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XV.

A MALIGNANT ADENOMA OF THE ADRENAL WITH TRANSFORMATION INTO SARCOMATOUS TISSUE.

By J. C. Meakins, M.D., Resident Pathologist.

Reports Presbyterian Hospital New York -

Malignant adenomata of the adrenal are uncommon, and especially uncommon are adenomata which show in the primary tumor or in the metastasis sarcomatous transformation. Such a condition is paradoxical, but the embryology of the adrenal affords an explanation. It was formerly believed that the cortex of the adrenal develops from the mesoblast and the medulla from the epiblast. The studies of Janosik and Gottschau, Minot[1] and Aichel,[2] have established the fact that the entire adrenal develops primarily from the mesoderm. The mesoderm divides into two parts: the mesochymal part forms the connective tissues, and from the mesothelial part develop the serous membranes, the genito-urinary tract (except the urinary bladder) and the striated muscles. The mesothelial structures undergo greater differentiation than mesochymal tissues and take on certain "epithelial" characters.

It may be assumed that the cells of a malignant tumor do not acquire new features but revert to a former state; there is reversion first to the characters latest acquired and finally to the original embryological condition. This view may help to explain peculiarities of the following case. Since the cells of the adrenal are mesothelial in origin and assume epithelial functions, tumors arising from them may exhibit epithelial characters of new growth, but revert to the primitive mesodermal type more readily than cells primarily of epithelial origin.

The patient with the tumor, which will be described, was ad-

mitted to the Presbyterian Hospital on January 6, 1908, in the service of Dr. Eliot. I wish to express my thanks to Dr. Eliot for permission to report the following facts concerning the history of the case:

The patient, W. N., was white, male, aged forty-five years, and by occupation a letter carrier. His family history is unimportant. He was born in the United States, where he has always lived. Many years ago he used alcohol in moderation; he had gonorrhœa in 1897. Otherwise his history contains nothing noteworthy.

In 1905 the patient had hematuria for a week without subjective symptoms. He remained in good health until December 24, 1908, when he noticed that his urine was dark brown. Three days later he suddenly developed severe pain in the left flank. It was not influenced by deep respiration or by movement, but on assuming the right lateral position it was greatly increased. No bright red blood was observed in the urine.

Physical examination revealed a prominence in the left flank and on palpation a large, tender tumor was found in this region. It disappeared under the costal margin and could be moved only in an antero-posterior direction. There was flatness from the fourth intercostal space to the crest of the ileum, concealing the splenic dullness. When the patient assumed the right lateral position the tumor approached almost to the median line. The heart, lungs and nervous systems were normal. Blood examination showed no abnormality.

The urine was dark brown, acid, and had a specific gravity of 1020. It contained about 0.1 per cent. albumin, and no glucose. Microscopical examination revealed hyaline and granular casts, many red blood cells, leucocytes and epithelium. Urea was 2.7 per cent. The ureters were catheterized and the urine from the two sides had practically the same characters, but the right kidney was excreting the greater amount.

On January 6, 1908, Dr. Eliot found at operation a large, firm, nodular mass, occupying the site of the left kidney. It

