

Journal (1956) various cures were proposed, but disappointingly little was mentioned about diagnosis. In our patient much time was wasted in conservative treatments of such kind: the logical and obvious cure is shown in Special Plate Fig. 3 and Graph 2.

In these cases one began by knowing little and believing much, and ended by inverting the quantities. The adenoids, long ago entered in the Gilbertian classification of things "that never will be missed," deserve some respect, if not a reappraisal, of their worth.

Finally, I would like to emphasize the advantages of early diagnosis and treatment in patients with speech disorders. These patients are invariably backward in reading and in their general education because of their speech defect. Some of them are of below-average intelligence and so require special help. Correcting the speech defect allows their education to proceed normally, and will also allow them to take advantage of extra coaching at school so that they may ultimately earn a living, as normal citizens, within their capacity for work and responsibility.

Summary

It is conservatively estimated that in England and Wales 250 children per year are born with potential speech defects or acquire such defects as the result of disease or of radical adenoidectomy. The mechanism of production of such defects by tonsil and adenoid operations is described.

A scheme for the investigation of children with defective speech is outlined, with particular reference to nasality. "Nasal escape" is defined and a summary of its causes given. The advantages of early diagnosis and treatment are stressed. A fairly complete palatopharyngeal analysis can be made on a simple lateral radiograph; even more accurate information can be obtained with a cephalometric tracing.

Children with speech disorders are invariably educationally backward, and correction of the defect allows their education to proceed normally so that ultimately they may earn their living as normal citizens.

Three illustrative cases are reported. These are discussed and their progress is charted.

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Lecturing at the Royal Institution on March 21, Professor C. D. DARLINGTON, F.R.S., said that man was already controlling his own evolution, as Francis Galton had predicted he would. The present methods of control operated at several levels. Irradiation induced mutations; cousin-marriage exposed them. Selective migration and education changed our breeding groups. The successes of medical treatment increased the proportion of individuals requiring medical treatment for birth or survival. These successes also favoured a differential fertility between social classes which tended to lower the proportion of educable individuals in the next generation. Artificial insemination and medical sterilization might be used to work in the opposite direction. On a higher level we could see that the development of class structure, and the rise and decline of nations which were connected with it, were genetic and evolutionary processes. These processes were influenced or controlled to-day by the action of departments of governments, especially in health, education, and taxation. We easily forgot that, though governments could provide us with education, only parents could endow us with the ability to profit by it.

LOCALIZED LEISHMANIASIS OF LYMPH NODES

REPORT OF FOUR CASES

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[WITH SPECIAL PLATE]

It is well known that lymph nodes may be affected in cases of kala-azar and that Leishman-Donovan (L.D.) bodies may be demonstrated in material obtained by lymph-node aspiration or biopsy (Cochran, 1912; Hu, 1936; Kirk and Sati, 1940; Lipscomb and Gibson, 1944; Rigg, 1957), but few records are available of human cases with lymph-node enlargement alone, and in which no other clinical manifestations of the infection could be found.

Chung (1944) described the case of a male student from Peiping who presented with an enlarged cervical lymph node. Microscopical examination of the node obtained by biopsy revealed the presence of L.D. bodies. Subsequent inoculation of a hamster with material obtained from an epitrochlear node gave rise to generalized leishmaniasis in the animal. The patient showed no other evidence of visceral disease over a period of four years' observation, at the end of which time he received a course of treatment ("neostibosan"—diethylamine-*p*-aminophenyl stibinate) following the development of a positive complement-fixation reaction.

Angevine *et al.* (1945) described two cases in U.S. Servicemen from the Mediterranean area who were admitted to hospital for investigation of lymph-node enlargement unassociated with any other abnormal physical signs. In both cases L.D. bodies were demonstrated in sections of the cervical lymph nodes, and, as in Chung's case, in the liver and spleen of a hamster which was inoculated with a culture made from a subsequent lymph-node biopsy from one of the cases. No other relevant case reports have been found in the literature.

