bronchiole, in a chemotactic way possibly, causes an ingrowth of the connective tissue from the bronchial wall, and in this way undergoes an organization. A possible bacterial origin of the disease is suggested by the sudden onset with a chill and the subsequent febrile course, both of which have been described clinically in association with the respiratory symptoms. In this connec-

5. Lange: Ueber die eigentümlichen Erkrankungen der kleinen Bronchien und Bronchiolen. *Deutsch. Arch. f. klin. Med.*, 1901, lxx, 342.

6. Wegelin, C.: Ueber Bronchitis obliterans nach Fremdkorperaspiration. *Beitr. z. path. Anat. u. z. allg. Path.*, 1908, xliii, 439.

7. Dunin-Karwicka, Marie: Ueber bronchiolitis obliterans. *Virchows Arch. f. path. Anat.*, 1912, ccx, 87.

tion, it may be added, acute parenchymatous changes have in some instances been found in the liver, the kidneys, and in the lymph-nodes. Although the condition of bronchiolitis obliterans may unquestionably be of secondary character, Dunin-Karwicka concludes from the study of her own case and a critical review of the literature that this disease of the bronchioles may be of a primary nature.

INFANTILISM ASSOCIATED WITH FUNCTIONAL AND ORGANIC LESIONS IN
THE KIDNEY—RENAL INFANTILISM

About two years ago Fletcher⁸ described a case of infantilism associated clinically with symptoms of polyuria and exhibiting post mortem advanced sclerotic changes in the kidney. Since this publication a number of other writers have reported similar cases of infantilism which apparently find as their chief visceral symptom a striking disturbance of renal function. Miller and Parsons⁹ divide renal infantilism into two groups. Group 1. Renal infantilism with organic renal disease (chronic interstitial nephritis). Group 2. Renal infantilism without organic renal disease (diabetes insipidus). The first group, the authors have again subdivided into cases of congenital nature exhibiting or not cardiovascular changes, and also a form of renal infantilism originating after birth.

Miller and Parsons have not alone followed clinically a number of these cases, but also have had opportunity of studying the lesions post mortem. The children of this type gave as a symptom during life a polyuria associated constantly with exaggerated thirst. The urine showed the presence of varying amounts of albumin and sometimes casts. The physical and the mental growth of the infant was very slow; so that, for instance, at the age of 9, one patient resembled a child of 3.

At autopsy the striking lesion was seen in the kidneys. Both kidneys as a rule were small, with coarsely granular surface. The cortex was found much decreased in size and the pyramids fibrous. Microscopically the principal change was a marked increase of connective tissue affecting the whole organ. The glomeruli showed extreme fibrous and hyaline changes, the tubules exhibiting dilatation and atrophy. The heart muscle gave evidence of hypertrophy and moderate fibrous changes in some instances. No detailed histological descriptions of the ductless glands are included in the autopsy reports and it is therefore assumed that these appeared normal. A case, exhibiting infantilism, polyuria without an albuminuria (Group 2, renal infantilism without organic

8. Fletcher, M.: Case of Infantilism with Polyuria and Chronic Renal Disease. Proc. Royal Soc. Med., 1910, Part 1, p. 93.

9. Miller, R. and Parsons, L.: Renal Infantilism. Brit. Jour. Child. Dis., 1912, ix, 289.

renal disease, diabetes insipidus), was reported only from the clinical standpoint. Miller and Parsons think that syphilis could be excluded as a factor causing the interstitial changes in the kidney; and they do not believe that the condition of infantilism is due to an internal renal secretion. This class of symptomatic infantilism the authors conclude, is secondary to a perversion of the renal functions, and they "regard the stunting of the growth as due to excessive drainage from the persistent polyuria and albuminuria."

THE HISTOLOGICAL CHANGES OCCURRING IN THE ADRENAL GLAND
DURING INFANCY

The studies of Kerr¹⁰ on the anatomy of the adrenal gland confirm, to a great extent, the earlier observations of Kawamura¹¹ and also Thomas,¹² both of whom have shown that the adrenal gland in the course of the first year of life undergoes a definite degeneration of its inner cortical cells. Kern's work aimed at a systematic study of the adrenal gland from the time of birth, through the various periods of childhood until the twelfth year. The technic employed for the examination of tissue was a simple one, and consisted in the preparation of frozen sections of adrenal tissue after fixation in Formal-Müller solution. The stains employed were those commonly used for tissues, including the stains for fat.

