

Acute cases of Hodgkin's disease (lymphadenoma) and the diagnosis of this disease from syphilis, tuberculosis, and atypical leukaemia / by F. Parkes Weber.

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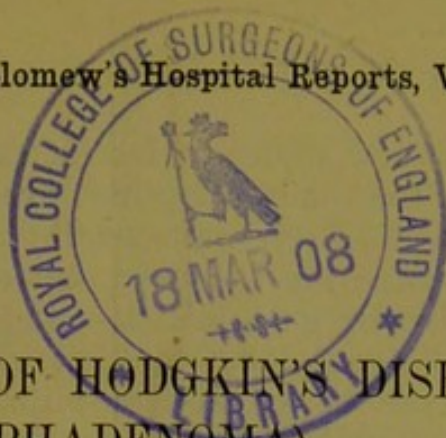
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ACUTE CASES OF HODGKIN'S DISEASE (LYMPHADENOMA)

AND THE DIAGNOSIS OF THIS DISEASE FROM
SYPHILIS, TUBERCULOSIS, AND
ATYPICAL LEUKÆMIA.

BY

F. PARKES WEBER, M.D., F.R.C.P.

Cases regarded as examples of "acute Hodgkin's disease" are from time to time recorded, and I have myself had an opportunity of studying some such cases. Recently W. R. Warrington¹ described the case of a patient who died within two months of the onset of the disease. Though in some of these acute cases doubts as to the correctness of the diagnosis may arise, there can hardly be any such question in recent cases such as Warrington's, in which microscopical examination of the lymphatic glands revealed the typical appearances of lymphadenoma as described by F. W. Andrewes,² Dorothy M. Reed,³ C. C. Simmons,⁴ W. T. Longcope,⁵ F. Warnecke,⁶ Robert Muir,⁷ &c. Andrewes himself⁸ referred to an example of acute lymphadenoma in a boy, seven years old, running its whole course up to a fatal termination in some four months and a half.

¹ Paper read at the Liverpool Medical Institution, October 24, 1907.

² "Discussion on Lymphadenoma." Transactions of the Pathological Society of London, 1902, vol. liii. p. 305.

³ "On the Pathological Changes in Hodgkin's Disease." Johns Hopkins Hospital Reports, 1902, vol. x. pp. 133-196.

⁴ "Hodgkin's Disease: A Pathological Analysis of Nine Cases." Journal of Medical Research, Boston, U.S.A., 1903, vol. ix. p. 378.

⁵ "On the Pathological Histology of Hodgkin's Disease." Bulletin of the Ayer Clinical Laboratory of the Pennsylvania Hospital, October 1903, No. 1, p. 4.

⁶ "Ueber die Hodgkinsche Krankheit." Mitteil. a. d. Grenzgebieten der Med. u. Chir., Jena, 1905, vol. xiv. p. 275.

⁷ "On Leucocythæmia, Lymphadenoma, and Allied Diseases." Glasgow Medical Journal, September 1905, p. 161.

⁸ Andrewes, *loc. cit.*, p. 310.

The existence of acute febrile cases and of a form characterised by "chronic relapsing pyrexia,"¹ the association of areas of necrosis (or occasionally of wide-spread hyaline or amyloid changes) in the liver and other viscera, the apparent dissemination or generalisation of the disease from a primary group of enlarged glands to other glands and to the spleen and liver, and the occurrence of miliary "metastases," possibly analogous to miliary tubercles, in various organs (including the bone-marrow), all suggest that Hodgkin's disease (or a portion of the cases now classed together under that heading)² is due to some unknown microbe resembling that of syphilis³ in not being able to live and propagate in the bodies of guinea-pigs, rabbits, and the animals ordinarily used for experimental inoculation.⁴ If further attempts were to be made to inoculate animals with Hodgkin's disease, anthropoid apes would have to be used for the experiments, since they have been successfully employed in regard to syphilis; the same consideration probably applies to various other diseases, such as acute leukaemia, multiple myeloma, and mycosis fungoides.