Four cases are now described of British Servicemen serving in Malta and Cyprus in whom the only clinical abnormality has been the presence of enlarged lymph nodes and in three of whom L.D. bodies have been demonstrated in material obtained by lymph-node biopsy or aspiration.

Case 1

A 19-year-old soldier arrived in Malta on August 14, 1956. He trained in various parts of the island before leaving for Cyprus at the end of November. In late October he first noticed enlarged "glands" in his neck, and over the next few weeks further enlarged lymph nodes appeared in both axillae and groins. These ached and were tender to touch, but otherwise he was well. He was admitted to hospital in Cyprus, and after a right cervical lymph-node biopsy on January 2, 1957 (first biopsy), he was invalided to the United Kingdom with a histological diagnosis of sarcoid. On admission to the Queen Alexandra Military Hospital on January 29 he looked well and was afebrile. Discrete rubbery lymph nodes were palpable in cervical, axillary, and inguinal regions. There was no splenomegaly or hepatomegaly.

Investigations

Hb 15.7 g. per 100 ml.; W.B.C. 7,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 6.8 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Chest radiograph and sternal marrow normal. Mantoux reaction positive (1/1,000 O.T.). Wassermann reaction, Paul-Bunnell test, *Brucella* agglutination reactions, brucellin skin test, and dye test and complement-fixation test for toxoplasmosis were all negative.

Aspiration of a right cervical lymph node on February 20 failed to demonstrate any parasites either in direct smears or after inoculation of Novy, MacNeal, and Nicolle's (N.N.N.) medium. A further lymph-node biopsy from the left cervical region was carried out on March 1 (second biopsy).

Pathology

First Biopsy.—A lymph node 1 cm. in its greatest diameter. Microscopically, the normal architecture of the lymph node is partially replaced by discrete, clearly defined collections of large macrophage or "endothelioid" cells with a weakly eosinophilic cytoplasm (Special Plate, Fig. 1). Only occasional lymphoid follicles are present, and these show little reactive change. The sinuses are dilated in parts and contain numerous macrophages and occasional lymphocytes. The larger collections of macrophages appear towards the periphery and extend to a thickened capsule. The periadenoid tissue and capsule are infiltrated by numerous plasma cells, lymphocytes, and foreign-body-type giant cells; "tubercle"-like aggregations of macrophages are also present (Special Plate, Fig. 2). No parasites could be identified in this material.

Second Biopsy.—A lymph node measuring 2.5 × 1.5 × 1.0 cm. The cut surface has a fleshy consistency. Microscopically, the appearances are broadly similar to those of the first lymph node, but the clumps of macrophages are larger and run together to form extensive sheets of cells. Signs of early necrosis are present at the centre of some of these macrophage clumps. Multinucleated giant cells of foreign-body and Langhans types are present throughout the lymph node. The pulp is oedematous and the medullary sinuses are dilated. Intracellular parasites morphologically identical with L.D. bodies are present in macrophages and giant cells, particularly in the periphery of the lymph node. Their distribution is very irregular and a careful search is required to identify them. Smears and culture from one-half of the lymph node on N.N.N. medium failed to demonstrate any parasites.

Progress

"Pentostam" (sodium stibogluconate), 6 ml. intramuscularly daily for 10 days, was given, and one month after completion of treatment all the nodes were smaller and firmer.

Case 2

A 19-year-old soldier arrived in Malta on August 20, 1956. After about two months he noticed enlarged

"glands" in the right side of his neck, but as he felt well and they were not painful he did not report sick. Soon after his arrival in Cyprus in late November the "glands" increased in size and he was admitted to hospital. On examination he was found to have enlarged, discrete rubbery lymph nodes in the cervical, axillary, and inguinal regions. The spleen was noted as "just palpable." Two lymph-node biopsies were performed, the first on January 11, 1957 (first biopsy), and the second on January 17 (second biopsy). He was invalided to the United Kingdom as a case of "generalized reticulosis." On admission to the Queen Alexandra Military Hospital on January 29 he looked well and was afebrile; the spleen was not palpable, the liver was not enlarged, and there appeared to be no change in the size and consistency of the lymph nodes as compared with their previous description. The biopsy scars were markedly indurated.