As a result of these studies Kern divides the changes occurring in the adrenals of infancy and childhood into four stages. The first stage, seen at the time of birth, shows as a characteristic distinction a marked hyperemia in the capillaries of the innermost zone of the adrenal cortex. The hyperemia gradually causes a separation of the cells of this layer with evidence of compression and beginning degeneration of the cytoplasm and nuclei of its cells. The second period occurs in children at about the end of the first month and extends to about the end of the first year. During this period the degeneration of the inner layer of the cortex becomes more distinct, and at the same time the cells of the medullary area are developed. The latter include both chromaffin cells and the perivenous cortical cells of the medulla. The third period is concluded on the average near the end of the first year. The characteristics of this period are the gradual subsidence of the hyperemia of inner cortex and the cessation of degeneration of its cells. The chromaffin cells of the medulla become well developed, and are separated from the cortex by circularly arranged interstitial tissue of the zone which had previously

10. Kern, H.: Ueber den Umbau der Nebenniere in Extrauterin Leben. *Deutsch med. Wehnsch.*, No. 21, p. 971, 1911, No. 21, p. 971.

11. Kawamura: *Die Cholesterinverfettung (Cholesterinsteatose)*. Fischer, 1911.

12. Thomas: Ueber die Nebennieren des Kindes und ihre Veränderung bei infectionskrankheiten. *Ziegler's Beitr. z. path. Anat. u. z. allg. Path.*, 1911, 1.

undergone degeneration. The fourth period extends indefinitely from the first year until period when growth ceases. In this period the connective tissue capsule separating medullary and cortical cells, gradually is reduced, and the final adult arrangement of cells is assumed.

In his studies on the adrenals of various animals Kern was not able to find anything analogous to the human stages of degeneration; nor could Delwitsky,¹³ after examining at different periods of life the adrenals of rats, find in the growth of the glands of this animal any of the phenomena of degeneration as seen in man.

In connection with the definite stages of growth exhibited in the adrenal of the normal child, it is of interest to note that in abnormal conditions of development as seen, for instance, in anencephaly, the degenerative processes of the cortex may be especially rapid in onset. R. Meyer¹⁴ who has recently studied the adrenal gland in cases of anencephaly found, however, that the adrenal may appear in such instances of anencephaly entirely normal in all its histologic details. Still, in half the cases of anencephaly in which the adrenal was found to be present in the body, Meyer noted that the medulla of the gland was hyperplastic and differentiated to a stage beyond what was the usual for a normal fetus of corresponding age. Where a diminution in the size of the gland exists in anencephaly, this occurs as a result of an early degeneration of the zona reticularis and the inner part of the zona fasciculata, the two zones which physiologically undergo degeneration during the first year of life. In nearly one-half the cases of anencephaly Meyer found that the whole adrenal on one or both sides was absent.

THE THYMUS

Although within a short period of time there have appeared publications, notably by Hammar,¹⁵ Biedl¹⁶ and Schridde,¹⁷ presenting in a most complete manner our present knowledge of the thymus in health and disease, still a number of recent communications have again fixed attention on this organ.

13. Delwitsky, W. L.: Beiträge zur Histologie der Nebennieren. Ziegler's Beitr. z. path. Anat. u. z. allg. Path., 1912, xxv, 431.

14. Meyer, R.: Nebennieren bei Anecephalie. Virchows Arch. f. path. Anat., 1912, ccx, 158.

15. Hammar, T. A.: Fünfzig Jahr Thymus forschung, Kritische Uebersicht der Normalen Morphologie. Ergeb. d. Anat. u. Entwicklungsgesh, 1910, XIX, 1-274.

