ing the tissues lying between the separated recti muscles, and, also, by excising a segment of the wall transversely, leaving a T-shaped scar. Our own impression is that it is better *not* to excise any of the tissues except skin, but, after making a long incision to close the abdomen in such fashion that the one rectus overlaps the other.

When beginning this paper it was our intention to describe, in detail, several of the operations devised for the cure of hepatoposis, but space forbids.

ORIGINAL ARTICLES.

HODGKIN'S DISEASE. A STUDY OF A CASE WITH RELAPSING FEVER.*

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THE main clinical features of Hodgkin's disease were first described by Hodgkin,¹ of Guy's Hospital, in 1832. He reported seven cases. Doubtless most of his cases were not Hodgkin's disease, according to our present conception, for at that time it was not possible to separate from each other the various groups of diseases in which there is glandular and splenic enlargement.

Since Hodgkin's article a voluminous literature has accumulated, which for the most part is of little scientific value because of the hopeless confusion by authors of the different pathological processes which may result in enlargement of the lymphatics and spleen. The disease with which Hodgkin's has been most frequently confused is lymphatic tuberculosis. There can be no doubt, in the light of recently acquired knowledge, that the two diseases are entirely distinct, but it must be conceded that the diseased glands of Hodgkin's disease frequently become the seat of a secondary tuberculous infection.

Recent articles of great value have been contributed by Clarke,² Reed,³ Simmons,⁴ and Longcope.⁵ Those of Reed and Longcope are, in my judgment, the best extant from a pathological standpoint, and I have drawn freely from them in the preparation of this paper.

In 1870 Murchison⁶ reported a case with a relapsing type of fever.

Pel,⁷ in 1885, and Ebstein,⁸ in 1887, each reported a case with fever of relapsing type. For such cases Ebstein suggested the

* Read before the Medical Society of the District of Columbia.

name "Chronic Relapsing Fever." Since Ebstein's paper a limited number of additional cases with relapsing fever have been reported.

The one constant symptom is progressive enlargement of the lymphatic glands. The enlargement always begins in the glands of the neck. It may be unilateral or bilateral in the beginning. More frequently it is unilateral, but later the glands of the opposite side enlarge. From the neck glands the disease spreads apparently by metastasis along the normal lymph channels to the nearest glands, attacking the axillary, intrathoracic, and abdominal lymphatics. The glands of the groin may be greatly enlarged, but usually they escape or are but slightly involved. The degree of enlargement is variable, in some cases being only moderate; in others very great, forming large tumor masses. The largest gland in the case below reported measured 7 by 3 cm. The size of the glands may vary from time to time within certain limits. During febrile movements they are apt to enlarge somewhat, and during periods of apyrexia to recede. The enlarged glands are painless and tend to remain discrete and movable. Involvement of the skin and other adjacent tissues is notably absent. Suppuration does not occur in the absence of secondary infection. When the glandular enlargement is sufficiently great, pressure effects may result—*e. g.*, dyspnoea from pressure on the trachea, oedema, etc.

The spleen is probably always enlarged. The enlargement may be great, suggesting that of splenomedullary leukæmia. More frequently it is moderate in degree. It may be so slight as to be difficult of recognition upon physical examination.

The liver also is often enlarged.

The general health may remain good for a considerable time after the glandular enlargement has become evident, but sooner or later there develop asthenia, anæmia, cachexia, and emaciation. Advanced Hodgkin's disease is distinctly a cachectic disease. There is nothing distinctive about the anæmia; it is of the secondary type. There is a reduction of the red cells, usually moderate in degree. There is no leukocytosis unless there is an acute infection; on the contrary, there may be a marked paucity of the white cells. Nucleated reds may be found as in other grave anæmias. A differential white count may or may not show a relative increase in the number of lymphocytes. The hæmoglobin is reduced and the color index usually minus. The blood examination is of diagnostic value only in a negative sense. By it leukæmia is positively excluded.

Hodgkin's disease is a febrile disease. The temperature curve may be that of an irregular, continuous fever, alternating with periods of apyrexia; it may be of an intermittent type; or it may be of a distinctly relapsing type, periods of continuous fever, which may reach a considerable height, alternating in a most striking manner with afebrile periods. It was for this last group of cases that Ebstein proposed the name of "Chronic Relapsing Fever."

