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LEUKAEMIC INFILTRATIONS*

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(With Special Plate)

What is the nature of these infiltrations? Three possible explanations may be given. The cells may accumulate in certain situations through being drawn out of the blood stream as they pass along the capillaries; some physical feature may detain them in their passage; or something in the nature of chemiotaxis may attract them; such arrested cells may multiply locally, the original arrested cells being few. Secondly, the accumulation of cells may be a response of local cells to some stimulus. Thirdly, the accumulation may represent the arrest of emboli of a true tumour process. In the cases under consideration extensive infiltration of the heart muscle or between the tubules of the kidneys cannot be explained by multiplication of local cells.

Another way in which the infiltrations differ from ordinary secondary malignant deposits is that the infiltration by cells is of a diffuse nature, the muscle bundles or renal tubules remaining for a long time distinct, though widely separated by masses of cells. This diffuse distribution is still maintained in parts where the deposit is of a circumscribed and nodular type. In the case of malignant deposits, although infiltration does occur slightly around the periphery, the original structure is entirely destroyed in the main portion of the deposit. The view, therefore, seems justifiable that the infiltrating cells reach their situation by the blood stream and then may undergo multiplication. But the method of infiltration is more diffuse than that of ordinary malignant deposits.

Causes of Death

The majority of leukaemic patients die as the result of a secondary anaemia and gradual asthenia, or from intercurrent infections. Among the rarer accidents that may lead to death leukaemic infiltration of the heart muscle must be considered, since this seems clearly to have been the cause of death of the male dement to be mentioned.

The intense leukaemic infiltration seen sometimes in the kidneys may obviously be in some cases so extensive as to interfere with renal function and lead to a form of uraemia of the anuric type. In these cases, however, the general disease is probably so far advanced that uraemic manifestations, if present, might be obscured in the dying patient. In some cases it seems possible that intense infiltration of the kidneys may occur with leukaemic lesions not far advanced elsewhere; under these circumstances death might result from uraemia.

Haemorrhages in the brain may be a cause of death; leukaemic infiltration does occur in this organ. In the effused blood white cells are present in large numbers, and this may suggest extensive infiltration. The Virchow-Robin space may contain many leukaemic cells.

In some leukaemic cases the capillaries in the alveoli of the lung may be stuffed with white cells, which, in sections, may be seen to have escaped in considerable numbers into the alveoli themselves. In such cases they probably appear eventually in the sputum.

Differentiation

It is hard to draw a sharp line of distinction between lymphatic leukaemia and lymphosarcomatosis, since there are cases showing infiltrations, sometimes extensive, which may be aleukaemic at the beginning and afterwards show a leukaemic change in the blood; these would seem to be connecting cases. Similarly, it is hard sometimes to decide whether a case is lymphosarcomatosis or an aberrant member of Hodgkin's group. As we have seen, Turnbull considers both these conditions to be granulomatous. In what are considered to be cases of lymphosarcomatosis, multinucleated cells may be seen occasionally. In some cases grouped under Hodgkin's disease we may see a general uniformity of cell type, although the cell is larger and paler than the large lymphocyte of lymphosarcomatosis.

Turnbull³ lays stress on enlargement of the spleen being essential for the diagnosis of leukaemia. In some of our examples of infiltration in what we have considered to be aleukaemic cases of leukaemia the spleen has not been enlarged, and in some of the definite cases with leukaemic blood the enlargement has only been trivial. It does not seem that enlargement of the spleen is a necessary condition for the post-mortem diagnosis of leukaemia.

In October, 1931, a male dement aged 57, who had been in the Parkside Mental Hospital for thirty-two years, and apparently had been a healthy man throughout his stay, collapsed and died within a few minutes, with signs of acute heart failure. The post-mortem examination revealed four pints of clear fluid in the pericardial cavity, and replacement of the heart muscle to a considerable extent by a glistening and slightly translucent whitish tissue, which projected slightly on the front of the right ventricle and on the posterior aspect of the left ventricle. The heart was hypertrophied, weighing 20 oz. The liver weighed 91½ oz., and the spleen 12 oz. Both the kidneys were large, and had one or two indefinite pale patches in the cortex. The mediastinal glands were normal. Microscopical examination showed infiltration of the heart muscle by rounded or somewhat oval

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cells (Fig. 1 on the Plate), and a similar infiltration between the tubules of the kidneys (Fig. 2), but no obvious infiltration in the liver. In the brain there was a definite slight increase of lymphocytes in places. Death was clearly attributable to heart failure from infiltration of the heart muscle by these cells.