16. Biedl, A.: Innere Sekretion. Ihre physiologischen Grundlagen und ihre Bedeutung für die Pathologie, 1910, p. 107.

17. Schridde, H.: Thymus, in Aschoff's Pathologische Anatomie, 1911, ii, 166.

Weidenreich,¹⁸ has apparently placed beyond doubt the fact that the thymus should be regarded as an organ which is active throughout nearly the entire period of life, in the production of white blood-cells. This conclusion was reached from the morphologic study of very freshly fixed material taken from normal persons who had been executed and from one who met death by drowning. Weidenreich found that in man the cortical cells of the thymus are typically lymphocytes which present not alone the morphologic characteristics of such cells, but possess also the peculiar property of differentiation in the direction of granular leukocytes. He noted that in the thymus both the eosinophil and neutrophil granular leukocytes developed from the non-granular lymphocytes, and also the remarkable fact that differentiated forms of granular leukocytes were developed in the thymus through mitotic division. He points out that this is the first time mitotic division of granular leukocytes has been observed under normal conditions outside of the bone-marrow.

The forms of leukocytes which Weidenreich found produced in the human thymus included the myelocytes, lymphocytes, plasma cells, mast cells and the eosinophil and neutrophil leukocytes, with transitional forms of leukocytes.

He believes that these forms of blood-cells after reaching their proper stage of development, are removed from the thymus by means of lymph-vessels and in this way reach the general circulation.

Weidenreich was unable in any case to demonstrate the formation of red blood-cells in the thymus, as nucleated red blood-cells or other embryonal forms did not appear. His findings, he believes, are of significance in proving that the formation of granular leukocytes does not occur exclusively in the bone-marrow. It is of interest to note that the evidence of active white blood-cell formation occurred even in a man who was 39 years old. This would lead to the belief that the activity of the gland is not limited merely to the earlier periods of life. Indeed, several writers of late have pointed out that the thymus may exist in a perfect state of development even after mid-life. It has been suggested that the well-known atrophy of this organ may in part be due to the decrease in size which is known to occur very rapidly under abnormal conditions of metabolism.

Weidenreich confines his observations entirely to the study of the thymus cortex. In his publication he makes no attempt to determine the relation of the cortex to the epithelial elements of the medulla. Whether or not the medullary part of the thymus with epithelial cells

18. Weidenreich, Franz: Die Thymus des Ernachsonen Menschen als Bildungsstätte ungranulierte und granulierte Leukobyten. München med. Wehnschr., 1912, *xlvi*, 2601.

developed from the branchial clefts is possibly associated with a specific function of the gland, is not discussed in the paper.

THE THYMUS IN CONGENITAL SYPHILIS

Ribbert¹⁹ has recently contributed to the subject of congenital syphilis of the thymus, approaching the subject from the standpoint of developmental disturbances in the thymus due to lues. He concerns himself with the lesion known as Dubois' abscesses which are known to occur in the gland in congenital syphilis, and which, as the result of the studies of Eberle,²⁰ are generally regarded as collections of pus occupying preformed cavity spaces representing the dilated epithelial canals of the thymus anlage.

The case in point, studied by Ribbert, was a syphilitic new-born infant, exhibiting typical symptoms of lues, including an osteo-chondritis. The thymus, the size of a pigeon egg, allowed on section an escape of pulpy, gray-yellow purulent material, representing the content of several cystic cavities occupying the substance of the gland. The microscopic examination of this exudate showed it to consist of masses of cells resembling pus cells, necrotic in character, with nuclei, for the most part, that could not be definitely distinguished. The organ, as a whole, was composed histologically of a system of cavities held together by loose connective tissue. The inner lining of the cavity wall consisted of a stratified squamous epithelium. Next to the epithelial layer was found a clear zone of connective tissue, external to which, in a third zone, were irregular masses of lymphoid cells. Ribbert, like Eberle, believes that these cystic cavities of the thymus represent the original spaces of the canal system of the thymus, dilated by an accumulation of cellular exudate. The original epithelium remaining as a lining to the cavities, undergoes a further development, and becomes a stratified squamous epithelium like that of the pharynx. No Hassall's bodies were found. In general, the relation of epithelium to lymphoid tissue resembles that seen in the region of the tonsils. Ribbert regards the cystic condition of the thymus as an arrest in the development of the gland, and believes that histologic study establishes the fact that the cortical cells of the thymus are not developed from the medullary epithelial cells. In this regard he opposes the well recognized view held by Stoehr.²¹ The histologic relations of Dubois' abscesses, Ribbert adds, vary in appearance according to period of development in which the syphilitic infection of the thymus has taken place; and therefore the

19. Ribbert, H.: Die Entwicklungsstörung des Thymusdrüse bei congenitales Lues. *Frankfurter Ztschr. f. Pathol.*, 1912, xi, 209.