In typical cases of acute Hodgkin's disease there is probably usually a history, if inquired into, of enlarged lymphatic glands⁵ on one side of the neck or in one axilla of some weeks' or months' or much longer duration before the acute and progressive symptoms develop, which doubtless signify the fatal generalisation of the disease. The acute dissemination of the disease throughout the body should, I think, be regarded as a "septicæmia of Hodgkin's disease," using the word septicæmia in the broadest sense of the term, as it is used in "gonococcal septicæmia," "pneumococcal septicæmia," "influenzal septicæmia," and, as it might justly be used in reference to the occurrence of fatal acute miliary tuberculosis, as a result of injury to some old tuberculous focus.⁶ According to this view

¹ For one of the most recent articles on this form of Hodgkin's disease see F. Taylor, "The Chronic Relapsing Pyrexia of Hodgkin's Disease." *Guy's Hospital Reports*, 1906, vol. lx. p. 1.

² There may still be more than one disease grouped together under the heading Hodgkin's Disease.

³ Quite recently indeed spirochætes have apparently been detected by the Levaditi and Giemsa methods of staining in enlarged lymphadenomatous glands. See Proescher and C. White (Pittsburg, U.S.A.). "Ueber das Vorkommen von Spirochæten bei pseudoleukämischer Lymphdrüsenhyperplasie." *Münchener Med. Wochenschrift*, 1907, No. 38, p. 1868.

⁴ Material from cases injected into animals has given negative results. See R. Muir, *loc. cit.*

⁵ According to Muir (*loc. cit.*) lymphadenomatous enlargement of glands usually begins in the cervical region. It may occasionally begin in the retroperitoneal region.

⁶ Rapidly fatal miliary tuberculosis has of course been occasionally set up by operations or injuries to old tuberculous joints, &c. A remarkable

the lymphadenomatous nodules in the viscera are of course not metastatic growths in the ordinary sense of the term (that is to say, in the sense in which secondary carcinomatous nodules are metastatic), but are due to metastasis or generalisation of the exciting cause of the disease; that is to say, of the hypothetical microbe. Granting, however, the existence of an hypothetical microbe of Hodgkin's disease, and that the microbe in question is present in the primary group of enlarged glands, its mode of entry into the body, unlike that of the parasite of syphilis, would still remain a mystery.

The case which I have first to describe is, I believe, one of acute Hodgkin's disease, though in its histological features it differs somewhat from typical cases, and the necrotic changes in the liver are very remarkable.

The patient, E. F., æt. 27, a commercial traveller, was admitted under my care at the German Hospital on October 28, 1905. He had apparently had no previous illnesses of any importance excepting gonorrhœa at about 20 years of age. In regard to alcohol he had been accustomed to take one or two glasses of red wine daily. Five or six weeks before admission the left axillary lymphatic glands, which were already apparently somewhat enlarged, began to increase rapidly in size. The patient felt pains in the left shoulder and in the region of the stomach and the liver; his abdomen became enlarged; he had little appetite and vomited almost everything that he ate; sometimes the vomited matter contained blood. Shortly before admission there had been some cough.

On admission (October 28) the patient, a delicate-looking man, had considerable enlargement of the lymphatic glands in the left axilla; smaller glands could be felt above the left clavicle, and the cervical, inguinal, and supracondylar glands on both sides were likewise somewhat enlarged. The area of cardiac dulness was very small; no murmur was heard on admission, but a systolic apical murmur was detected later on. There was pleuritic effusion at the base of the right lung and considerable enlargement of the liver and spleen. No tubercle bacilli were found in the mucopurulent sputum. The urine, of specific gravity 1030, contained a trace of albumen. A blood examination on October 30 showed that there were 4,000,000 red cells and 3800 white cells in the cubic millimetre of blood. The differential count of white cells gave polymorphonuclears 83 per cent., large mononuclears 1 per

example of acute miliary tuberculosis of the lungs in a man, 33 years of age, apparently following an injury to a tuberculous epididymis, was recorded by me in the *Lancet*, August 7, 1897, p. 306.

cent., intermediate forms 2.5 per cent., lymphocytes 4.5 per cent., eosinophiles 1.5 per cent., myelocytes 7.5 per cent. There was fever up to 101° or 102° F., and at the commencement of November jaundice was noticed. On November 1, paracentesis was performed on the right side of the chest, and 1450 cc. of a nearly clear, bile-stained fluid were withdrawn, of specific gravity 1016, loaded with albumen, and giving a positive reaction to Gmelin's test for bile-pigments. On November 7, 1350 cc. of similar fluid was withdrawn. About this time there was likewise evidence of slight ascites. From November 11 to the patient's death on November 19 there was practically no fever and the temperature remained mostly subnormal. The jaundice had decidedly increased towards the end. In the treatment of the case strychnine, quinine, digitalis, and other drugs were tried for a time.