Two years later another patient in the mental hospital, a man aged 42, suffering from dementia praecox, was transferred to the infirmary ward for special care and treatment on account of influenza. His temperature continued to oscillate, he became very anaemic, and died on December 9th. At the necropsy it was found that the heart muscle was rather pale but firm. The liver weighed 59½ oz. and the spleen 4½ oz. The kidneys were not enlarged, but the medulla of both was pale. Microscopical examination of a papillary muscle and of a portion of the septum of the heart showed some irregular diffuse infiltration with rounded cells, among which were definite myelocytes. In some foci the cells seemed to be breaking down and the nuclei disintegrating. In the liver there was some infiltration with myelocytes and polymorphonuclears, but there was no infiltration in the kidneys or testes. The marrow of the shaft of the femur, which appeared greyish white, showed numerous myeloblasts and nucleated red cells. Death was attributable to the profound anaemia, with dilatation of the heart and early hypostatic pneumonia.

In January, 1929, a schoolboy, aged between 12 and 14, was treated at home for an illness of a vague nature with a raised temperature. He was then sent to a private hospital, where after a stay of two or three days he developed what seemed to be a fit, and died before his medical attendant could see him. There was a history of his having been hit on the head by a cricket bat or ball; the blow apparently had not been a severe one. At the post-mortem examination scattered softened foci with haemorrhages were found in the brain. He had a large liver and a fairly large spleen, with an enlargement in the neighbourhood of the thymus, but the lymph glands were not noticed to be enlarged. Sections of the brain showed extensive areas packed with cells of a myeloblastic or myelocytic type (Figs. 3 and 4). The areas looked like haemorrhages in which white cells were taking the place of red cells. There was also an infiltration of a diffuse nature in the kidneys (Fig. 5) and in the liver.

About twelve years ago a child aged 18 months died at the Children's Hospital with, among other symptoms, a sloughing ulceration of the pharynx. Post-mortem examination showed that the kidneys were very extensively infiltrated with myelocyte-like cells with indented nuclei—to such an extent that tubules were only to be seen at wide intervals, and the glomeruli appeared isolated in the mass of cells (Fig. 6). There was a very extensive infiltration of the pancreas (Fig. 7), and an infiltration (apparently by myelocytes) with many mitoses in the region of the thymus. Groups of Charcot-Leyden crystals were frequent in the infiltrations. The case was evidently an acute form of leukaemia, a condition which had been suspected before death, though a blood count had not been made.

In the first three of these cases no suspicion of their possible leukaemic nature existed before death. One patient died in a few minutes; the others were ill for from ten days to two months. No blood count estimations were made. Nevertheless, the extensive nature of the infiltrations suggests that an overflow into the blood stream had very likely taken place, and that a leukaemic picture would have been presented therein. Problems that present themselves for investigation are:

1. Do these and similar types of infiltration, sometimes diffuse and sometimes nodular, in the heart or kidneys or liver or subcutaneous or other tissues, represent one process or several different entities, some leukaemic and some not leukaemic?

2. Is there a clear-cut means of distinguishing between leukaemic infiltrations, lymphosarcomatous infiltrations, and the infiltrations met with in some cases of acute Hodgkin's disease?

Definitions

Diffuse infiltrations by the appropriate cells of the liver, kidneys, and other organs and tissues are common features of ordinary cases of myeloid and lymphatic leukaemia. In true pseudoleukaemia (systemic aleukaemic lymphomatosis) the picture is that of lymphatic leukaemia, with numerous groups of enlarged lymph glands, and, possibly, deposits in such organs as the spleen, liver, kidneys, and gastro-intestinal lymphatic system, but without the leukaemic blood picture. In Sternberg's leucosarcomatosis a lymphatic leukaemic blood picture is associated with more atypical characters in the cells which form tumour-like infiltrations. The appearances suggest a neoplastic process, but there seem to be all varieties of transitions to ordinary cases of lymphatic leukaemia. In chloroma, lymphomatous masses are found particularly in the skull, with groups of enlarged lymph glands and enlargement of the spleen, and with, or even without, a leukaemic blood picture.