Investigations

Hb 13.1 g. per 100 ml.; W.B.C. 8,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 6.5 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Mantoux reaction positive (1/1,000 O.T.). Wassermann reaction, Paul-Bunnell test, *Brucella* agglutination, and complement-fixation and dye tests for toxoplasmosis—all negative. Sternal marrow normal. Lymph-node puncture was carried out on February 19, and the smears showed many macrophages and lymphocytes. Numerous L.D. bodies were present in macrophages (Special Plate, Fig. 3). Fluid aspirated from the lymph node was inoculated on to N.N.N. medium, but no growth took place.

Pathology

First Biopsy.—A collection of small lymph nodes, the largest being 1.0 × 0.5 × 0.5 cm. Cut section is firm. Microscopically, the lymph node shows a normal follicular pattern. Small congeries of macrophages with occasional multinucleated giant cells are scattered throughout the parenchyma, some being present in the sinuses and others in the outer zone of follicles. The peripheral and medullary sinuses show moderate dilatation and contain mainly lymphocytes and macrophages. There is no capsular thickening or periadenoid reaction. L.D. bodies are present in small numbers, both in giant cells and macrophages.

Second Biopsy.—A lymph node 1.5 cm. in its greatest diameter. Microscopically, the lymphoid follicles show marked reactive hyperplasia and there is proliferation of reticulum cells in the pulp. Clumps of macrophages, which are larger and more numerous than in the first biopsy, and giant cells are present. L.D. bodies are present within the macrophages.

Progress

After a course of pentostam there was a marked reduction in size of the lymph nodes.

Case 3

A 21-year-old soldier arrived in Malta on August 20, 1956, and trained in most areas of the island. Two months later he noticed a lump in his right groin which gradually increased in size. Unlike the other patients, he was admitted to hospital while still in Malta. On examination he was found to have enlarged femoral lymph nodes. There was no evidence of a primary focus of infection in legs or perineum. There was no other lymphadenopathy; he looked well and was afebrile. Results of investigation at that time, including white cell count, E.S.R., and chest radiography, were all normal. Two femoral lymph nodes were removed on November 28, 1956, and subsequently a histological diagnosis of sarcoid was made and the patient invalided to the United Kingdom for further investigation. The biopsy wound was slow to heal, and on the patient's admission to the Queen Alexandra Military Hospital on January 24, 1957, there was still considerable surrounding

induration. Apart from this, physical examination was negative and there were no symptoms.

Investigations

Hb 15.0 g. per 100 ml.; W.B.C., 7,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 7.9 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Mantoux reaction positive (1/1,000 O.T.). Sternal marrow normal. Wassermann reaction, Paul-Bunnell test, *Brucella* agglutination, and complement-fixation and dye tests for toxoplasmosis—all negative.

Pathology

Two lymph nodes each approximately 1.5 cm. in their greatest diameter. Microscopically, the normal architecture is widely replaced by ill-defined clumps and cords of large macrophages, amongst which are scattered numerous multinucleated giant cells of foreign-body and Langhans types. Occasional isolated giant cells are present in the pulp and lymph follicles (Special Plate, Fig. 4). L.D. bodies are present in moderate numbers in giant cells and macrophages (Plate, Fig. 5); these are more numerous in the periphery of the node and show an irregular distribution. The medullary and peripheral sinuses are dilated and the capsule is thickened and densely infiltrated by plasma cells and lymphocytes.

Progress

The patient was treated with pentostam and has remained well.

Case 4

A 19-year-old soldier arrived in Malta on August 14, 1956. Two months later he noticed enlarged "glands" in his neck, but at no time did he have any constitutional upset. He went to Cyprus in late November, where he was admitted to hospital and a left cervical lymph-node biopsy performed (first biopsy). A diagnosis of sarcoidosis was made and he was invalided to the United Kingdom. When admitted to the Queen Alexandra Military Hospital in early January, 1957, he looked well and was afebrile. He was found to have enlarged lymph nodes in the right cervical and submental regions and in the left axilla, and there was marked induration surrounding the biopsy scar. There were no other abnormal findings.