At the *necropsy* there was much clear, bile-stained fluid in the right pleura and also some effusion in the left pleura. The middle lobe of the right lung contained a yellowish-white nodule of the size of a small cherry. The bronchial glands were somewhat enlarged and much pigmented. The heart was small, weighing only 6 ounces, and the mitral valve was slightly thickened, but there was no evidence of any recent endocarditis; the pericardium contained a good deal of clear, bilious fluid. In the abdominal cavity there were firm peritoneal adhesions in various parts, but especially over the liver and spleen. The peritoneum contained a good deal of clear, bilious fluid. The liver was enlarged (weight, 87 ounces), of fairly firm consistence, and partially adherent from old perihepatitis to the surrounding structures. There were several ecchymoses under the capsule. On section its substance appeared swollen, bile-stained, congested with blood, and mottled all over with ecchymoses. The spleen was enlarged (weight, 16 ounces), of rather firm consistence, and very dark red colour. It contained a few blackish-red nodules of various sizes and of harder consistence than the rest of its substance; parts of one or two of these nodules were yellowish-white in colour, evidently having undergone some degenerative change. There was an ulcer in the duodenum close to the pylorus. One of the kidneys contained a little hard whitish nodule.¹ There were a few reddish

¹ Subsequent microscopic examination showed this nodule to consist of fibrous tissue through which some of the renal tubules passed. It apparently belonged to the class of tumour-like structures described by F. Genewein in his paper, "Ueber Hamartome (Geschwulstartige Fehlbildungen) der Niere und Leber," published in Chiari's *Zeitschrift für Heilkunde*, 1905, vol. xxv. p. 430. There is therefore no connection between the patient's disease and the presence of this fibrous nodule in the kidney.

enlarged lymphatic or hæmo-lymphatic glands at the sides of the aorta. Some of the mesenteric glands were enlarged; at one part there was a group (adherent to the surrounding structures), one or two of which were caseous or calcareous.

The left axillary lymphatic glands varied considerably in size, one of them being as large as a hen's egg. They were of firm texture and pinkish-red colour, some of them containing patches of pale, yellowish, degenerated material. The left humerus was sawn through longitudinally and the bone-marrow of the shaft was found to be of red colour and gelatinous consistence.

Microscopical examination.—Sections of the diseased lymphatic glands showed the characteristic growth of endothelioid cells met with in cases of lymphadenoma according to the descriptions of Andrewes, Reed, and others.¹ The glandular tissue, however, seemed (at least in the case of the axillary glands) very vascular and the blood-vessels engorged with blood. Various portions of the sections showed respectively necrotic, hæmorrhagic, and fibrotic changes. One relatively large blood-vessel was seen invaded by lymphadenomatous growth, and this reminds one of a figure in Longcope's work on Hodgkin's disease,² showing a nodule extending through the wall of a blood-vessel. Such occlusion of blood-vessels probably plays a part in the production of the necrotic areas which form so characteristic a feature in the macroscopic and microscopic appearances of the parts affected by this disease. No typical tuberculous structure was seen in any of the sections examined. Some sections were stained by Levaditi's method for the "spirochæta pallida,"³ but with negative results.

Sections of the liver showed numerous scattered areas of necrotic change accompanied by much extravasation of blood and much small cell infiltration. I take it that the appearances in the liver were complicated by the presence of cirrhotic changes, and I am not sure that the necrotic areas in this organ were completely analogous to the necrotic areas in the lymphatic glands. At one part I saw a blood-vessel invaded by lymphadenomatous growth⁴ like the vessel I have already mentioned in speaking of the lymphatic glands.

¹ See previous references.

² Longcope, *loc. cit.*, Fig. 11.