H. M. Turnbull³ depicts "lymphosarcoma" as follows: a condition in which cells resembling large or small lymphocytes or lymphoblasts lie in the meshes of a fibrillar reticulum, replacing the normal tissues like an infiltrating neoplasm; a single group of lymph glands or several areas of adenoid tissue may be affected; several foci may be affected simultaneously, as in lymphoid tissue in the intestine; the periadenoid tissues become infiltrated; and secondary foci may appear in organs where adenoid tissue is normally present, as in the spleen, bone marrow, and portal system of the liver, or even in those in which it is not normally present, as in the skin, kidney, and myocardium. The spleen, he states, is the key organ in differentiating "lymphosarcoma" from lymphatic leukaemia. If the spleen is unaffected leukaemia is excluded. If it is affected the lesion is confined to the Malpighian bodies in lymphosarcoma, while in lymphatic leukaemia it affects the pulp primarily. He considers lymphosarcoma a lymphogranuloma rather than a neoplasm, and closely allied to Hodgkin's disease.

Ordinary cases of Hodgkin's disease present a characteristic histological picture, with large and small lymphocytes, eosinophil cells, often plasma cells, proliferating reticulum cells, and usually reticulum giant cells, followed by fibrosis. In Hodgkin's sarcoma as described by Ewing¹ the picture varies from a close resemblance to the ordinary form to a tissue composed of large round cells with faintly staining granular cytoplasm and moderately chromatic vesicular nuclei; large round giant cells with multiple or multilobed nuclei may predominate. Pullinger² considers these various cells in this disease as probably all derived from the reticulum cells, constituting, in fact, a reticulosis.

Clinical Considerations

In the course of 3,142 post-mortem examinations at the Adelaide Hospital, and 358 at the Parkside Mental Hospital—a total of 3,500 cases—the incidence of leukaemia, lymphosarcoma, and Hodgkin's disease was as follows: ordinary myeloid leukaemia, nine; myeloblastic leukaemia, four; ordinary lymphatic leukaemia, seven; lymphatic leukaemia with extensive infiltrations, three; pseudoleukaemia (aleukaemic leukaemia), three; leukaemic infiltrations found but blood counts not made, four; atypical cases, perhaps leukaemias, three; lymphosarcomata, six; multiple myelomata, two; chloroma (?) (no increase of white cells in the blood), one; ordinary Hodgkin's disease, seven; acute Hodgkin's disease with multinucleated cells, six; and Hodgkin's disease with sarcoma (reticulo-endothelioma), three. In the 358 mental patients only two cases occurred; they are grouped as

"leukaemic infiltrations found but blood counts not made," being the two examples given of infiltration of the heart muscle. The schoolboy with the cerebral haemorrhage and unsuspected leukaemic infiltration, and the infant of 18 months from the Children's Hospital, are not included in the above. An epitome of those cases in the above series showing unusual degrees of infiltration will indicate the scope of these, and the difficulty often experienced in deciding on the correct diagnosis.

Infiltrations in Known Leukaemic Cases

Myeloid Leukaemia: Nodules in the Peritoneal Cavity, Ovaries, and Liver, with Ascites.—No. 99/31: A woman aged 40 had received deep x-ray treatment for myeloid leukaemia. The white cell count during her last period of admission was reduced to 18,600 per c.mm., with 69 per cent. myelocytes. The spleen weighed 86 oz. and the liver 102 oz. There were nodules over the peritoneal cavity tending to fuse, from a pin's head to a walnut in size, with ascites. Myelocytes infiltrated the liver and kidneys, and composed the nodules; mitoses were present.

Lymphatic Leukaemia with Infiltration at the Sites of Soamin Injections and a Surgical Incision.—No. 143/20: A man aged 66 had a sore on the back of the right hand, which was followed by a painless lump near the elbow. Six months later he was admitted with enlargement of the glands at the right elbow, in the right axilla, on both sides of the neck, and in the inguinal regions. No increase in his white cells had been detected six weeks before admission. When admitted they numbered 422,000, consisting almost entirely of large lymphocytes. The spleen weighed 36 oz. and the liver 50 oz. Where soamin injections had been made in the left arm the subcutaneous tissues were infiltrated. There was a similar infiltration over the site where a supratrochlear gland had been removed. There was infiltration of the skin over the right biceps. Besides the glands mentioned, those along the vertebral column and common iliac arteries and the femoral glands were enlarged.