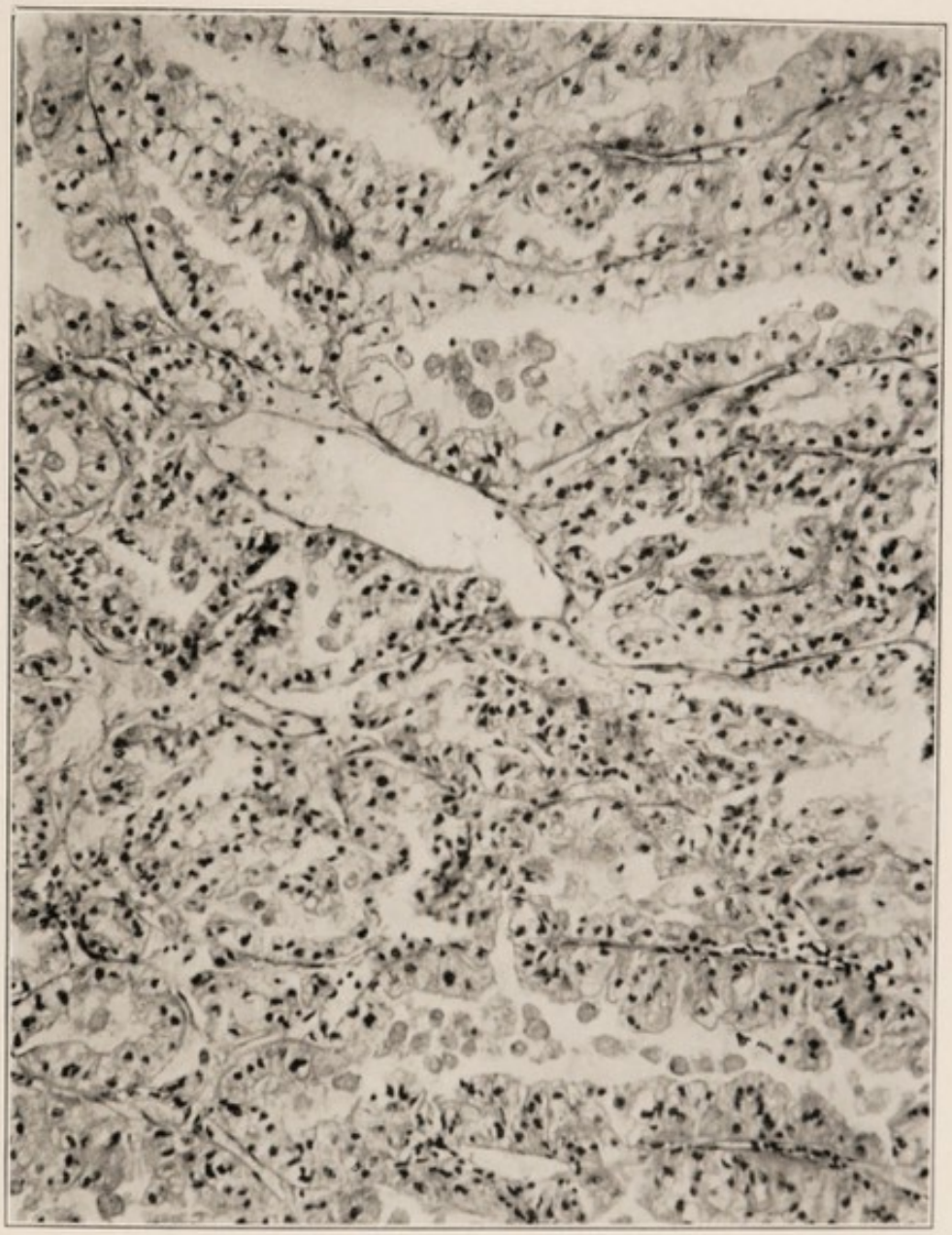

FIG. 1—ADENOMATOUS TISSUE

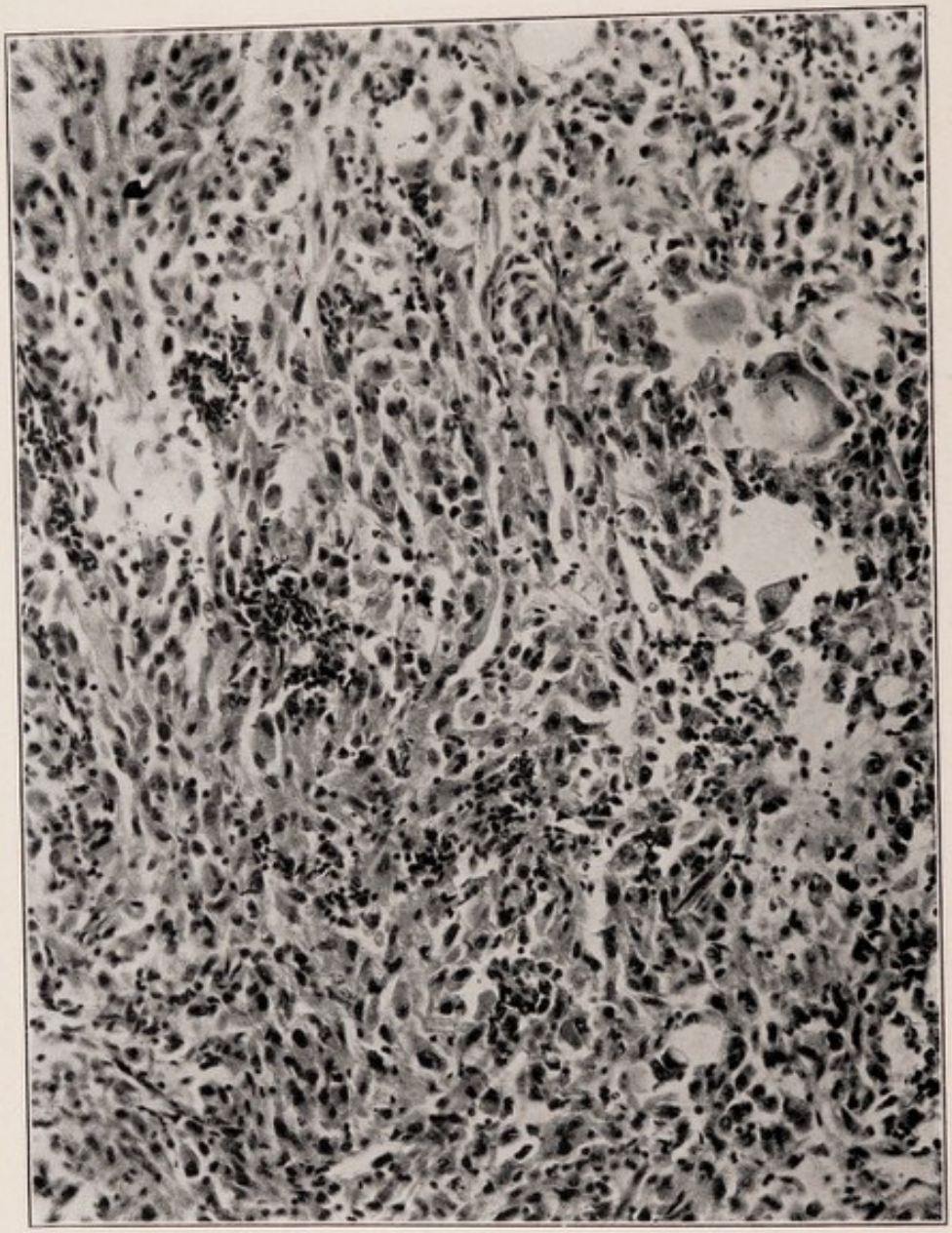

FIG. 2—SARCOMATOUS TISSUE

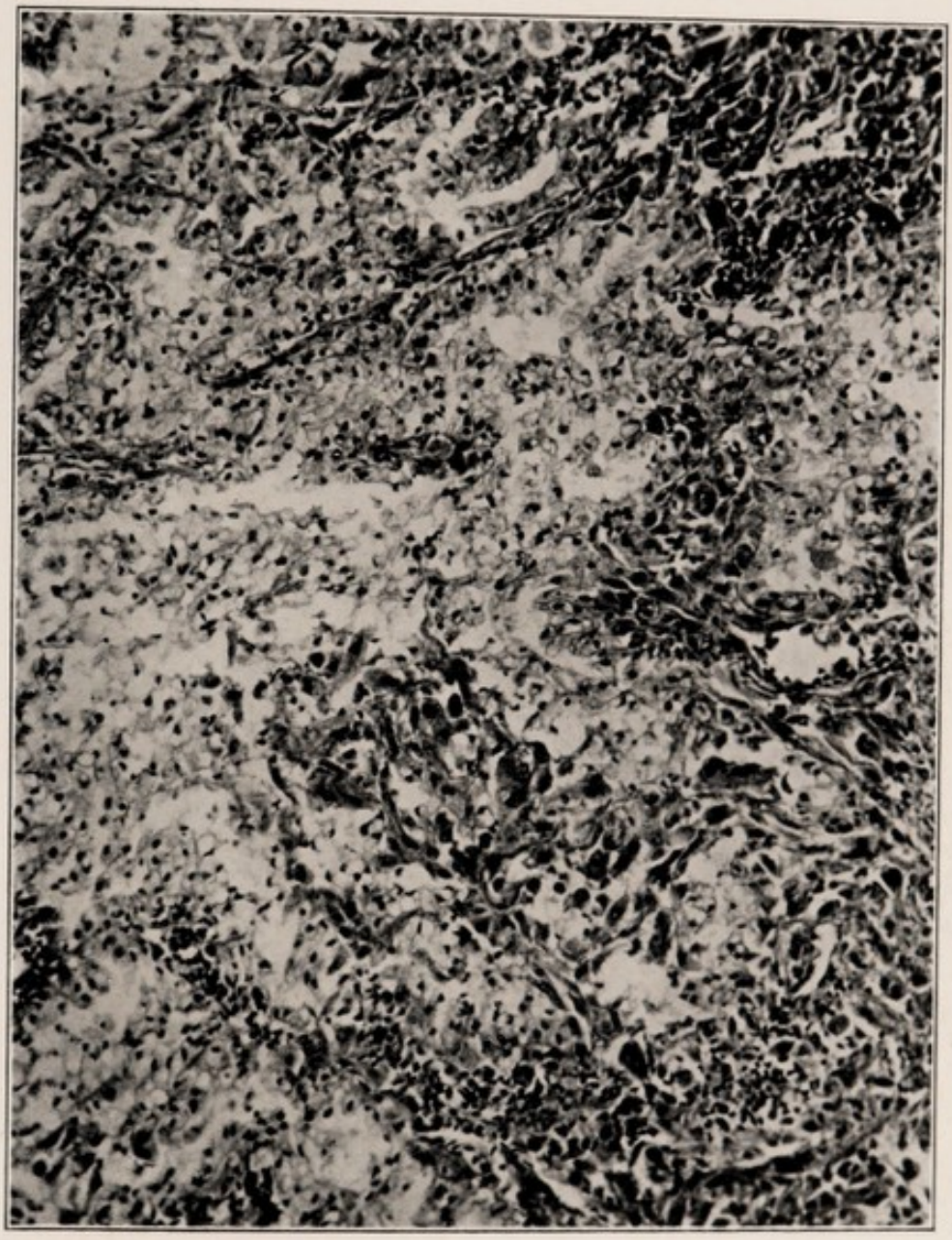

FIG. 3—TRANSFORMATION FROM ADENOMATOUS INTO SARCOMATOUS TISSUE

extended from above the costal margin downward almost to the crest of the ileum. The tumor pushed the peritoneum forward and to the right, but was completely retroperitoneal. It was removed with great difficulty and there was considerable hemorrhage.

Pathological Examination.

The specimen has the general shape of a kidney, measuring 18 x 11 x 10 cm. The outer part consists of a thick layer of perirenal fat in which are imbedded tumor nodules of various sizes. These tumors are yellowish white and very friable. They contain many blood-vessels and into some of the nodules hemorrhage has occurred. Many of the larger masses seem to infiltrate the surrounding fat. This perirenal mass, although thickest at the upper pole, completely surrounds the kidney and is removed with little damage to the kidney substance.

The kidney measures 13 x 7 x 4 cm. The posterior surface is smooth and the anterior surface and the borders contain tumor nodules similar in character to those in the perirenal fat. After longitudinal section through the pelvis the kidney is found almost entirely replaced by new growth. The only part of the cortex which remains intact is upon the posterior surface of the organ. The tumor nodules may be divided into two varieties, according to the color and consistence. The nodules of one variety are white, more or less granular and very friable. Those of the other variety are yellowish and firm. In some nodules the two varieties are combined and merge into each other. The white nodules exhibit a tendency to infiltrate the surrounding structures. Reference will be made later to this distinction.

