III. HODGKIN'S DISEASE.

Definition.—An affection characterized by progressive hyperplasia of the lymph glands, with anæmia, and occasionally the development of secondary lymphoid growths in liver, spleen, and other organs. The disease has also the names *pseudo-leukæmia*, *general lymphadenoma*, and *adénie*.

Hodgkin, the well-known morbid anatomist of Guy's Hospital, first described cases in detail, and by the labors of Wilks, Virchow, Billroth, and Cohnheim the disease attained definite recognition.

Etiology.—A majority of the cases are in young persons. In Gowers' table of 100 cases, 30 were under twenty years, 34 between twenty and forty, and 36 above forty. Three fourths of the cases are in males. In a few instances heredity has been adduced as a possible cause, and antecedent disease, such as syphilis, but this is doubtful. More important is local irritation, upon which Trousseau lays special stress, and gives instances in which chronic irritation of the skin, chronic nasal catarrh, or the irritation of a decayed tooth gave rise to local gland swellings, which preceded a general development of the disease. In a large majority of the cases the disease comes on insidiously, without any recognizable cause.

Morbid Anatomy.—*The Lymph Glands.*—In a few cases the enlarged glands are hard and firm, but in a majority the growth is soft and elastic. In the early stage the individual glands are isolated, not larger than almonds or walnuts, and readily separated and movable. When advanced the glands fuse together, and a group, as in the neck, may form a large tumor, the size of an orange or even of a cocoa-nut. About such masses the capsular tissues are hard and dense, forming a firm investment. A growth may perforate the capsule and invade contiguous parts, such as the muscles, skin, or the solid organs. On section, the tumor has a grayish-white appearance; it is smooth, and of variable consistence, either firm and dry or soft and juicy. Suppuration is most frequently seen when the growth reaches the skin. In the deep glands the formation of pus is rare. Caseation is not common; occasionally there are areas of necrosis very like it. The superficial glands are most often attacked, particularly the cervical groups, and the glands may be traced as continuous chains along the trachea and the carotids, uniting the axillary and mediastinal glands.

The axillary group is involved next in order of frequency, and the masses may pass beneath the pectorals and beneath the scapulæ. The inguinal glands occasionally form very large masses. Of the internal groups, those of the thorax are most often affected, either the chain in the posterior mediastinum or the bronchial group, or those of the anterior mediastinum. The trachea and the aorta with its branches may be completely surrounded by the growths, and be but little compressed. From the anterior mediastinum the masses may perforate the sternum and appear as an external tumor.

Of the abdominal groups, the retroperitoneal is most frequently involved and may form a continuous chain from the diaphragm to the inguinal canals, and extend into the pelvis. The glands may compress the ureters, involve the sacral or lumbar nerves, or compress the iliac veins. Occasionally they adhere to the uterus and broad ligament so as to simulate fibroids. I saw, some years ago, one of the most distinguished gynæcologists of Germany perform laparotomy in a case of this kind, in which the diagnosis of myomatous tumors of the uterus had been made. Occasionally the mesenteric or hepatic lymph glands may form large abdominal tumors.

Histologically the chief change is an increase in the cells, with or without thickening of the reticulum. In the early stage there is simple hyperplasia and the relations of the lymph paths are maintained, but when the glands are greatly enlarged the normal arrangement is disturbed. The reticulum varies extremely; in the softer growths it is expanded and can scarcely be found; in the harder structures the network of fibres is very distinct, and there is probably an increased development of the adenoid tissue.

Spleen.—In seventy-five per cent of the cases collected by Gowers this organ was hypertrophied, and in fifty-six of these cases it presented lymphoid growths. The enlargement is rarely great, and does not approximate to the large leukæmic spleen. The lymphoid tumors form grayish-white bodies ranging in size from a pea to a walnut, and may resemble lymph glands in appearance and consistence. Histologically, they consist of lymph corpuscles in a fibrous reticulum.

The marrow of the long bones may be converted into a rich lymphoid tissue; in a few instances the pyoid form, such as is more common in leukæmia, has been found. The tonsils may be involved and the follicles at the root of the tongue. Occasionally secondary growths are seen in the intestines.

The liver is often enlarged and may present scattered lymphoid tumors. The kidneys are occasionally involved and are the seat of growths similar to those of the spleen and liver. The lungs are occasionally directly attacked from the bronchial glands at the root, and secondary nodules may be found throughout their substance. Pleural effusions are not uncommon. Involvement of the nervous system is rare, but paraplegia may be induced by invasion of the spinal canal. The skin may be the seat of adenoid growths, as in a case reported by Greenfield.