20. Eberle: *Ueber Congenitale Lues des Thymus*. Dissert., Zurich, 1894.

21. Stoehr, P. L.: *Ueber die Abstammung der kleinen Thymusrindenzellen*. *Anatomy*, 1910, xl.

findings in his case, representing an unusually early affection of the thymus do not necessarily picture the condition when syphilitic involvement of the thymus has occurred at a stage of later fetal development.

STATUS THYMUS LYMPHATICUS

Schridde,²² during the past year, has had opportunity to study a number of cases of death associated with status thymus lymphaticus and has grouped the lesions found in these cases as characteristic of this condition. At autopsy, he found the skin in cases of status lymphaticus death to be of a peculiar pallor, the subcutaneous fat well developed, pale yellow, and unusually moist. The normal thymus, weighing 12 gm. in the new-born and between 20 and 25 gm. at puberty, involutes, according to the author, so that between the twentieth and twenty-fifth years only traces of the thymus are found. In instances of status lymphaticus Schridde has found that the thymus might weigh between 60 and 80 gm. As a rule the hypertrophy is not so marked, occasionally the organ is normal, or, indeed, below the normal in weight. The microscopic changes in the thymus, the writer considers to be constant and characteristic. These consist of a distinctive hyperplasia of the medulla associated with an underdeveloped yet otherwise normal cortex. Hassall's corpuscles are, however, relatively few in number yet large in size. They do not exhibit the usual morphology, but consist, for the most part, of centrally located fatty masses without nuclei. This typical hyperplasia of the medulla of the thymus is present as a lesion in instances of status thymolympathicus not alone found in children but also in adults. It is characteristic of both the small thymus as well as of the enlarged thymus that may be found in this condition.

Besides the changes in the thymus, Schridde finds that a hyperplasia of the malpighian corpuscles of the spleen is constantly present, which at times lead to a visible enlargement of the organ. Conspicuous hyperplasia of the lymphatic tissue of the gastro-intestinal tract is also encountered. In this connection, Schridde emphasizes the enlargement of the lymphatic follicles at the base of the tongue and the tonsils. The constant hyperplasia of the lymph follicles of the tongue, Schridde considers to be especially important in distinguishing clinically cases of status thymus lymphaticus. Two specific instances are cited in which death in patients with status lymphaticus followed the injection of salvarsan, the first in a boy 10 years of age, the second in a woman of 50.

EXPERIMENTAL OBSERVATIONS ON THE THYMUS

The slowly accumulating evidence that the thymus has a rôle as an organ of internal secretion has gained support by the remarkable obser-

22. Schridde, H.: Die Diagnose des Status thymolympathicus. München. med. Wehnschr., 1912, xlviii, 2605.

vation on the metamorphosis of the tadpole, made by Gudernatsch²³ in feeding experiments. The experiments have been conducted since 1911 and are published as a preliminary note in 1912. In brief, tadpoles of different ages were fed various mammalian tissues, and among these thyroid and thymus. The effects on the developing tadpole fed on thyroid and thymus were opposite in character. Fed with thyroid, growth of the tadpole ceased but metamorphosis began at once, with the final result that small dwarfed frogs were produced. On the other hand, animals fed with thymus, continued to grow rapidly and formed large tadpoles. In some of these animals fed on thymus, a metamorphosis failed entirely to make its appearance.