Among less constant and less important symptoms may be mentioned deafness due to lymphoid growths in the pharynx, pigmentation of the skin, and nose-bleed.

The disease is invariably fatal. The average duration is from one to four years. Cases in which the progress is unusually rapid may terminate within a few months; and cases in which the progress is unusually slow may extend beyond the four-year period. During the course of the disease there may be remissions, during which the glands remain stationary in size, or even recede, and there may be improvement of the general health, with gain of weight and strength. The lowered vitality of the subject of advanced Hodgkin's disease is a constant invitation to secondary infections. The tuberculous infection is the one to which he is especially liable, and in many cases, during the latter part of the disease, there is a combined lymphatic tuberculosis.

Some of the gross anatomical facts have already been mentioned—viz., the variable size of the glands, their tendency to remain discrete and movable, the circumstance that they are painless, and the fact that in the absence of secondary infection there is no involvement of the skin or other adjacent tissues, and no suppuration within the glands. That the glands remain discrete and movable is due to the fact that their capsules do not share in the diseased process in the gland substance proper. The consistency of the diseased glands is variable: generally speaking, the small glands are soft and elastic to the feel, while the larger ones are firm and even quite hard. On section the smaller and younger growths present a uniform, slightly opaque, grayish, bulging surface. The larger and older growths on section show a partially translucent, grayish surface, which is traversed by opaque, yellowish lines. The yellowish lines represent degenerating fibrous tissue. There are no large areas of caseation or other necrosis unless there has been a secondary infection.

Metastatic lymphomatous growths may be found wherever there is lymphoid tissue—*e. g.*, in the tonsils, pharynx, intestine, spleen, etc. The constancy of splenic enlargement is very striking, and in a majority of cases there are in the enlarged spleen distinct lymphoid tumors, resembling in appearance ordinary lymph glands. Lymphoid nodules may also be found in the marrow of the long bones.

The microscopic picture is not that of a simple hyperplasia, as is so frequently stated, but rather of a chronic inflammatory process. It varies with the stage of the disease. In the small and recently diseased glands the most striking feature is an increase of the cellular elements; while in the larger glands, which have been diseased longer, fibrosis is a marked feature. The difference in the consistency of the glands is thus explained.

The first change consists of proliferation of the free endothelial cells and the large lymphocytes of the germinal centres, resulting

in obliteration of the lymph sinuses and reticular spaces. Epithelioid cells are formed by the proliferated endothelium, and from the epithelioid cells are formed giant cells, which possess numerous large vesicular epithelioid nuclei, with one or more prominent oxyphile nucleoli. The giant cells are a constant, striking, early, and characteristic feature of the histology. Lymphoid cells of the usual type are also found. They also are derived from endothelial proliferation, and may be very numerous. Eosinophiles are not an essential part of the picture, but are apt to be present. They may be found everywhere except in the germinal centres of the follicles, and may be so abundant as to outnumber all of the other cellular elements. Plasma cells are apt to be found, and may be very numerous.

Increase of connective tissue begins early, but marked fibrosis belongs to an advanced stage. It has its origin from the connective tissue of the vessels and trabeculae, pre-existing reticular cells, and endothelial fibroblasts. Its growth is gradual and at the expense of the compressed cellular elements. Finally, coarse contracting fibrous bands are formed which may be seen with the naked eye as yellowish lines traversing a section.

The bloodvessels are numerous and full early in the process, but later many of them may be obliterated by perivascular thickening. Areas of anæmic necrosis, with centres containing fragmented nuclei and infiltrated with polynuclear cells, may be found, but contain no demonstrable micro-organisms.

The histology of the lymphomatous growths which may be found in the various parts of the body—*e. g.*, spleen, kidneys, etc.—is the same as in the diseased glands.

The pathogenesis of Hodgkin's disease is still unknown. It is certain that it is not a glandular tuberculosis, but there is an increasing belief that it is an infectious disease. This belief is supported by the facts that it is a febrile disease, and that it sometimes runs an acute instead of a chronic course. Assuming the disease to be infectious, the fact that the cervical glands are the first to be attacked would suggest that the causative organism effects an entrance through the mucous membrane of the upper air passages, or of the upper part of the digestive tract. Diseased tonsils are well known to be a very vulnerable point. Organisms may pass through them and infect the neck glands, without infecting the tonsils themselves.