Microscopical sections were made through different parts of the new growth and the changes which were found may be divided into two groups. In some sections the cells had the typical appearance and arrangement of adenoma, while in others the arrangement was sarcomatous.

Adenomatous Tissue.—The histological appearance presented by the tumor tissue of this type is entirely different from that observed in the sarcomatous areas. The difference is not so much in the character as in the shape and arrangement of the cells. The cells are cuboidal with a faintly staining protoplasm which is finely granular. The nucleus is usually situated near the periphery of the cell. It is round and vesicular, with a deeply stained nucleolus and a pale chromatin network. These cells closely resemble those of the adrenal cortex.

The cells in a single layer are arranged to form tubular alveoli. The alveoli are usually straight, but occasionally are tortuous. The lumina are patent and frequently contain débris derived from desquamated cells. Between the alveoli there are fibrous trabeculæ fairly rich in cells. The reticulum is well demonstrated by Van Gieson's stain, and does not extend between the tumor cells. Broad bands of connective tissue separate the tumor into lobules, and from these bands the trabeculæ between the alveoli are derived. (Plate I).

In some of the larger tumor masses of this type the cells at the periphery of the mass differ from those in the centre. In the centre the cells tend to lose their distinctly alveolar arrangement. The lumen disappears and the trabeculæ become less distinct. The cells at the same time become longer, although the nucleus does not change.

Sarcomatous Tissue.—There are found in such parts of the tumor various types of cells which may be grouped in three classes. (1) Some of the cells closely resemble those of the normal adrenal cortex. They have a large, deeply staining nucleus, which, as a rule, is round, but occasionally assumes an oval shape. The cell body is small and, corresponding in shape to the nucleus, is round or oval. The protoplasm takes eosin poorly. These cells are not numerous or uniformly distributed but occur in small collections, chiefly about the blood-vessels. Under the low power of the microscope they closely resemble lymphocytes but, with a

high magnification, a difference is apparent. (2) Closely associated with these cells there are large spindle-shaped cells which form the greater part of the tumors. The protoplasm of these cells stains poorly and contains fine granulations and sometimes small vacuoles. The nucleus is large and as a rule spindle-shaped, but frequently is irregular in shape. It stains poorly and has a fine chromatin network; there is a deeply staining nucleolus which is situated towards one end of the nucleus. (3) Besides these cells there is a large irregular cell with a faintly staining irregular nucleus. The cell body contains many vacuoles, some of which are large and appear to fill the whole protoplasm, displacing the nucleolus. (Plate II).

A series of transitions between the three kinds of cells described above indicates that they are all derived from the same source, namely, the cortical cells of the adrenal. Mitotic figures are very common, and both regular and irregular types are observed. Multinucleated cells are frequently found and the nuclei are usually arranged at the periphery of the cell.

In sections stained with Van Gieson's stain broad bands of connective tissue are found, separating the tumors into lobules. In addition a few fine strands of reticulum are occasionally found between the cells, but as a rule the cells are closely packed together. This is especially true where the spindle cells predominate. These cells are arranged with their long diameters more or less parallel, but without any evidence of alveolar arrangement.

The blood-vessels are abundant and are in intimate contact with the tumor cells. In fact the walls of the veins in many places are formed by tumor cells covered by endothelium, and occasionally a vein was found whose lumen the tumor had invaded. A section through the vessels at the hilus of the kidney shows one of the smaller veins almost completely obliterated by a parietal thrombus. A mass of tumor cells found at the point of attachment of the thrombus appears to be the cause of the thrombosis.