The studies of Klose²⁴ and Matti²⁵ on thymectomized dogs have also revealed the close relationship between the thymus and processes of development, especially with regard to the growth of bone. Klose found that puppies about 10 days old are most suitable for these experiments because at this age the gland is relatively large, bearing a relation of 1 to 170 to the body-weight, and is then possibly most active. Reduction of the size of the gland is rapid soon after the tenth day, so that at the end of the third month the proportion to the body-weight is 1 to 1,200 or 1,600. Excision of the thymus was performed under most careful surgical technic in order to insure a complete removal of the gland. Small gland rests left behind proved to be the source of a rapid regeneration of the whole gland. Matti²⁵ like Klose, found that practically no changes occurred in thymectomized dogs until after a period of latency of about four weeks, when the animal developed a general weakness, various curvatures of the long bones, and a definite inhibition in the growth of the bones of the legs which was very apparent when compared with the normal control dogs of the same litter. Interference with growth became gradually more conspicuous from this time on. The development of the skull was retarded and even a typical "rosary" was noted at the costochondral junction of the ribs. The slow but progressive cachexia resulted eventually in the death of the animals. Matti believes that morphologically the changes in bone found in thymectomized animals agrees closely with those described as occurring in human and also animal rachitis and that these depend chiefly on the fact that a calcium assimilation by newly-formed and over-produced osteoid tissue does not take place. The characteristic weakness in voluntary muscles exhibited by the thymectomized animals, was found histologically to be

23. Gudernatsch, T. F.: Fütterungsversuche an Amphibienlarven. *Zentralbl. f. Physiol.*, 1912, xxvi, 323.

24. Klose, H.: Nerve Thymus forschungen und ihre Bedeutung für die Kinderheilkunde. *Arch. f. Kinderh.*, 1911, lv, 1-50.

25. Matti, H.: Untersuchungen über die Wirkung experimentelles Ansschaltung der Thymusdrüse. *Mitteil a. d. Grenzgeb d. Med. u. Chir.*, 1912, xxiv, 665.

associated with atrophy and evidences of other forms of degeneration in the muscle cells. The study of the various other organs of the dogs in whom the thymus had been removed at an early age leaves still in doubt the question of interrelation between thymus and these organs. Hypertrophy of the medulla of the adrenal appeared, however, to be a constant finding associated with the removal of thymus in the young dogs of Matti's experiments.

MELENA NEONATORUM

Advances in the study of the physiology of blood coagulation have resulted in throwing considerable light on a number of hemorrhagic diseases occurring not alone in adults but also in children. Whipple²⁶ by an analysis of the elements of coagulation has been able to demonstrate the fact that, in a number of hemorrhagic diseases, the normal balance between the elements instrumental in the production of coagulation may become so affected as to bring about the occurrence of hemorrhages with the sequence of symptoms and lesions which have become recognized as characteristic of disorders of this nature. Of interest, in particular, was the study of a case of melena neonatorum. A new-born child apparently healthy at the time of birth, developed bleeding from the nose, foreskin and intestine, together with jaundice. Death occurred on the fifth day. The blood from this patient remained uncoagulated even after twenty-four hours contact with tissues in the body and the absence of antithrombin, in consequence, was excluded as a causative factor of non-coagulation. Fibrinogen and calcium were tested for and found present in the usual amounts. Thrombin and prothrombin were found to be the essentials lacking in the production of the coagulation process in the case in point. Of interest were the histologic findings in the lung alveoli, which showed the presence of old fibrin, but none of fresh formation, indicating, as Whipple points out, that the necessary elements of coagulation were present at the time of birth, yet disappeared in the next few days during which the fatal symptom developed.

The use of injections of blood-serum with its thrombin becomes, as a result of these observations, a valuable therapeutic measure in cases of melena of this nature.

PATHOLOGY OF ACUTE POLIOMYELITIS

Peabody, Draper and Dochez²⁷ in a monograph on acute poliomyelitis devote a chapter to a consideration of the pathology of this disease. The authors emphasize at the outset that acute poliomyelitis is essentially a general infection, although heretofore chiefly the lesions of the central

26. Whipple, G. H.: Hemorrhagic Disease. Septicemia—Melena Neonatorum, and Hepatic Cirrhosis. *Arch. Int. Med.*, 1912, ix, 635.