Bacteriological study has yielded very unsatisfactory results. In some cases the ordinary pyogenic cocci have been obtained from the blood and the diseased glands; in other cases various unidentified organisms have been obtained. From the fact that a variety of organisms has been found, and that no one organism to the exclusion of others has been demonstrated, it is evident that if Hodgkin's be an infectious disease, the specific causative agent is yet undiscovered. Certainly it seems improbable that a number

of different organisms could cause the definite pathological picture of the disease.

In opposition to the more or less generally accepted belief that it is an infectious disease, there are arrayed some important facts. In some cases blood cultures and cultures from the diseased glands have been sterile, and animal inoculations have been negative. Fischer⁹ has reported twelve such cases. In my case reported below cultures of splenic blood withdrawn during life gave no growth on bouillon or agar. On the day of the autopsy (made fourteen hours after death) a rabbit was inoculated intravenously with 0.75 c.c. of an emulsion made by rubbing up some diseased glandular tissue removed from the mediastinum with sterile physiological salt solution, and a guinea-pig was inoculated intraperitoneally with a like amount of the same emulsion. One month after inoculation the guinea-pig died, and on autopsy showed a well-marked lobar pneumonia, without other discoverable lesion. Several uninoculated guinea-pigs died at about the same time, which corresponded to a sudden change in the weather. Nearly five weeks after inoculation the rabbit, which had remained well, was killed with chloroform and autopsied. The examination showed no evidence of disease. I am indebted to Mr. George W. Stiles, Jr., of the United States Bureau of Animal Industry, one of my fourth-year students, for making the inoculations and doing the autopsies.

In one case reported by Fischer,¹⁰ in which there was relapsing fever, organisms were present in blood cultures made during the febrile periods and absent from those made during periods of apyrexia, suggesting that the periods of fever were due to secondary infection. In my case negative blood cultures were made on the second day of the third febrile period, and on the twelfth day of the fourth febrile period. Bacterial poisons are certainly the most frequent and most important causes of fever, but other causes must be recognized as adequate to disturb the heat equilibrium. In uræmia, for instance, we may encounter a considerable elevation of temperature which we are only able to explain on the theory that the diseased kidneys have manufactured some toxic substance which disturbs the normal activity of the heat mechanism. It may be that in Hodgkin's disease the diseased glands manufacture a toxic material capable of causing fever; or that because of imperfect tissue drainage due to an extensively diseased lymphatic system material is retained which may exert a disturbing influence upon the heat centres.

We have, then, in considering the question as to whether Hodgkin's disease is an infection or not, good reasons *pro* and *con*. The weight of evidence, perhaps, points to infection, but at present the question must be left open. If it is not an infectious disease, it is

difficult to explain the nature of the irritant responsible for the inflammatory changes in the glands.

The diagnosis is apt to present considerable difficulty.

Syphilitic adenitis is separated by the absence of other evidence of syphilis and of a syphilitic history, and by the negative effect of specific treatment.

Lymphatic leukæmia in which the diseased glands are associated with enlarged spleen is readily excluded by the absence of the characteristic blood picture which belongs to that disease.

Lymphosarcoma has unfortunately been used as a synonym for Hodgkin's disease. The two diseases are entirely distinct, though clinically they may resemble each other very closely and the differential diagnosis may be quite difficult. In lymphosarcoma the disease process is not restricted to the parenchyma of the glands, but invades the capsules and adjacent tissues (which is not true of Hodgkin's disease), and extension is not limited to metastatic advancement from one gland group to another. The histology of sarcoma and Hodgkin's disease is radically different, and the diagnosis may be made if the removal of a superficial gland be permitted.