Investigations

Hb 15.0 g. per 100 ml.; W.B.C., 9,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 6.7 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Wassermann reaction, *Brucella* agglutination, Paul-Bunnell test, and complement-fixation and dye tests for toxoplasmosis—all negative. Mantoux reaction negative (1/1,000 O.T.). Sternal marrow normal. Biopsy of a left axillary lymph node was performed on March 1, 1957 (second biopsy).

Pathology

First Biopsy.—A soft lymph node 2 × 1 × 1 cm. Microscopically, the normal lymph-node architecture is completely replaced by poorly defined clumps and sheets of macrophages. Multinucleated giant cells are infrequent and occur near the lymph-node capsule, which is thickened and infiltrated by lymphocytes, plasma cells, and macrophages. The periadenoid tissue shows marked involvement in the granulomatous process, and in addition there are several foci of fibrinoid degeneration, many of which are in the walls of vessels. Eosinophilic material is also present in the centre of macrophage clumps. Despite a careful search of many sections, no L.D. bodies were found.

Second Biopsy.—Three small lymph nodes. Microscopically, all three nodes show a similar pattern. The general architecture is normal. Reactive hyperplasia and sinus catarrh are present, and two or three small conglomerates

of macrophages with an occasional giant cell lie in the pulp. No parasites are present. Direct smears and culture on N.N.N. medium from these lymph nodes failed to show any leishmania.

Progress

Following the patient's admission to hospital in England the induration in the scar and the lymph-node enlargement gradually subsided, and after a course of pentostam the nodes became even smaller and firmer. He has remained well.

Discussion

Agius-Ferrante (1955, 1957), discussing the incidence of leishmaniasis in Malta, states that the visceral form in adults is rare on the island, and that between 1947 and 1954 only 10 cases out of a total of 777 occurred in patients over 10 years of age. He further states that there has been a significant decline in incidence of the disease on the island in the last few years, only 14 cases being notified in 1956 as compared with 204 in 1948. He makes a third observation, that the cutaneous form of the disease is never seen on the island. Debono (1957) says that, while leishmaniasis in adults does occur in Malta, it is exceptional. It is of interest, therefore, that the infection should have occurred in these four adults, within two months of their arrival in Malta, in a year in which the low incidence of the disease among the indigenous population suggests a satisfactory reduction in the number of vectors on the island. The patients were drawn from two units only, but there was no intimate contact between the personnel of these two units, and camp sites were not adjacent. In spite of repeated clinical examination over a fairly long period of observation, no further evidence of leishmaniasis was found; and, although in Case 2 it was noted in Cyprus that the spleen was "just palpable," it has not been felt on any subsequent occasion, whereas the natural history of the disease would lead one to expect a progressive enlargement if there had been a true leishmanial infection of this organ. The induration of the biopsy scars in Cases 2, 3, and 4 was a noticeable feature, and this is in accordance with the histological evidence of capsular and periadenoid infiltration.

Following a course of intramuscular injections of pentostam there was a measurable reduction in the size of the lymph nodes in Cases 1, 2, and 4 but this could not be observed in Case 3, as the only group of enlarged lymph nodes had already been surgically removed. Case 4 has been included, as there were the same movements in timing, geography, and duration as Case 1, the case presented a parallel clinical picture and showed definite clinical response to treatment, with reduction in size of the lymph nodes, and the histological picture was similar to that of the other cases. It was this basic similarity of the histological appearances of the lymph-node biopsies that first made us consider the possibility of a common aetiology. The main features are aggregations of macrophages associated with a varying number of giant cells, and in two cases severe involvement of the capsule and periadenoid tissue. Within this framework the picture varies from a few scattered foci of macrophages with occasional giant cells (vide Case 2, first biopsy) to almost complete replacement of the normal lymph-node structure by the granulomatous process (vide Case 4, first biopsy).