Symptoms.—Enlargement of the glands of the neck, axilla, or groins is usually the first symptom noticed. In a few cases the anæmia and constitutional symptoms attract attention before the glandular involvement is evident. When the trouble begins in the deeper groups, pressure effects may be first noticed; thus, paroxysmal dyspnœa with pain in the chest may result from enlargement of the bronchial glands before any physical signs can be detected. Œdema of the feet and shooting

pains in the nerves were the first symptoms in one case which I dissected for Ross, and in another case at the Montreal General Hospital there was paraplegia from pressure on the cord. Such instances, however, are exceptional, and in the majority of cases the swelling of the superficial glands is the earliest symptom. Epistaxis has occasionally been noted, but not so frequently as in leukæmia. With progressive enlargement of the glands the patient becomes anæmic.

Usually, the cervical group is first affected, and it may be impossible to decide whether the enlargement is syphilitic, tuberculous, or lymphadenomatous. One side is first affected as a rule, and it may be months, or even, as in one of my cases, three years before the affection extends to other groups Ultimately huge tumors may develop, which obliterate the neck and extend upon the shoulders and over the clavicles and sternum. The trachea is surrounded, great dyspnœa is produced, and not infrequently tracheotomy is necessary. In the later stages, the skin becomes involved and ulcerates. The axillary group may form large tumors, which compress the brachial or axillary veins and cause swelling of the arms. The inguinal glands are not so often involved, but may form large or even pendulous tumors

In the thoracic glands, as mentioned, the various groups may be involved and produce pressure upon the veins or upon the trachea. In a case at present under observation the superior cava is completely obliterated and a very extensive collateral circulation has been established by means of the mammary and epigastric veins. The skin over the sternum is a mass of fluctuating veins, some of which contain phleboliths. In the abdomen the mesenteric glands may be enlarged, or more commonly the retroperitoneal group. When the patient is thin there may be no difficulty in detecting these, but in stout persons the diagnosis may be impossible. In connection with the affections of the abdominal glands there may be bronzing of the skin, which was well marked in Case IV of my series. A remarkable feature is the variations in the rate of growth and in the size of the glands. They may reduce rapidly and almost disappear from a region, and before death the tumors may diminish very much. The spleen may be enlarged and readily palpable. The thyroid also may be involved, and in a few instances the thymus has been affected. Though present in a majority of the cases, there may be enormous enlargement of the lymph glands without marked anæmia. In one of my cases the blood-corpuscles did not sink below 4,000,000 per cubic millimetre, and in only one instance have I counted the blood below 2,000,000. The red blood-corpuscles rarely show extreme poikilocytosis. The white corpuscles may be moderately increased and the lymphocytes most abundant. Occasionally the leucocytes are greatly increased and the characters of the blood become those of a lymphatic leukæmia. Nucleated red blood-corpuscles may be present, but not in such numbers as in leukæmia.

Of cardiac symptoms, palpitation is common. Hæmic murmurs are often heard over the heart. Shortness of breath may be due to the anæmia, to pressure upon the trachea, or, in some instances, to pleuritic effusion associated with mediastinal growths. Fever is observed in nearly all cases; even in the early stages there is slight elevation. It may be of an irregular hectic type, or continuous, with evening exacerbation. Very remarkable are the cases with ague-like paroxysms, which may persist for weeks or months. They were present in Case I of my series. Pel, of Amsterdam, has given a thorough description of these attacks, and Ebstein has described a case under the remarkable title of "Chronic Recurrent Fever, a New Infectious Disease." In his case during nine months the attacks were present for periods of from twelve to fourteen days and alternated with apyrexia for ten or eleven days.

The digestive symptoms are usually not marked. It is not uncommon to find albumen in the urine. Headache, giddiness, and noises in the ear may be associated with the anæmia. Delirium and coma may be present. Deafness may be produced by growth of the adenoid tissue in the pharynx close to the Eustachian tubes. Inequality of the pupils may be present, owing to pressure of the glands on the cervical sympathetic. The skin may show definite secondary lymphatic tumors, bronzing may occur, and occasionally a most intense and troublesome prurigo.

Diagnosis.—A tuberculous adenitis may at first be very difficult to differentiate. The chief points of distinction are as follows: Tuberculous adenitis is more common in the young and involves the submaxillary group of glands more frequently than those of the anterior and posterior cervical triangles, which are usually affected first in Hodgkin's disease. The enlargement may last for years in a group without extending. The bunches are often, when small, welded together and, most important of all, tend to suppurate—a feature rarely seen in true lymphadenoma, except when it has attained very large size. Strict limitation to one side of the neck or to the axilla is suggestive of tuberculous disease rather than lymphadenoma.

There is an acute tuberculous adenitis, which may involve the lymph glands of the neck, producing enormous enlargement. A man, aged twenty-four, was admitted to the General Hospital, Montreal, with great swelling of the cervical glands on both sides, tonsillitis, and sloughing pharyngitis, with irregular fever and diarrhœa. The case was at first regarded as one of Hodgkin's disease. The occurrence of rigors and intermittent pyrexia is in favor of lymphadenoma. There are cases in which it may for a time be impossible to make a diagnosis. When the glands are only moderately enlarged on one side of the neck or axilla, they should be removed, and the diagnosis can then be thoroughly established.