³ *Vide* E. Gierke, *Münchener Med. Wochenschrift*, Feb. 27, 1906, p. 393. The spirochæta pallida has occasionally been detected in tertiary syphilis, even if we do not include under this heading the diffuse changes in the liver, &c., of congenital syphilis, in which its presence has been abundantly recognised. See especially E. Tomaszewski, "Ueber den Nachweis der Spirochæte pallida bei tertiärer Syphilis." *Münchener Med. Wochenschrift*, July 3, 1906, No. 27, p. 1301.

⁴ Compare Longcope, *loc. cit.*, Fig. 11.

In the spleen I think there can be no doubt that the changes were of essentially the same nature as those in the lymphatic glands. The small nodule in the lung, which, like the spleen, liver, and glands, showed necrotic and hæmorrhagic changes, was probably also of the same nature. The red colour of the bone-marrow seemed to be due chiefly to engorgement with blood. I have to thank Dr. Schuh, Dr. Daser, and Dr. Petersen, then residents at the German Hospital, for their kind assistance in the examination of the case.

The following case of acute Hodgkin's disease I am permitted to refer to by the courtesy of my colleague, Dr. Fürth, for which I take this opportunity of thanking him. The patient, a single woman, aged 30 years, was admitted under his care at the German Hospital on August 23, 1905. The history was that she had had large lymphatic glands on the right side of the neck for some months, and for the last three weeks or so she had apparently suffered from pyrexia. Several years ago she had had a joint affection, probably acute rheumatism. In the hospital she had high, continued fever, and besides the glandular enlargement there was evidence of stenosis of the mitral valve of the heart. A blood-count (August 24, 1905) gave 3,816,000 red cells and 8437 white cells in the cubic millimetre of blood; the hæmoglobin value was estimated as 55 per cent. of the normal. Ophthalmoscopic examination showed nothing special. Death occurred on September 26, a little more than a month after admission. Towards the end there were catarrhal signs in the lungs, and albumen was detected in the urine.

At the *necropsy* the liver (not enlarged) and the spleen (only slightly enlarged) both contained white patches. Macroscopic examination of the enlarged cervical glands did not show caseation. There was enlargement of the mediastinal and abdominal lymph-glands. The heart showed stenosis of the mitral valve with some recent fibrinous vegetations. Microscopically a cervical gland showed the characteristic structure of Hodgkin's disease with degenerative changes, and similar partially degenerated nodules were present in the liver, bone-marrow (from the shaft of the left humerus), and in part of one lung. Sections of a lymph-gland and the liver were likewise examined for tubercle bacilli, but with negative result. The spleen was not examined microscopically. A section of one kidney showed only a little interstitial inflammatory or fibrotic change in the cortex. I may add that of the whitish nodules in the various organs (liver, spleen, bone-marrow) some appeared as large as a lentil, others were only miliary

in size. The pale nodules in the bone-marrow (which was abnormally red, as in the first case) were visible to the naked eye.

DIAGNOSIS OF HODGKIN'S DISEASE FROM SYPHILIS.

Unusual enlargement of groups of lymphatic glands (neck, axilla, &c.) in the late secondary and (more especially) the tertiary stages of syphilis has undoubtedly been sometimes mistaken for Hodgkin's disease. Such an error in diagnosis is more likely to occur when progressive cachexia and pyrexia are associated with the glandular enlargement, and when there is complete absence of any history of syphilitic infection. Some forms of "late syphilitic pyrexia" might easily be mistaken for lymphadenomatous pyrexia,¹ and the liver may be obviously affected (enlargement, jaundice) in Hodgkin's disease (the patient whose case I have just described was an instance), as it notoriously may be in the syphilitic cases. I need hardly emphasise the possible absence of any history of infection in really syphilitic cases. Even in medical men infected on the finger the primary chancre and the secondary skin symptoms may be so insignificant as to lead to at least temporary errors of diagnosis. A man, whom I saw at the German Hospital for a curious affection of the mouth yielding to antisymphilitic treatment, on being questioned, at last remembered that he did have something on the penis once, which was treated during a voyage by the captain of the ship on which he was sailing, and then apparently gave him no further trouble. Out of 58 men with unquestionable late syphilis, in only 45 of them could G. Pernet² obtain the history of a primary sore. Moreover, in patients with tertiary syphilis, and probably especially in the hospital class of patients, the history of a chancre may sometimes be obtained without one of secondary symptoms.