The microscopic appearance of organs involved in visceral leishmaniasis are well known, and are clearly described by Ash and Spitz (1945): "The basic pathologic changes in visceral leishmaniasis result from localization of the leishmania within the cells of the reticulo-endothelial system and consequent proliferation of these cells." Meleney (1925), reporting the histology of lymph nodes in experimentally infected hamsters, describes appearances very similar to those seen in our cases. He noted large clumps of clasmato-cytes and multinucleated cells, and that parasites were often only present at the periphery of the clumps. Hu (1933), in reporting his work on experimentally infected hamsters,

D. W. BELL *ET AL.*: LEISHMANIASIS OF LYMPH NODES

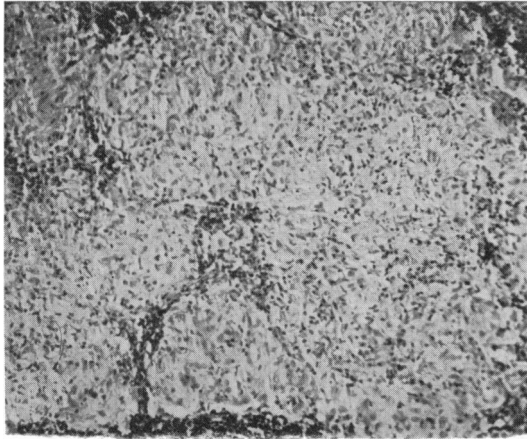


FIG. 1.—Case 1. Lymph node: focal collections of macrophages. (Haematoxylin and eosin. $\times 60$.)

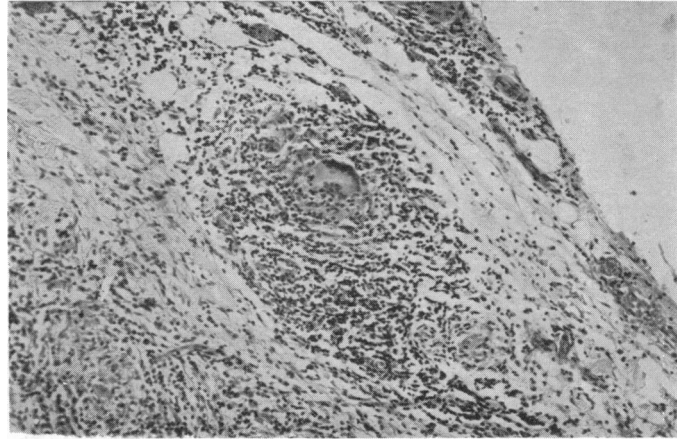


FIG. 2.—Case 1. Lymph node: capsular and peradenoid reaction. (Haematoxylin and eosin. $\times 60$.)

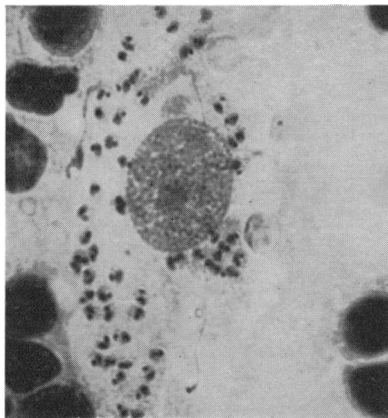


FIG. 3.—Case 2. Lymph-node puncture: L.D. bodies. (Leishman. $\times 750$.)

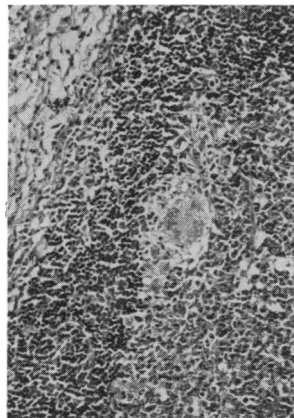


FIG. 4.—Case 3. Lymph node: giant cell in follicle. (Haematoxylin and eosin. $\times 60$.)