The sarcomatous type of tissue is present alone in the white,

friable nodules, described above, and is the predominating form of tissue in the perirenal mass; these tumor nodules invade the surrounding tissues. In the kidney substance the nodules of this type are large and ill defined, showing invasive characters. The yellowish nodules have the histological structure of adenoma and are circumscribed. In some of the tumor masses both white and yellow tissue is found, and in these nodules sarcomatous and adenomatous structures are side by side. As a rule, the two types are well isolated by bands of fibrous tissue, but in some places the adenomatous structures exhibit the loss of alveolar arrangement described above; the cells become spindle-shaped and their nuclei take on an oval form and become paler. A complete transition may be traced in the same tumor from a purely adenomatous structure to one with typical sarcomatous cytology and arrangement. (Plate III).

In accordance with the embryology of the adrenal, all malignant tumors of the gland should be classed as sarcomata, but from the histology of the normal gland carcinomata might be expected to develop. In the present case the larger masses exhibit the cellular characters of sarcoma. There is, however, evidence to show that these tumors may have had originally a carcinomatous structure, and as the growth progressed the reversion to the mesothelial or sarcomatous type of cells occurred. In fact such transformation or reversion is demonstrated in some of the tumor masses. If these tumors had had opportunity to continue their growth, reversion to sarcomata would, perhaps, have become complete.

Jores[3] has described a sarcoma of the adrenal in which a direct transition could be traced from the normal adrenal cells to the cells of the sarcoma. In this case metastases in the brain were of the same structure as the main tumor. In another case he describes an alveolar sarcoma of the adrenal which in places resembles slightly the histological structure of carcinoma. On the evidence afforded by these cases Jores believes that all malignant tumors

of the adrenal are sarcomata, although they may resemble in some parts carcinomata.

Rolleston and Marks,[4] after a careful study of tumors of the adrenal, make the following statement: "Our own impression is that malignant tumors of the suprarenal bodies are peculiar and form a special class. They may approach structurally either the carcinomata or sarcomata, and sometimes one and the same tumor may in different parts resemble both."

Woolley[5] has reported a case in which a transition was demonstrable between the adrenal cells and a primary adenoma of the adrenal, accompanied by metastases, all of which were sarcomatous. He believes this condition is explained by the embryology of the adrenal, and thinks that such malignant tumors should be called "mesothelioma."

Such cases show that tumors of the adrenal may begin as sarcoma or as carcinoma and revert to a sarcomatous type of tissue. Such reversion may occur as a direct transformation from the normal adrenal cells to sarcomatous or carcinomatous cells, or may occur in metastases from the original adenoma; or, as in my own case, may be followed by a series of transitions within the same tumor nodule.

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XVI.

A CASE OF GANGRENE OF THE OMENTUM DUE TO TORSION.

By George Woolsey, M.D.

Torsion of the omentum is of such uncommon occurrence that the following case seems worthy of record:

Mr. A. A., twenty-three years of age; Russian; single; druggist; was admitted to the Presbyterian Hospital July 26, 1908 (Hosp. No. 6353). Family history negative. Previous history: seven years ago he was ruptured playing football. In May, 1906, he had pain in the hernia, but this soon disappeared. In March, 1907, it became irreducible and painful, and he was operated upon. The patient says that the wound was allowed to granulate up from below. Present history: Saturday afternoon, July 23, he was suddenly seized with severe pain across the lower part of the abdomen which he attributed to pears eaten the day before. As the bowels had not moved that day or the previous one he took magnesium citrate, and then other cathartics, without relief. The pain became a dull continuous ache and extended into the right inguinal region, so that he thought the old hernia had reappeared. That night he felt prostrated, and weak in the lower limbs. On going to bed he noticed a swelling the size of a small egg in the right inguinal region, which did not disappear on lying down. The pain continued, but did not increase, in the lower abdomen and the right inguinal region, and there was sharp pain here on deep inspiration. There was no passage of gas or stool. Hot and cold local applications gave no relief. There was no vomiting. Micturition was normal.