The importance of remembering the possible presence of syphilis in supposed cases of Hodgkin's disease has been referred to by various writers, certainly by N. J. Tschistowitsch, in his recent paper on Hodgkin's disease with periodic fever,³ J. Galloway,⁴ H. J. Paterson,⁵ and (in regard to congenital

¹ See F. P. Weber, "On Tertiary Syphilitic Fever and the Visceral and other Changes connected with it." *Lancet*, London, March 16, 1907, p. 728.

² "Transactions of the Life Assurance Medical Officers' Association," London. Volume for the years 1906-1907, p. 281.

³ "Ueber Pseudoleukämie mit periodischen Fieber." *Deutsche Med. Wochenschrift*, March 28, 1907, p. 502.

⁴ *Clinical Journal*, London, March 21, 1906, p. 356.

⁵ *St. Bart.'s Hosp. Journ.*, London, October 1899.

syphilis) R. Pott in Germany,¹ and doubtless also by many others. Probably in all cases of supposed Hodgkin's disease when there is any question whatever of syphilis, antisyphilitic treatment should be given a trial. Owing, however, to better knowledge of the histological distinction between syphilis and lymphadenoma² the "biopsy" method of diagnosis (microscopical examination of an excised gland) is likely to yield more satisfactory results in the future than it has in the past.

The question, however, arises whether cases of true Hodgkin's disease may not sometimes have been (at least temporarily) benefited by antisyphilitic treatment, as they undoubtedly have been by arsenic. Hodgkin's disease, or rather some of the cases now classified as Hodgkin's disease (or lymphadenoma), may, as already suggested, be due to a microbe similar to, but not identical with, the microbe of syphilis.³

If this were really so, it would explain any benefit derived from antisyphilitic treatment. Atoxyl, the arsenic preparation which has recently been found to exert a decided action in experimental syphilis in anthropoid apes, deserves, I think, as fair a trial in Hodgkin's disease as it has already obtained in many other affections.

DIAGNOSIS OF HODGKIN'S DISEASE FROM TUBERCULOSIS.

In 1898 Carl Sternberg published an important paper⁴ on the subject, and proved that true tuberculosis was present in a large proportion of cases classified as pseudoleukæmia (Hodgkin's disease). He maintained that such cases could not be regarded as combinations of pseudoleukæmia with tuberculosis (such as earlier writers had supposed them to be); that the presence of a form of tuberculosis in such cases was certain; and that a great number, probably most, of the cases of so-called pseudoleukæmia were in reality instances of a peculiar form of tuberculosis of the lymphatic system characterised by the production of a special form of granulation tissue (rich in large cells, &c.). In 1902 J. Sailer,⁵ from a study of four cases and from a search into the literature of the subject, concluded that what evidence there as yet was, rather tended to confirm the

¹ "Das Schicksal hereditär-syphilitischer Kinder." *Münchener Med. Wochenschrift*, February 19, 1901, p. 293.

² See the works of Andrewes, Reed, Muir, &c., already referred to.

³ Cf. Præcher and White, *loc. cit.*

⁴ "Ueber eine eigenartige unter dem Bilde der Pseudoleukämie verlaufende Tuberkulose des lymphatischen Apparatus." *Zeitschrift für Heilkunde*, Berlin, 1898, vol. xix. pp. 21-90.

⁵ "The Relation of the Tubercle Bacillus to Pseudoleukæmia (Sternberg's Disease)." *Philadelphia Med. Journal*, 1902, vol. ix. pp. 615, 669.

supposition that the majority of cases of pseudoleukæmia, if not all, would ultimately be recognised as tuberculous in nature.