Lymphatic Leukaemia with Tumour-like Infiltrations (Leucosarcoma), Nodules in the Kidneys, Liver, and Pericardium, Plaques on the Ribs and in the Spinal Canal. Low Leucocyte Count.—No. 10/23: A man aged 38 had a white blood count of 11,000, of which the lymphocytes contributed 80 per cent. There was an infiltrated neoplastic-looking mass on the posterior aspect of the bladder in the depths of the rectovesical pouch, and extending to the prostate. The kidneys were studded with nodules with rather ill-defined outlines; there was a diffuse infiltration, with the remains of tubules still showing in many places. A few ill-defined nodules were present in the liver and also in the pericardium. There were diffuse whitish elevations on some of the ribs and in the spinal canal. A plaque in the pia mater pressed on the subjacent cord near the commencement of the cauda equina; microscopical examination of this mass was not made owing to the accidental loss of the specimen.

Lymphatic Leukaemia with Tumour-like Masses (Leucosarcoma) around the Abdominal Aorta, in and around both Kidneys, in the Mediastinum, and in the Left Scrotal Sac.—No. 82/26: A man aged 51 had a white cell count of 48,000, of which the lymphocytes contributed 89 per cent. The spleen, which was said to have been enlarged for eleven years, weighed 92 oz., and the liver 82½ oz. The tissues in front of the abdominal aorta showed a diffuse firm pinkish-white infiltration surrounding this vessel and the inferior vena cava; they extended laterally to form cuirasses around each kidney, as well as infiltrating each kidney by way of the hilum and pelvis. The suprarenal glands were lost in the mass of infiltration, and the pancreas was surrounded. The left scrotal sac was infiltrated. There was an infiltrating mass partly embracing the lower portion of the trachea, and another behind the heart. The glands in the axillae and groins were also enlarged. Microscopically there was infiltration in the liver—of Glisson's capsule more particularly—and in the kidneys a diffuse infiltration affecting also the surrounding fat.

Infiltrations in Pseudoleukaemia

In the examples above detailed the leukaemic nature of the cases is beyond question. In the two following cases, placed under "pseudoleukaemia," the leucocyte count was either reduced or not greatly increased, and the differential counts were normal. Otherwise the pathological pictures were those of a leukaemia, and the cell infiltrations were similar in characters to those met with in leukaemic cases. As it is well known that cases, later showing typical leukaemic blood pictures, may be met with in an aleukaemic (presumably early) stage with enlarged glands, there is no reason to consider these cases as being aetiologically distinct from leukaemia.

Pseudoleukaemia with Infiltration in the Liver.—No. 205/30: A girl aged 13½ had a profound secondary anaemia and a white cell count of 3,700; a differential count revealed no abnormal cells, but the polymorphonuclears were reduced. The spleen weighed 14 oz. and the liver 81 oz. There was slight enlargement of the external lymph glands and the mesenteric glands. The liver was stuffed with enormous numbers of round cells in patches, obscuring Glisson's capsule; there were also small groups between the liver cells suggestive of blood-forming islands. In the spleen the medulla was full of red cells, contrasting with the lymphoid areas. In the kidneys, cells with indented nuclei accompanied the blood vessels in the medullary and glomerular regions.

Pseudoleukaemia, with Extensive Infiltrations in the Liver, Kidneys, and Testis, and Infiltration of the Heart Muscle.—No. 123/34: A boy aged 13 had a white cell count varying from 6,000 to 14,000; the cells being present in normal proportions. The spleen weighed 27 oz., and the liver was large. There were very large glands around the pancreas, along the abdominal aorta and iliac vessels, and in the groin. The mesenteric glands were enlarged, as were the tracheal glands. There was an extensive infiltration of the liver with large mononuclear cells. In the kidneys the renal tubules in places were only seen at wide intervals on account of the infiltration. There was some diffuse infiltration in the heart muscle, and extensive infiltration of the testis. Lymphocytes were present also in the pial vessels, and accompanying the small vessels in the pons, cerebellum, medulla, cortex, and basal nuclei. These cells were like large lymphocytes, with rounded nuclei occupying most of the cell.

Infiltrations Believed to be Leukaemic

Under this heading, comprising cases in which no blood count was taken, come the four mentioned at the beginning of this paper, and the case which follows.

No. 121/32.—A lad aged 18 died thirty-two hours after admission. The spleen weighed 40½ oz. and the liver 110 oz. The lymph glands were generally enlarged. There was enlarged tissue in the mediastinum, and the kidneys were infiltrated.