Tuberculous adenitis is the disease most frequently confused with Hodgkin's disease. Tuberculosis of the cervical lymphatics is frequent; generalized tuberculous adenitis sometimes occurs; Hodgkin's disease is comparatively rare. It is believed that a large majority of cases reported as Hodgkin's disease were in reality tuberculous adenitis. Musser,¹¹ as late as 1902, considered Hodgkin's disease to be a lymphatic tuberculosis, and it is only since the careful histological studies of Reed¹² (1902), Simmons¹² (1903), and Longcope¹² (1903) that the line of separation has been sharply drawn between the two diseases. In their general clinical appearance they may resemble each other so closely as to be inseparable. We do not expect to find enlargement of the spleen in tuberculous adenitis; it may be slight and undiscovered in Hodgkin's disease. Cervical tuberculous adenitis occurs especially in children; Hodgkin's disease is also frequent among children as compared with its occurrence in adults. In both diseases there has often been a preceding catarrh of the nose or throat, or chronic tonsillar enlargement. In cervical tuberculous adenitis the submaxillary glands are the first to be diseased; in Hodgkin's the submaxillary glands may be primarily invaded. In tuberculous adenitis the enlarged glands tend to fuse and to become knotted together in large masses; the skin remains movable for a longer or shorter time, but later is apt to become adherent to the underlying masses; the glands tend to suppurate, open through the adherent skin, and discharge their contents; the abscess tends ultimately to heal. In Hodgkin's disease the enlarged glands remain discrete and movable; they do not adhere to the skin or other adjacent structures, or suppurate, unless there is a secondary infection; spontaneous cure never occurs.

Tuberculous cervical adenitis is, as a rule, unilateral at first; subsequently the glands of the opposite side may or may not become infected. Hodgkin's disease may be bilateral in the beginning, but more frequently, like tuberculous adenitis, it is at first unilateral, the glands of the opposite side subsequently enlarging.

In tuberculin we have a valuable test for tuberculous adenitis as for other forms of tuberculosis. There is a prompt reaction even in the early stage. In Hodgkin's disease the tuberculin test is negative.

E. A. S., aged thirty years; male; white; driver; was admitted to University Hospital March 14, 1903.

Family History. Unimportant.

Personal History. Ordinary diseases of childhood; recoveries good. General health had been good, but there had been gatherings about chin and under lower jaw off and on for ten years, some of them associated with bad teeth. One gathering had broken and discharged pus; other swellings had disappeared without gathering. Gave up work a month before admission because of malaise, anorexia, and loss of flesh and strength. Glands of both sides of neck had begun to enlarge a few weeks earlier. Had had fever and been confined to bed since February 20, 1903.

Condition on Admission. Height 5 feet 8 inches; weight 122 pounds 12 ounces. Expression good; because of swollen neck, face seemingly that of a much larger man. Face flushed; was slightly cyanotic about cheeks, lips, and ears. Cervical glands much enlarged on either side; the highest were most enlarged; from above downward size diminished; small glands felt immediately above clavicles; all moderately firm and painless. Axillary, inguinal, and epitrochlear glands slightly enlarged on either side; firm, movable, and painless. Teeth in poor condition. No enlargement of liver or spleen discoverable. Nutrition only fair. Circulatory, respiratory, nervous, and genitourinary systems negative.

March 24th cervical gland removed for microscopic examination. During the next few weeks the neck glands gradually increased in size. On April 18th small patches of dark-brown pigment were noted in skin of cheeks and on various parts of body; these gradually increased. On May 10th axillary glands of right side were noted to have increased in size. On May 14th a dermatitis began to develop on either side of neck, the result of a number of x-ray exposures. On May 17th dermatitis was very marked. On May 21st cervical glands were somewhat softer; appeared to be larger than before beginning x-ray treatment. On June 2d five minims of Trudeau's tuberculin were given hypodermically at 6 p.m.; temperature normal; reaction prompt; temperature remained normal for eight hours and then rapidly ascended reaching 103.7° fourteen hours after injection; remained practically stationary at that level for twenty hours, and then rapidly declined to normal.

From date of admission to April 6th (twenty-three days) there was continuous, irregular fever, temperature ranging between 99° and 103.3°. From April 6th to 27th temperature was lower, irregular, sometimes of simple continued type, sometimes remittent, and at other times intermittent. From April 27th to date of administering tuberculin temperature was normal or subnormal, with the exception of two or three trifling short-lived exacerbations, during one of which it momentarily reached 101°.

Two blood examinations were made: March 16th, red cells, 4,500,000; white cells, 3200; hæmoglobin, 92 per cent.; normal leukocytes present in normal percentages; April 22, red cells, 4,040,000; white cells, 3000; hæmoglobin, 85 per cent.

Weight diminished steadily from admission to May 15th, on which date it was 112 pounds. From May 15th to June 5th it increased to 120 pounds.