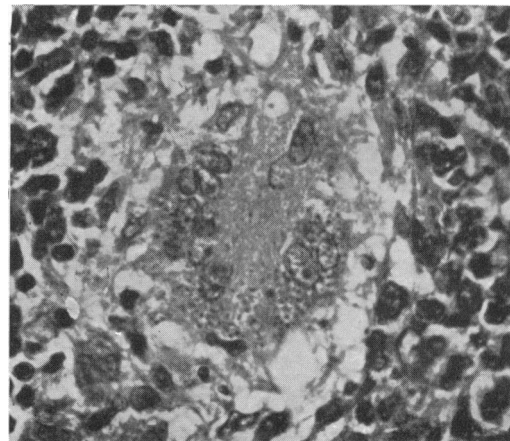


FIG. 5.—Case 3. Lymph node: L.D. bodies in giant cell. (Haematoxylin and eosin. $\times 480$.)

R. O. K. SCHADE. EXFOLIATIVE CYTOLOGY OF GASTRIC CARCINOMA

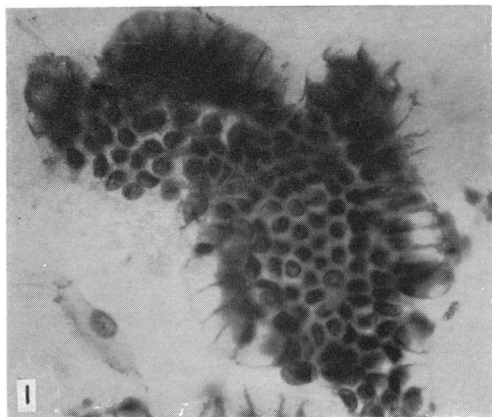


FIG. 1.—Clump of normal gastric epithelium with regular structure and nuclei of equal size. Cell boundaries are well defined. ($\times 712$.)

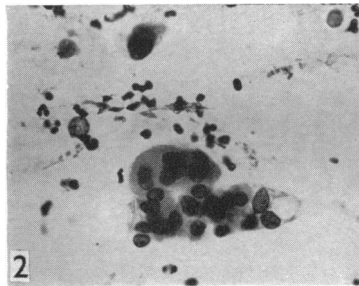


FIG. 2.—Clump of malignant cells showing overlapping and variation in size of nuclei. The background is formed by squamous cells, organisms, and polymorphs. ($\times 475$.)

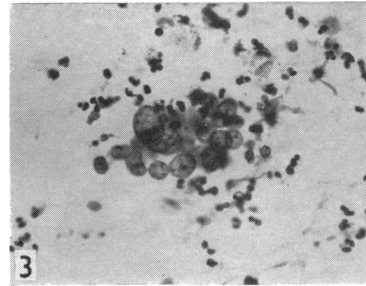


FIG. 3.—Group of malignant cells denuded of cytoplasm. Note variation in size of nuclei and prominence of nucleoli. Polymorphs and organisms form the background. ($\times 475$.)

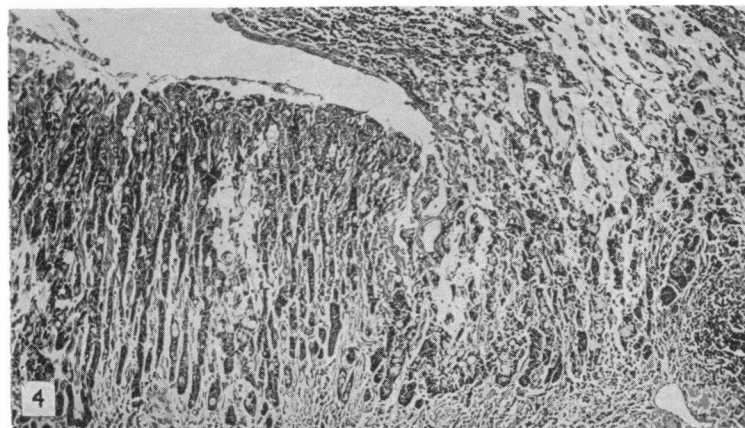


FIG. 4.—Typical mucoid carcinoma, entirely confined to the mucosa. ($\times 165$.)

described tubercle-like collections of macrophages in lymph nodes and an increase in the number of plasma cells in the medullary cords of lymph nodes. Angevine *et al.* described similar changes in the lymph nodes of their two cases.