This last-mentioned case, with much enlarged liver, spleen, and lymph glands, seems unquestionably one of leukaemia. The boy who died with softened areas and haemorrhages in the brain had obviously leukaemic blood, as indicated by the white cell accumulations in the effused blood. The child of 18 months seems also an undoubted case. The first dement had a very large liver, but only a slightly enlarged spleen and no enlarged lymph glands. Nevertheless the cell infiltration of his heart muscle had caused his sudden death, and the accumulation of cells in his kidneys was considerable. In the second dement the only important features linking it with a possible leukaemic process were the infiltration of the cardiac muscle by myelocytes and the presence of similar cells between the liver columns, the spleen and lymphatic glands being not appreciably enlarged. Blood counts in these dements might have settled their leukaemic nature beyond dispute. Even had such an examination shown a normal blood

picture this would not exclude leukaemia, perhaps in an early stage. Both men died from what might be called "leukaemic accidents" (if they are leukaemic cases); the complete pathological picture might be considered as not having yet become developed.

Possible Chloroma

No. 99/34.—A woman aged 52 had a white count varying from 4,100 to 8,000 per c.mm. The differential count was mostly normal, though metamyelocytes varying from 2 to 12 per cent. were noted on two occasions, and several abnormal cells were seen on two occasions. A fleshy mass attached to one of the costal cartilages was continuous with a similar mass in the anterior mediastinum. An extradural sheet of tissue pressed upon the dorsal cord. The abdominal glands were slightly enlarged. The spleen weighed about 30 oz. and the liver 64 oz. The infiltrating cells resembled large lymphocytes.

Lymphosarcoma with Infiltrations

Four examples from the six cases which were diagnosed as lymphosarcoma in these necropsies are epitomized. The differentiation of these from cases considered to represent leukaemic infiltrations, but without leukaemic blood changes, is difficult if not impossible. The details show that the distribution of the infiltrations follows similar lines to those in the leukaemias. In typical lymphosarcoma a delicate reticulum passes between the cells, but it may not be readily demonstrable.

No. 36/26.—A man aged 40 had extensive infiltration of the ilio-psoas muscle, of the recto-vesical space, between the stomach and liver, in and around both kidneys, in the pericardium, and in the mediastinum. He had haemorrhage from a secondary malignant ulcer of the stomach. The spleen was not weighed.

No. 173/27.—A woman aged 40 had infiltration of the head of the pancreas, the base of the mesentery, along the abdominal aorta, and into both ischia, with resulting caries and secondary gangrene of the labium majus. The spleen weighed 12 oz. and the liver 56 oz.

No. 119/34.—A young woman aged 21, in whose case no blood count had been done, showed infiltration of the mediastinum, pericardium, and pleura; there were enlarged glands in the abdomen and base of the neck, and deposits in the kidneys (Fig. 8 on Plate). The spleen weighed 8½ oz. and the liver 51 oz. There were mitoses in the coeliac glands.

No. 46/35.—A young woman aged 22 had a mediastinal mass surrounding the great vessels, infiltrating the heart muscle, and invading the right pleura over the diaphragm, with nodular masses and hydrothorax. The glands in the coeliac axis and in the portal fissure were enlarged. The spleen weighed 3 oz. and the liver 56 oz. The infiltrating cells resembled lymphocytes, with nuclei 3.5 to 5 μ in diameter.

Acute Hodgkin's Disease with Multinucleated Cells and Infiltrations

No. 170/29.—A woman aged 64 had deposits in the peritoneum, enlarged glands along the abdominal aorta, deposits in the liver up to one inch in diameter with necrosed centres, and deposits in the right kidney. There were enlarged glands in the neck, around the thoracic aorta, and in the roots of the lungs, with infiltrations of the lungs. The spleen weighed 6½ oz. and the liver 65½ oz. The cells appeared to be reticulum cells, and the multinucleated cells were unusually large and numerous.

No. 162/34.—A lad aged 18 had a white cell count of 12,500 per c.mm., with 5 per cent. of eosinophils. Masses in the mediastinum and interior portion of the pericardium extended into the right lung, with right pleural effusion and with nodular infiltration of the left lung. There were deposits in both kidneys (Fig. 9 on Plate), suprarenals, and the pancreas, with a large mass round the abdominal aorta. The spleen weighed 4½ oz. and the liver 53½ oz. Microscopically there was fibrosis, necrosis, eosinophil infiltration, and proliferating reticulum cells, many with compound nuclei.

No. 77/35.—A man aged 26 had been treated for seven years with deep x rays for Hodgkin's disease. There were enlarged glands in the mediastinum, the neck, around the pancreas, along the abdominal aorta into the left groin, and in the axillae. The bronchial glands were enlarged on the right side, and there was invasion of that lung with miliary spread. There were umbilicated deposits in the liver and spleen up to the size of 3¼ inches and 2 inches respectively. A sheet of tissue pressed on the cauda equina.