On June 6th patient returned to his home considerably improved in health. It was learned that he was shortly afterward able to resume his work of driving.

This case is referred to somewhat in detail for the purpose of emphasizing the clinical parallelism between Hodgkin's disease and lymphatic tuberculosis, and to illustrate the value of tuberculin as a means of differential diagnosis. Many features pointed to Hodgkin's disease: the age of the patient (thirty years); the fact that the glandular involvement was extensive, and especially that it was bilateral (according to history) from commencement; the pigmentation; and the fact that the glands were for the most part discrete and movable. There was no suppuration or extension to adjacent tissues. For a time the case was suspected to be one of Hodgkin's disease, and was shown clinically as such. The report upon the gland removed for examination was delayed, and it was not until the tuberculin test was used that the tuberculous nature of the disease was positively recognized. Subsequently it was reported that the gland was tuberculous and did not present the picture of Hodgkin's disease.

But the crucial test between the two diseases lies in the removal of a diseased gland and microscopic study of sections. Each has its definite histological picture. In those cases in which the two diseases coexist it is quite possible to recognize the distinctive characters of each. (Reed.¹²)

Those cases of Hodgkin's disease in which there is fever of a relapsing type may clinically simulate piroplasmiasis (*kala azar*; *Dumdum fever*). In patients who have been in the tropics where piroplasmiasis prevails a differential diagnosis may only be possible by microscopic examination of a gland and the finding of the histological appearances peculiar to Hodgkin's disease, on the one hand; or on the other, by examination of splenic blood and the finding of the Leishmann-Donovan bodies pathognomonic of piroplasmiasis.

C. V., aged twenty-four years; male; white; fireman U. S. N.; was admitted to University Hospital October 30, 1904.

Family History. Unimportant.

Previous Personal History. Birthplace, Plymouth, North Carolina. No history of diseases of childhood or other illnesses. From age of three to nineteen years lived in the country near Washington, North Carolina. In 1900 entered U. S. N. as fireman. During the following four years visited ports of Cuba, Philippines, Hawaiian Islands, and China.

History of Present Illness. In October, 1903, enlargement of the glands on left side of neck began. Was sent to hospital in February, 1904, and the enlarged glands were removed. Recovery good. Since operation has had regular periods of illness, which were thought to be bilious attacks. During these attacks, which lasted from three to five days, there were malaise, weakness, and fever. During the intervals, which usually lasted seven or eight days, felt comparatively well and appetite was good. A few months after operation the glands on left side of neck again began to enlarge. Upon admission to University Hospital patient considered that he was in the midst of one of his periodical attacks.

Condition on Admission. Expression poor; marked anæmia and sallowness; "fishy" appearance of eyes.

Skin. Dry and harsh. Extensive evidence of scabies, with numerous excoriations from scratching.

Glands. On right side of neck not palpable; on left side one gland enlarged to about the size of a hickory nut and two others smaller, but easily palpated; all movable, discrete, and firm. Axillary glands of left side and inguinal glands slightly enlarged.

Digestive System. Teeth in good condition; diffuse epigastric tenderness; spleen easily palpated; liver not enlarged; nutrition fair.

Respiratory System. Respiration rapid (28); otherwise inspection and palpation negative. Extending from midsternal line to left for a distance of nearly two inches, and from clavicle downward to lower margin of second rib distinct area of dulness. Breath sounds feeble over dull area and shifting moist rales audible over various parts of chest.

Circulatory, nervous, and genitourinary systems unimportant. Temperature, 103.2°; pulse, 128.

Clinical Notes. November 8, 1904. Glands on left side of neck show no change; slight cough and expectoration; slight attack of nose-bleed; fever continues, but has become more remittent.

11th. Temperature subnormal; patient brighter; appetite improved; spleen and glands on left side of neck smaller.

12th. In collapse; temperature at noon yesterday 94.8°; pulse, 62.

17th. Temperature still subnormal; spleen not now palpable, and glands of neck are reduced in size.

21st. Great pain in feet and plantar surfaces are very sensitive to pressure; temperature beginning to ascend.

27th. Spleen again palpable; glands of neck enlarging, and a gland about the size of a chestnut is felt in left axilla; patient is complaining of weakness and dyspnoea; fever has been continuous since last note.