On examination the abdomen is symmetrical, but moves less

Our conclusions then, from Table III, would be:

1. A polymorphonuclear count between eighty-five and ninety per cent. indicates the presence of a severe process.

2. Above ninety per cent., a dangerous condition, probably complicated by peritonitis.

3. Below eighty per cent., safety, for the time being.

4. Between eighty and eighty-five per cent., doubtful.

5. These rules hold good for about four-fifths of this series of cases, there being many exceptions to each rule.

It is not the object of this paper to form any definite rule by which we can tell from the blood count when to operate and when not to operate in a given case of appendicitis. In fact, one point, and probably the most important that this investigation has taught the writer, is that it is impossible to decide from the blood count what pathological condition we shall find, or even determine whether the case is severe or not. There are many exceptions, and these we must learn to recognize by other means at our command.

One of the most recent methods, and one which has aroused more investigation along the line of the value and interpretation of the blood count in appendicitis, is that suggested by Dr. C. L. Gibson of New York City.* He advanced the idea that the relation between the total leucocyte count and the percentage of polymorphonuclears gave the most valuable information; 10,000 leucocytes with seventy-five per cent. of polymorphonuclears was taken as a base line representing the normal relation. With every rise of 1,000 leucocytes there should be a corresponding rise of one per cent. of polymorphonuclears to maintain the normal relationship. Lines were drawn from the leucocyte count to the polymorphonuclear count and designated as horizontal, rising or falling lines, according to the relationship between the leucocyte and the polymorphonuclear count. In brief he says: "If the line

*Annals of Surgery, April, 1906. "The Value of the Differential Leucocyte Count in Acute Surgical Diseases."

connecting the levels of the leucocyte count and the polymorphonuclear count runs pretty nearly horizontal, whether up or down, with only 2-4 points of difference, it indicates that a lesion, whether severe or not, is well borne and therefore of good prognosis. If the difference of level between the two points is considerable, say ten or more units, we are quite sure to have a pretty severe lesion."

The following table (Table IV) gives the result of applying Dr. Gibson's method to our series of cases:

TABLE NO. IV.

Variety.	Rising Line.	Falling Line.	Horizontal Line.	Rising Line. 5 units or more.	Total cases.*
Chronic	13	41	9	3	63
Simple Acute	24	15	8	9	47
Gangrenous	14	10	4	7	28
With Abscess	9	5	0	5	14
With Local or Spreading Peritonitis	58	37	6	36	101
With General Peritonitis	23	23	1	19	47

*To explain the totals it must be remembered that the cases in column four—namely, those showing a rising line of five units or more—are included in column one—namely, those cases showing a rising line.

On examining Table No. IV we see that the conclusions suggested by Dr. Gibson hold good in only about one-half of the cases of this series. For example, of the 47 cases of general peritonitis, only nineteen, or less than half, showed a rising line of over five units, which is supposed to indicate a pretty severe lesion. Twenty-three of the cases of general peritonitis showed, on the other hand, a falling line, and this is supposed to indicate a mild process. Yet we must admit that no case of general peritonitis should be considered a mild process. Again, only fifty-eight, or a trifle over one-half, of the 101 cases of localized or spreading peritonitis showed a rising line, and of these 58 only 30 showed a rising line of over five points. In other words, less than one-third of the cases of

localized or spreading peritonitis would be considered severe cases according to Dr. Gibson's chart, and more than two-thirds of the cases would be considered cases of good prognosis. By far the greater part of these cases, however, proved on the operating table to be severe cases.

Dr. R. H. Fowler, of St. Luke's Hospital in this city, reports* 278 cases of appendicitis. After a thorough examination of these cases he comes to the conclusion that the standard chart of Dr. Gibson offers the most advantages.

Dr. Noehren, of the German Hospital in this city, reports 69 cases.† He concludes that the estimation of the percentage of polymorphonuclears alone is more reliable than any method that has so far been suggested, also that a polymorphonuclear percentage of ninety per cent. or more indicates a severe process, which calls for immediate operative interference; a percentage below seventy-eight per cent. means a "safe" or mild process; a percentage between the two extremes speaks for the one condition or the other according as it approaches the one extreme or the other.