F. W. Andrewes,¹ however, criticises the inoculation-test as a criterion of the presence or absence of tuberculosis in glands. He takes it that lymphatic glands are bacterial filters, and that normal glands may temporarily contain living tubercle bacilli. Therefore, when inoculated into the susceptible soil provided by a guinea-pig, pieces of lymphatic glands, whether normal or lymphadenomatous, might produce tuberculosis in the guinea-pig, even when not themselves (in the true sense of the term) tuberculous. He adds that D. L. Pizzini actually inoculated guinea-pigs with lymphatic glands from forty bodies, dead of non-tuberculous affections, and found tuberculosis to result in 42 per cent. of the cases.²

From careful microscopical examination in various cases³ he concluded that lymphadenoma is a distinct disease, not due to the action of the tubercle bacillus; that there is a form of tuberculosis of the lymphatic glands clinically indistinguishable from lymphadenoma; that a fair number of cases of lymphadenoma occur in which secondary infection with tubercle has taken place; and that this secondary infection may be local and unimportant, or the patient may die from generalised tuberculosis with a mixture of lesions of the most puzzling kind. An apparent example of this association is the following case.⁴

The patient, a girl, had some enlarged glands removed from the right side of the neck in March 1898. In March 1901, when 14 years old, she was an in-patient under my care at the German Hospital with anæmia, an enlarged spleen, and moderate pyrexia. She improved considerably under arsenic treatment, and after the middle of April was practically free from fever. Whilst under treatment I may mention she had a slight attack of arsenical herpes zoster. In April 1902 the patient was again in the hospital, and in June I noticed that the spleen reached to within half an inch of the anterior superior spine of the ilium. The liver could be felt below the costal margin. In the latter part of June the patient suffered from a short acute attack of pneumonia at the base of the left lung. She left the hospital in July, but was troubled with a good

¹ *Loc. cit.*, p. 310.

² D. L. Pizzini, "Tuberkelbacillen in den Lymphdrüsen Nichttuberkulöser." *Zeitschrift für Klin. Med.*, Berlin, 1892, vol. xxi. p. 329. The bronchial glands were those which most frequently yielded a positive result.

³ Andrewes, *loc. cit.*, p. 314.

⁴ F. P. Weber, "Remarks on the Relations of Pulmonary Tuberculosis to Other Diseases." *Lancet*, April 2, 1904, p. 924.

deal of cough and occasionally a little mucous expectoration, sometimes streaked with blood. She was readmitted on November 7, 1902, with moderate ascites and œdema. Some crepitation could be heard over the left lung. No tubercle bacilli were found in the sputum. The blood showed extreme anæmia with relative leucocytosis; the hæmoglobin was only 30 per cent. of the normal. The urine contained a trace of albumin. There was very little fever, but the general weakness increased and death occurred on December 1. The necropsy showed enlarged glands in the neck, posterior mediastinum, and abdomen. A few of the glands seemed slightly caseous, especially some not very large ones at the root of the lungs. A hard fibrous mass situated at the back of the upper part of the abdomen and displacing the stomach and liver forwards had microscopically the appearance of chronic hard lymphadenoma. The spleen weighed 26 ounces, and contained some whitish masses ("hardbake" type), one of them approaching caseation. There was a considerable serous effusion in the peritoneum, with some matting together of the abdominal viscera (probably due to peritoneal tubercle). The lungs showed scattered tubercles, and by microscopic examination minute tubercles were detected in the liver and spleen. Tubercle bacilli were seen in specially stained sections of the liver, and (what is more noteworthy) in the bone-marrow from the shaft of the left humerus. This case to some extent recalls one of Mr. Butlin's, referred to by Dr. Andrewes¹ as a case of apparent lymphadenoma, in which the patient died of acute general tuberculosis, with his lymphadenomatous glands seemingly cured by arsenic.

Amongst the more recent writers on the association of Hodgkin's disease with tuberculosis, Andrewes,² Reed,² Simmons,² Longcope,² Warnecke,² and Muir,² all come to the conclusion that Hodgkin's disease (lymphadenoma) is pathologically distinct from tuberculosis, though the two diseases are not rarely associated together in the same patient. It seems that lymphadenomatous tissue offers a soil favourable to the growth of tubercle bacilli, so that bacilli which would be destroyed in normal lymphatic glands are able to establish themselves and flourish in the glands of Hodgkin's disease. Thus, children with Hodgkin's disease often ultimately develop fatal disseminated miliary tuberculosis. It is possible that the development of tuberculosis in cases of Hodgkin's disease sometimes causes retrogression of the lymphadenomatous process analogous to the retrogression of the leukæmic process which has been observed, according to some authorities, in

¹ *Loc. cit.*, p. 313.