30th. Temperature subnormal; spleen not palpable; glands on left side of neck softer and reduced in size; appetite voracious.

December 9th. Temperature again ascending; patient feels comparatively well, but is troubled with nose-bleed; spleen again palpable; scabies has disappeared under treatment.

19th. Fever has continued; patient weak and refuses nourishment; glands on left side of neck again larger (movable, firm, and discrete); liver and spleen palpable; some abdominal tenderness. Patient is deaf, and it has been observed that his hearing becomes much impaired during febrile periods, improving during periods of apyrexia.

22d. Repeated examinations of chest have shown persistence of dulness below left clavicle and under left half of upper portion of sternum. The area of dulness has varied, increasing during febrile periods and diminishing during periods of apyrexia.

28th. Temperature again normal; glands in neck and axilla smaller; spleen not palpable; some delirium at night and more or less stupor throughout day; hearing improved; great tenderness of feet.

January 15, 1905. Temperature again ascending; glands on left side of neck again more enlarged; spleen again palpable.

February 4th. Pigmented areas noticed for the first time upon side of face and abdomen; skin dry and scaly; for the first time glands of right side of neck are palpable; glands of the left side of neck somewhat larger; spleen palpable; some cough and blood-tinged expectoration; some nausea and vomiting; increasing deafness; temperature has remained high since last note, and the morning remissions are slight. The inguinal glands have varied slightly in size from time to time; they are not now materially larger than on admission. Examination of abdomen shows slight accumulation of fluid in either flank. Repeated palpation has failed to show enlargement of abdominal glands.

11th. General condition very asthenic; fever high; pulse rapid and weak; respiration labored; glands on both sides of neck palpable; spleen palpable; abdomen distended and somewhat tender; patient unable to retain nourishment.

13th. Death by asthenia, one hundred and six days after admission.

Summary of Temperature. The temperature was of a decidedly relapsing type, showing four distinct periods of continuous pyrexia

and three periods of apyrexia. At the commencement of each febrile period the ascent of the temperature was of step-ladder fashion, reaching the fastigium in about three days, and at the close there was a corresponding step-ladder defervescence. During the afebrile periods the temperature remained subnormal, several times going as low as 95°, and on one occasion reaching 94.8°. The length of the periods of pyrexia and apyrexia was as follows:

First period of pyrexia	13 days.
“ “ apyrexia	8 “
Second “ pyrexia	10 “
“ “ apyrexia	7 “
Third “ pyrexia	23 “
“ “ apyrexia	10 “
Fourth “ pyrexia	35 “

The accompanying chart shows morning and evening temperatures from admission to death.*

Blood. Examination as follows:

	Reds.	Whites.	Hæmoglobin.	Color index.	Polynuclears.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Mast cells.	Myelocytes.	Total counted.
			%	%	%	%	%	%	%	%	
October 30, 1904	4,112,000	5,096	60	0.75	79.7	3.5	12.0	2.5	1.9	0	315
November 10, “	2,948,000	2,920	50	0.85	71.0	5.0	22.0	2.0	0	0	100
“ 13, “	3,588,000	5,900	50	0.75	76.0	13.7	8.2	1.9	0.2	0	1000
“ 25, “	2,804,000	5,500	50	0.88	83.4	2.2	14.2	0.2	0	0	500
December 4, “		4,400									
“ 8, “	4,316,000	8,360	60	0.70	75.0	5.6	13.6	5.0	0.8	0	500
“ 17, “	2,512,000	2,400	45	0.90							
January 3, 1905	2,552,000	2,850	33	0.64							
“ 30, “	3,032,000		38								

The small percentages of small lymphocytes and the large percentages of large lymphocytes are worthy of note.

Numerous examinations for malarial organisms were made. Two were made of blood drawn from the spleen by puncture. All negative.

Numerous Widal tests for typhoid fever were also made. All negative.

* Because of great length of chart it was found impracticable to publish in entirety. The above section covers a period of forty days, and serves to illustrate the strikingly relapsing type of fever.

Two splenic punctures were made (December 9, 1904, and January 24, 1905). These were done to secure specimens to study for malarial organisms and for the Leishmann-Donovan bodies of piroplasmosis. Examination of a large number of stained smears for the Leishmann-Donovan bodies yielded no result.