With the first conclusion, namely, that the percentage of poly morphonuclears is the most reliable method, the conclusions reached in this paper agree. But with the second conclusion namely, that operation is indicated, or not indicated, according as the percentage of polymorphonuclears is above ninety per cent. or below seventy-eight per cent.—we cannot agree. It may hold good in a certain number of cases, but the larger the series, the more exceptions occur, and it seems best not to draw any hard and fast rules from our blood counts and still less from our polymorphonuclear counts alone.

The writer wishes to thank Drs. McCosh and Eliot for permitting him to use their cases as material for this article.

*Surgery, Gynecology and Obstetrics, Sept., 1908. "The Relation of the Lesion in Appendicitis to the Leucocyte Count."

†"The Value of the Differential Leucocyte Count in Acute Appendicitis." Annals of Surgery, Feb., 1908.

XVIII.

A CASE OF SYRINGOMYELIA WITH PARTIAL MACROSOMIA.

By M. G. Schlapp, M.D., Head of the Class of Nervous Diseases in the Dispensary

(*Reprinted from The Medical Record, May 5, 1906*).

Not many years ago, cases showing hypertrophy of one or more extremities, or other parts of the body, in connection with symptoms of syringomyelia, were described as acromegalia with accidental association of syringomyelia. These two groups of symptoms were looked upon as not having any special relationship to each other. It was not until recent years that this combination of symptoms was recognized as being caused by the same lesion, syringomyelia. This condition has been given a special name by Schlesinger—"Partial Macrosomia." For the enlargement of the whole hand, Hoffman and Marie have chosen the name "Cheiromegalia;" for the enlargement of the foot, Schlesinger has suggested the name "Podomegalia."

This hypertrophy usually begins in one extremity, spreading from there to the trunk, or jumping to the other extremity. It seems, sometimes, to involve the soft tissue alone; other times, and less frequently, it involves the soft and skeletal tissues. The length of an extremity is not found increased as often as is the thickness, nor does the length increase as much, when increased at all, as does the thickness.

In connection with the hypertrophy of the tissue, arthropathies are frequently found—thickening of bones about the joints, hardening of articular ligaments, and, as in the case described by Nolbandoff, softening of the bones.

XIV.

THE ASSOCIATION OF TUBERCULOSIS OF THE LUNGS WITH DIABETES MELLITUS.*

By Henry L. Shively, M.D., Physician in Charge of the Tuberculosis Clinic.

(*Reprinted from the New York Medical Journal of May* 16, 1908).

For two diseases so essentially different in their nature as are pulmonary tuberculosis and diabetes mellitus, there are certain points of analogy between them which are at once curious and striking. Diabetes is to be considered a typical example of a disease of metabolism, of disturbed function due to the action of unknown toxines originating within the body itself. The production of these toxines is apparently related in some way to the internal secretion of the islands of Langerhans, and there is accumulating evidence, for which we are largely indebted to the investigations of von Mering and Minkowski, and the recent researches of Hansemann, Opie, Herter, and Bosanquet, that the pathological basis of true diabetes is a congenital or acquired insufficiency of these histological elements of the pancreas. Hansemann found the pancreas diseased in seventy per cent. of all of his cases which came to autopsy. In nineteen cases Opie showed the gland to be affected in fifteen, Bosanquet in seventeen out of nineteen cases.

Tuberculosis of the lungs is perhaps the best known and most carefully studied example of a chronic, infectious disease due to a specific micro-organism introduced from without the body. Both diseases are usually progressive in their course and are regularly

* Read before the West End Medical Society, February 22, 1908, and before the Section in Medicine of the New York Academy of Medicine, April 21, 1908.

opened, than it had been at any time before, the counter pressure from intestinal distension being then removed. Whether in this case the peritoneum would have been able to take care of the presumably sterile urine which had accumulated there before the operation, had the exploratory opening into the peritoneum not been made and the rupture area in the bladder simply treated by drainage, is of course hard to say. That conditions somewhat similar to those disclosed by the order of operative procedure in this case may well have existed unrecognized in a number of the reported cases of extraperitoneal rupture of the bladder, seems not at all unlikely, the relative toxicity of the urine being one of the factors, perhaps, in the end result in such cases where the peritoneal cavity had not been opened.