² *Loc. cit.*

leukæmic patients who have become tuberculous.¹ O. Reunert² of Hamburg has described the case of a boy, 8 years old, supposed to be suffering from pseudoleukæmia (Hodgkin's disease), who developed a tuberculous iritis. Under treatment with new-tuberculin not only was the tuberculous affection of the iris cured (adhesions of course remained), but some of the lymphatic glands could no longer be felt, and the spleen was reduced to only one-third of its previous size. Reunert concluded that the tuberculosis was the cause both of the eye disease and of the glandular and splenic enlargements; but this conclusion cannot be accepted as quite proved if we believe (as we are inclined to) that tuberculosis (and tuberculin also) are in some way antagonistic to true lymphadenoma.

From all the foregoing considerations it appears that in every case of supposed Hodgkin's disease not only the presence or absence of the characteristic lymphadenomatous changes in the glands has to be considered, but likewise the presence or absence of tuberculosis. In children the two affections are probably more apt to be associated than in adults. The presence of true Hodgkin's disease can often be determined by a "biopsy" examination of one of the enlarged glands, and the results of the biopsy method are not necessarily to be regarded as wrong if the patient subsequently reacts to tuberculin or develops undoubted signs of tuberculosis. Doubtless there are cases of multiple tuberculosis of lymphatic glands (especially, I think, in children) in which clinically the diagnosis is very difficult, for even the presence of clinical signs of tuberculosis (including evidence obtained by the various tuberculin tests) does not, as has been already pointed out, make it impossible that the original disease may have been lymphadenoma.

There are, however, certain cases of chronic multiple tuberculosis of lymphatic glands, especially in adults, in which the diagnosis of lymphadenoma may be fairly readily excluded by ordinary clinical examination (1) by there being no, or only very slight, enlargement of the spleen or liver, and (2) by there being evidence of associated chronic pulmonary tuberculosis.³ Examples of such chronic glandular tuberculosis in adults, though not very common, are, of course, occasionally met with

¹ H. Quincke (*Deutsches Archiv. für Klin. Med.*, Leipzig, 1902, vol. lxxiv. p. 445) has even suggested the therapeutic employment of tuberculin in leukæmia.

² "Ueber die durch Tuberculose bedingten pseudoleukämischen Erkrankungen und ihre Behandlung mit Neutuberkulin." *Deutsche Med. Wochenschrift*, 1905, No. 23, p. 907.

³ Cf. Professor Baümeler's paper, "Multiple Lymphdrüsentuberkulose," at the *Oberrheinischer Aerztetag* on July 16, 1903. (*Münchener Medicinische Wochenschrift*, 1904, No. 1.)

at hospitals and sanatoria for pulmonary tuberculosis as well as at general hospitals.

DIAGNOSIS OF HODGKIN'S DISEASE FROM ATYPICAL LEUKÆMIA.

The only leukæmic cases which after the most superficial examination of the blood could be mistaken for Hodgkin's disease are the cases of so-called atypical leukæmia, including "leukanæmia," in which the number of white cells in the blood is not very greatly increased. In a case of "leukanæmia" which I described in 1904,¹ the white cells on one occasion were counted as only 3000 to the cubic millimetre of blood. But a differential count of white cells gave 49.4 per cent. of small lymphocytes and 9.6 per cent. large lymphocytes to only 37.5 per cent. polymorphonuclear neutrophiles; whilst there were also 3.0 per cent. myelocytes present. A differential blood-count would therefore probably distinguish such cases from Hodgkin's disease. In the latter disease the white cells are generally not much changed, but there is sometimes a relative increase in polymorphonuclears, and there may be an increase of the eosinophile leucocytes. Some of the cases formerly regarded as "pseudoleukæmia," with decided relative increase of lymphocytes, as spoken of by Pincus, constitute, doubtless, a form of disease quite distinct from Hodgkin's disease—namely, a kind of "sublymphæmic lymphomatosis," or rather "a leukæmic sublymphæmic lymphomatosis."

For the diagnosis of Hodgkin's disease there ought to be *great* enlargement of some one or more regional groups of lymphatic glands. It is doubtful whether any of the so-called "pseudoleukæmia" cases showing a universal but *only slight* enlargement of lymphatic glands can be included as examples of Hodgkin's disease.

¹ Trans. Path. Soc., London, 1904, vol. lv. p. 288.