From both of the specimens of splenic blood cultures were made on bouillon and agar. No growth obtained.

Stools. October 31, 1904. No parasites or ova; no blood cells.

November 13th. Eight ova of *uncinaria Americana* found after searching seventeen preparations on seven-eighths inch cover-glasses. No undigested food or blood cells. Subsequently the ova were repeatedly found, but always in small numbers.

December 2d (the day following third course of thymol) three adult *uncinariae* were found.

4th. One ovum.

During the following two months neither parasites nor ova could be found.

Sputum. Repeated examination for tubercle bacilli negative.

Necropsy Excerpt. Examination fourteen hours after death. One litre of straw-colored fluid in peritoneal cavity. Peritoneum transparent and glossy.

Spleen. Enlarged; weight, 800 grams; smooth, firm, brownish red. On section is strikingly dry; surface thickly studded over with pearly white, irregular areas, 2 to 5 mm. in diameter.

Liver. Somewhat enlarged; pale; cut surface dry and slightly mottled. On anterior surface immediately beneath capsule are a few pearly white, translucent areas, 3 to 5 mm. in diameter.

Kidneys. No nodules found.

Lymphatic Glands. (a) Those of neck are enlarged, both sides; larger on left side; largest gland 3 cm. in diameter; discrete. Toward left axilla nodes the size of chestnuts are felt. A group of fused glands 1.5 x 2 cm. projects downward from left side of neck into apex of thorax. (b) Those of mediastinum enlarged; discrete. Around trachea are the largest glands in the body; they are continuous above with the cervical glands; the largest individual gland is on the right side of the trachea, 3 x 7 cm. A short distance below the bifurcation there is a node in each lung 2 cm. in diameter, and about left bronchus are a few smaller ones. (c) Those of abdomen also enlarged. On under side of diaphragm are two groups of fused nodes. Extending from vertebral column to spleen is a chain of about twenty glands, 1 to 5 cm. in diameter. On either side of vertebral column from diaphragm to pelvis are the largest masses found; capsules adherent, but glands for the most part discrete. The enlarged glands found in the above localities differ slightly in consistency; all firm; largest are the firmest. Where they are fused the fusing is a mere welding of the capsules. On section they are

pale yellow and translucent, except that an occasional gland shows a darker yellow band or spot, extending toward its centre.

Bone-marrow. Not examined.

Lungs. In places minute drops of mucopus escape from bronchioles under pressure. No tubercles or other evidence of tuberculosis.

Intestines. Minute examination of mucous surface and of contents fail to show uncinariæ.

Histology of Tissues. Glands. The smaller glands are not favorable for study, because of a faulty method of preservation. The larger glands are well preserved. In the latter almost all traces of normal structure have disappeared. Those studied show a distinct proliferative change, marked by endothelial proliferation, the formation of new bloodvessels, and increase in the connective-tissue framework. Lying in this meshwork there is found a variety of cell types—namely, epithelioid, uni-, and multinucleated giant cells, endothelial, plasma, and lymphoid cells, and an occasional polymorphonuclear leukocyte. The characteristic giant cells are abundant, as are also cells representing the transitional changes from epithelioid to giant cells. The characteristic giant cells have from one to eight or more nuclei, which are pale, with deeply staining chromatin rim, a distinct nuclear network, and one or more prominent nucleoli. The shapes of the nuclei are sometimes bizarre. One giant cell is seen containing between twenty and thirty comparatively small and densely staining nuclei. The accompanying photomicrographs were made from a moderately firm mediastinal gland 2.5 cm. in diameter, and show many of the histological features of the disease.

Spleen. In this are found single and conglomerate lymphomatous areas possessing an identical structure to that of the lymph glands. Considerable golden-brown pigment and small areas of cell necrosis presenting fragmented nuclei are seen.

Liver. Minute lymphomata are found immediately beneath the capsule growing by infiltration into the subjacent parenchyma. In them are liver cells, singly and in small islands, undergoing fatty degeneration and atrophy; otherwise their structure corresponds to that of the large lymph glands. There are moderate fatty infiltration and cloudy swelling of liver cells.

Kidneys. Show capillary engorgement, albuminous and dropsical degeneration of epithelium, and granular and epithelial casts. In the capsular spaces of some of the glomeruli and in some of the tubules are found hyaline material, a few red cells, and desquamated epithelium.