Prognosis.—Recovery is very rare. The course of the disease is extremely variable. Early and rapid growth in the mediastinal groups may produce pressure effects and cause death before the development is extreme. In some cases the enlargements spread rapidly and group after

group becomes involved in a few months. These acute cases may run a course in three or four months. Chronic cases may last for three or four years. Periods of quiescence are not uncommon. The tumors may not only cease to grow, but gradually diminish and even disappear, without special treatment. Usually a cachexia develops, the anæmia progresses, and there are dropsical symptoms. The mode of death is usually by asthenia; less commonly by pressure from a tumor; and occasionally by coma.

Treatment.—When small and localized the glands should be removed. Local applications are of doubtful benefit. I have never seen special improvement follow the persistent use of iodine or the various ointments.

Arsenic has a positive value in the disease. It should be given in increasing doses, and stopped when unpleasant effects are manifested. The results have in many instances been striking. Due allowance must be made for the fluctuations in the size of the growths which occur spontaneously. I have seen no ill effects from the administration of Fowler's solution for months at a time, and many patients have taken from fifteen to twenty minims three times a day for weeks, and in some instances for months. Recoveries have been reported under this treatment. Personally, no instance of recovery has come under my notice in the cases of which I have notes. Phosphorus is recommended by Gowers and Broadbent, and should be used if the arsenic is not well borne. Quinine, iron, and cod-liver oil are useful as tonics. Every possible means must be taken to support the patient's strength.

IV. ADDISON'S DISEASE.

Definition.—A constitutional affection characterized by asthenia, depressed circulation, irritability of the stomach, and pigmentation of the skin. In a majority of the cases it is associated with tuberculous disease of the adrenals, in other instances with wasting of these organs or with changes in the abdominal sympathetic system.

The recognition of the disease is due to Addison, of Guy's Hospital, whose monograph on The Constitutional and Local Effects of Disease of the Suprarenal Capsules was published in 1855.

Etiology.—Males are more frequently attacked than females. In Greenhow's analysis of 183 cases 119 were males and 64 females. A majority of the cases occur between the twentieth and the fortieth year. A congenital case has been described in which the skin had a yellow-gray tint. The child lived for eight weeks, and post mortem the adrenals were found to be large and cystic. Injury, such as a blow upon the abdomen or back, and caries of the spine have in many cases preceded the attack. The disease is rare in America. Eight cases have come under my personal observation, either clinically or anatomically.

Morbid Anatomy and Pathology.—There is rarely emaciation or anæmia. In a great majority of the cases the adrenals are affected. There may be (*a*) atrophy of one or both glands, due to an interstitial cirrhosis, of which cases have been described by Hadden and Goodhart. (*b*) Tuberculosis, which is the common condition. The capsules are thickened and present firm caseous masses, surrounded by connective tissue. There is usually much fibrous thickening and matting of the adjacent structures, and the affection has definitely been shown to be tuberculous. Tuberculous lesions are common in other parts, particularly in the lungs, though in a number of the cases tuberculosis has been limited to the adrenals. (*c*) There may be malignant disease of the adrenals, which has been present in a few instances of genuine Addison's disease. Among other anatomical features the condition of the abdominal sympathetic has been specially studied. The nerve-cells of the semilunar ganglia have been described as degenerated and deeply pigmented, and the nerves sclerotic. The ganglia are not uncommonly entangled in the cicatricial tissue about the adrenals. The spleen has occasionally been found enlarged; the thymus may persist and be larger than normal.

It is difficult to explain satisfactorily all the symptoms of this remarkable disease. The theories which have been advanced are briefly as follows: (*a*) That the disease depended upon the loss of function of the adrenals. This was the view of Addison. It is held that the blood is gradually poisoned by the retention of some material, the destruction or alteration of which is a function of the suprarenals; (*b*) that it is an affection of the abdominal sympathetic system, induced most commonly by disease of the adrenals, but also by other chronic affections which involve the solar plexus and its ganglia. According to this view, it is an affection of the nervous system, and the pigmentation has its origin in changes induced through the trophic nerves. The pronounced debility is the outcome of disturbed tissue metabolism, and the circulatory, respiratory, and digestive symptoms are due to implication of the pneumogastric. The changes found in the abdominal sympathetic are held to support this view, and its advocates urge the occurrence of pigmentation of the skin in tuberculosis of the peritonæum, cancer of the pancreas, or aneurism of the abdominal aorta. Opposed to it are the facts that the lesions described in the sympathetic system are indefinite, and identical changes occur without the symptoms of Addison's disease.

Symptoms.—In the words of Addison the characteristic symptoms are "anæmia, general languor or debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of color in the skin."

The pigmentation is the symptom which, as a rule, first attracts attention. The grades of coloration range from a light yellow to a deep brown, or even black. In typical cases it is diffuse, but always deeper on the exposed parts and in the regions where the normal pigmentation is