No. 109/35.—A man aged 21 had a leucocyte count falling from 6,000 to 1,600 per c.mm.; the differential count showed a polymorphonuclear leucopenia. There were large soft glands around the pancreas, along the abdominal aorta extending into the left groin, and one soft gland in the right side of the neck. The spleen was much enlarged and weighed 40 oz., but did not show white nodules; the liver weighed 62½ oz. There were ulcers in the stomach and duodenum.

Hodgkin's Disease: Sarcomatous Type

No. 111/32.—A man, aged 50, on whom no blood count had been done, had enlarged soft pinkish glands in the mediastinum and along the abdominal aorta, in the neck, axillae, groins, and the mesentery, with infiltration of the pericardium and wall of the heart. The infiltrating cells suggested reticulum cells.

Summary

1. Examples are given of: (a) leukaemic infiltration of heart muscle, in one case causing sudden death in a hitherto seemingly healthy man; (b) leukaemic infiltration of the kidneys or pancreas to a degree calculated to embarrass the functions of such organs; (c) leukaemic cerebral accidents in which white cells form conspicuous accumulations, mostly from the associated haemorrhage; and (d) neoplastic-like deposits of seemingly leukaemic cells in various organs and tissues in known or presumed leukaemic cases, and in cases which have not shown any alteration in the blood picture (pseudoleukaemia).

2. Examples are given of infiltrations in lymphosarcomatosis. The author finds it difficult to decide in some cases whether the condition is a lymphosarcoma or a pseudoleukaemia. He is not satisfied that there is a sharp line of demarcation between these.

3. Examples are also given of infiltrations in acute cases of Hodgkin's disease and Hodgkin's sarcoma of Ewing. The presence, even in small numbers, of reticulum cells with compound or multiple nuclei is a help in diagnosis, and enables some cases resembling lymphosarcoma to be reasonably transferred to this group.

REFERENCES

- ¹ Ewing, James: *Neoplastic Diseases*, 1928.
- ² Pullinger, B. D.: *Rose Research on Lymphadenoma*, 1932, p. 117.
- ³ Turnbull, H. M.: *Proc. Roy. Soc. Med.*, 1929, xxiii, 220.

L. v. Szathmáry (*Zentralbl. f. Gynäk.*, October 19th, 1935, p. 2477) describes an extreme case of uterine hypertrophy induced by hormone production in granulosa-cell ovarian tumours. The patient, 63 years old, had had procidentia since two years before the menopause (at 43), and an ulcerated os externum was noted on a bluish-red tumour, larger than a child's head, which protruded from the vulva. After rest it proved to be replaceable, and was found to be connected with a pelvic swelling reaching to three fingerbreadths below the navel. There was a copious cervical discharge of pus, and a diagnosis of myoma and pyometra was made. The uterus on removal was twice the size of the fist; it was free from myoma or other tumour, but there was cervical hypertrophy. The myometrium was 6 cm. thick. The remains of the endometrium showed glandular hyperplasia and penetration of the myometrium, in the stroma of which were numerous cells resembling those of the decidua. A yellow granulosa-cell cyst was found in one ovary, and the urine after operation contained 360 mouse units of folliculin to the litre.

FIG. 1.—Male dement, aged 57. Sudden death from acute heart failure. Extensive cellular infiltration of heart muscle.

FIG. 2.—Same case as Fig. 1. Diffuse cellular infiltration of kidney.

FIG. 3.—Schoolboy. Sudden death following a fit after a few days of vague illness. Softened haemorrhagic focus in brain packed with myeloblasts or myelocytes.

FIG. 4.—Same case as Fig. 3. Virchow-Robin space round a vessel in brain packed with cells.

FIG. 5.—Same case as Fig. 3. Extensive cellular infiltration in kidney.

FIG. 6.—Child, aged 18 months, with sloughing ulceration of the pharynx. Very extensive infiltration of kidney with myelocyte-like cells.

FIG. 7.—Same case as Fig. 6. Very extensive cellular infiltration of pancreas.

FIG. 8.—Woman, aged 21, with lympho-sarcomatous infiltration of mediastinum, pericardium, and pleura, and enlarged glands in abdomen and neck. Deposit in kidney showing diffuse infiltration.

FIG. 9.—Lad, aged 18. Hodgkin's disease. Masses in mediastinum, pericardium, lungs, and round abdominal aorta. Deposits in kidneys, suprarenals, and pancreas. Section of kidney.