Lungs. The bronchioles are filled with polynuclear leukocytes and epithelium, and a few leukocytes are seen in their walls. The alveoli surrounding the bronchioles are similarly distended.

Pancreas. Apparently normal.

FIG. 1

Mediastinal gland, showing typical cellular arrangement and diffuse fibrosis.
Magnified 150.

FIG. 2

Mediastinal gland, showing giant cells, etc. Magnified 500.

Animal Inoculations. Immediately after autopsy a rabbit was inoculated intravenously with 0.75 c.c., and a guinea-pig intraperitoneally with a like amount of an emulsion made by rubbing up diseased glandular tissue (mediastinal) with sterile physiological salt solution. A month later the guinea-pig died. Autopsy showed lobar pneumonia, without other lesion. Several uninoculated guinea-pigs died at about the same time, which corresponded to a sudden change in the weather. Five weeks after inoculation the rabbit was killed with chloroform and autopsied. No disease was discovered.

The diagnosis of this case was difficult. The patient's anæmic appearance and history of temporary tropical residence at once suggested uncinariasis. Study of the stools confirmed the suspicion. It is believed the disease was of long standing, and dated back to the patient's residence in North Carolina.

Typhoid fever, suggested by the enlarged spleen, temperature curve, and nose bleed was early excluded by repeated Widal tests, and subsequently by the course of the illness.

Malarial cachexia, suggested by enlarged spleen and profound anæmia, was excluded by examinations of the peripheral and splenic blood.

Piropasmosis was strongly suggested by the enlarged liver and spleen, scabies and dry skin, severe anæmia, and recurring attacks of fever. It was positively excluded by examinations of splenic blood.

Lymphatic tuberculosis was excluded by the fact that the glands remained firm and discrete. No adhesions to the skin or other adjacent structures occurred. The tuberculin test was not used. Removal of a gland during life was frequently urged, but not permitted.

A provisional diagnosis of Hodgkin's disease was made several weeks before death. It rested upon the history of an operation for enlarged cervical glands in February, 1904; the presence of firm, discrete, movable, painless glands in the left side of the neck, in the left axilla, and in the groins; the subsequent appearance of similar glands in the right side of the neck; the dulness beneath the left clavicle and left half of the upper portion of the sternum, which was believed to be due to enlarged mediastinal glands (verified by autopsy); and the typically relapsing type of fever. The autopsy findings and the histological study of tissues made the diagnosis conclusive.

I am indebted to Drs. James Carroll and H. H. Donnelly for careful study of tissues and specimens sent to the laboratory.

CONCLUSIONS. Hodgkin's disease shows histological changes peculiar to itself, as found by Reed, Longcope, and others.

The easiest and surest method of diagnosis lies in the removal and histological study of a diseased gland. It may be impossible to make a conclusive diagnosis during life in any other way.

Glandular tuberculosis may be excluded by the tuberculin test. Some cases are characterized by a typically relapsing fever.

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**BACTERIOLOGICAL FINDINGS IN FIFTEEN CASES OF EPI-
DEMIC CEREBROSPINAL MENINGITIS, WITH SPECIAL
REFERENCE TO THE ISOLATION OF THE MEN-
INGOCOCCUS FROM THE CONJUNCTIVA
AND FROM THE CIRCULATING
BLOOD.**

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DURING the recent epidemic of cerebrospinal meningitis in Philadelphia there were in the wards of the Pennsylvania Hospital 15 cases of that disease from which the diplococcus intracellularis meningitidis was isolated. Three of the cases occurred in 1904, while the remaining 12 were seen during the late winter and spring of 1905. All of these cases were quite typical clinically, and this phase of the disease will not be here generally considered. The bacteriological findings of these 15 cases are tabulated in the accompanying table.

The organism isolated from these 15 cases of epidemic cerebrospinal meningitis was practically the same in all cases. As seen in the exudates obtained by lumbar puncture and at autopsy from the central nervous system it was always in pure culture and appeared as a medium-sized or fairly large biscuit-shaped diplococcus somewhat irregular in size. It sometimes occurred in tetrads and small groups. Definite chain formation was never noted. The organism was usually found both within and outside of the polymorphonuclear leukocytes. Of the eleven times in which the position in regard to the leukocytes was noted, the organism was