27. Peabody, F. W., Draper, G., Dochez, A.: A Clinical Study of Acute Poliomyelitis. *Monographs Rockefeller Inst. Med. Research*, 1912, p. 18.

nervous system have been studied. The probable path of entry of the virus through the lymphatics of the nasal passages to the meninges is discussed and the anatomic relation of the perivascular lymph spaces of the meningeal vessels to the cerebrospinal fluid is pointed out. The earliest changes in the cord are found in the hyperemia and round-cell collections in the lymph spaces that surround the blood-vessels entering the anterior and lateral aspects of the spinal cord. The cellular exudate, edema, small hemorrhages and probable direct toxic action of the virus, are regarded as responsible for the degenerative changes in the nerve cells of the cord, affecting both the gray and the white matter. Histologic changes in the posterior root ganglia are found to be of constant occurrence. The brain, medulla and pons may also show a hyperemia, cellular infiltration about the vessels and degeneration of the nervous elements. In organs other than the nervous system changes of constant occurrence were noted. In brief, lymphatic glands, thymus and spleen reacted to the virus by swelling, and histologically the endothelial cells of the germinal centers were found large, swollen and pale. Phagocytosis was active in the lymphatic glands; degeneration of both lymphoid and endothelial cells with even extensive necrosis are described. A proliferation of the endothelial cells of the lymph-sinuses was also seen. Conspicuous histologic changes were found in the liver, where, like in typhoid fever, areas of necrosis with lymphoid cells and polynuclear leukocytes were seen.

TUBERCULOSIS OF BONE

Fraser²⁸ has studied the tuberculous lesions of bone in eighty human cases, beside the experimental lesions of bone produced in rabbits and guinea-pigs. The subject of bone tuberculosis he discusses from the following standpoint: (a) The development of the primary tubercle; (b) associated changes in the marrow, periosteum, bone lamellae and blood-vessels; (c) the gross pathologic varieties of bone tubercle; (d) necrosis and sequestrum formation.

Fraser finds that the tubercle bacillus enters the marrow either through the blood-stream (intravascular infection) or through the lymphatics closely associated with the blood-vessels (perivascular infection). The tubercle developed as a result of intravascular infection is rare, and is thought to be produced by the occlusion of a small blood-vessel of the marrow by an embolus of tubercle bacilli. The perivascular infection is secondary to tuberculous inflammation of adjacent synovial membranes and the development of the tubercle is characterized as a gradual process. The histology of tubercle formation differs in a number of ways, dependent on one or the other method of infection. The final appearance of

28. Fraser, T.: The Pathology of Tuberculosis of Bones. *Jour. of Pathol. and Bacteriol.*, 1912, xvii, No. 2, p. 254.

tuberculous tissue is, however, much the same in each mode of infection. A central cystic degeneration of the tubercle is found to be of frequent occurrence in later stages of the disease. Calcification of nodules is rare, although this may occur after a primary deposit of calcium in a giant cell has extended to the rest of the tubercle.

Of considerable interest is the detailed study of the associated changes taking place in the affected bone during the period of tubercle development. In the earliest stages of the disease immature forms of polymorphonuclear leukocytes and shortly afterward polymorphonuclear neutrophil leukocytes appear, both types exhibiting high phagocytic powers. Nucleated red cells increase in number and gigantoblasts at times are found. The polynuclear leukocytes are replaced by the lymphocytes and mononuclear cells. Fibrous changes in the marrow follow on the cessation of active growth in the tubercle, the connective tissue cells being derived from the connective tissue cells lying among the fat cells, and also from the perivascular tissue. The bone lamellae now undergo either rarefaction or thickening. In the former process bone absorption is effected through the cellular activity of osteoclasts or through a chemical change in the lamella, noted by characteristic staining reaction associated with the disappearance of calcium. The fibrous elements of the bone lamellae alone remain. Lamellar thickening was found in most of the chronic forms of bone tuberculosis, commonly accompanied by an obliterative endarteritis. The fibrosis of blood-vessels, the author believes, is due to the circulation of a tuberculous toxin, through the vessel. The lesion affects the smaller vessels and occasionally the primary divisions of the nutrient artery. Fibrous changes in the bone-marrow are attributed to disturbances of nutrition induced by the vascular changes in the blood-vessels. Besides the general discussion of tuberculosis affecting bone, the author describes in detail the changes found in six different forms of tuberculous disease of bone. These are (1) the encysted tuberculous lesion, (2) the infiltrating lesion, (3) intermediate form of lesion, (4) atrophic, (5) hypertrophic and (6) the acute miliary lesion. Spina ventosa and the formation and characters of different kinds of sequestra have also received careful description.

10 North Kingshighway.