Identification of the parasites requires a careful search of many sections. Angevine *et al.* also noted this and found parasites were more numerous at the periphery of the node. They suggest that if fixation does not reach the parasites quickly they degenerate. The difficulty of finding the parasites is well illustrated in Case 1 (second biopsy). After surgical removal the lymph node was bisected, one-half being placed in 10% formol saline for histological processing, and smears and imprints made from the other half. Parasites were identified in the paraffin sections, but none could be found in the smears.

Various staining methods were used, including Giemsa, but the most satisfactory results were obtained with routine haematoxylin and eosin. It was noted that the parasites were P.A.S.-negative. No tubercle bacilli or fungi were demonstrated in any of the lymph nodes.

Our lack of success in culturing the parasites was disappointing. One of the reasons for this failure may have been that only a very small amount of fluid was obtained by aspiration of the lymph nodes, and most of this was used in the preparation of the smears, leaving only traces in the needle for cultural purposes. Unfortunately the cultures prepared from the excised lymph nodes were contaminated.

Many disease processes involving lymph nodes, including sarcoidosis, tuberculosis, and histoplasmosis, may present similar microscopical changes to those described above, and the differential diagnosis on histological grounds may be difficult. It is a matter of interest that in three of our cases an initial diagnosis of sarcoidosis was made.

The possibility of the occurrence of this condition should be considered by both clinicians and pathologists in the differential diagnosis of lymphadenopathy in patients from areas of endemic leishmaniasis.

Summary

Four cases of leishmaniasis are described in which the disease appears to have localized to the lymph nodes. The literature on this subject is briefly reviewed.

Histologically, the lymph nodes showed a chronic granulomatous reaction, and the presence of Leishman-Donovan bodies was demonstrated in three of the cases.

Attention is drawn to the possibility of the occurrence of this condition in the differential diagnosis of lymph-node enlargement occurring in patients who have been in areas of endemic leishmaniasis.

We are indebted to Dr. I. A. B. Cathie, of the Hospital for Sick Children, Great Ormond Street, for performing the toxoplasmosis complement-fixation and dye tests, and to Mr. D. E. Tomkinson, of the Royal Army Medical College, for the photomicrographs.

ADDENDUM

Since this paper was written a further case has come to light: in a soldier aged 20 from the same unit as Cases 1 and 4. He presented with cervical lymph-node enlargement, and biopsy revealed a similar histological picture with L.D. bodies.

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EXFOLIATIVE CYTOLOGY OF GASTRIC CARCINOMA*

BY

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[WITH SPECIAL PLATE]

Although it is generally assumed that cytological studies of gastric material are recent in origin, the literature of the last century contains several papers which point out the importance of a histological study of gastric washings. Rosenbach in 1882 observed tumour particles in gastric washings, and Samuel Fenwick in 1895 described the presence of gastric mucosal fragments in gastric aspirations. Similar observations were made by French workers. However, these studies were not pursued until Papanicolaou's work gave us a renewed stimulus for this type of investigation.

At the request of my surgical colleagues I began the cytological examination of gastric cellular material about four years ago in an attempt to achieve earlier diagnosis of gastric carcinoma. In preparation for this task I made smears from fresh operation specimens of benign and malignant conditions of the stomach in order to obtain some idea of the cellular structures that one may find in gastric aspirations. The next step was to decide which of the many methods for obtaining cellular material should be used.

At the time two essentially different ways of obtaining cellular material were in use: (1) those methods which aimed at a mechanical removal of mucosal tissue, and (2) lavage techniques which used a fluid with or without mucolytic agents. The gastric brush and the abrasive balloon belonged to the first group; lavage with saline or Ringer's solution of a fluid containing papain or α -chymotrypsin belonged to the second.

Technique

We decided to use the least-complicated lavage method, a method advocated by the group of cytologists working in the Vincent Memorial Hospital (1950). This technique is as follows.

The patient fasts for 12 hours before the test. In the morning a Levene tube with additional openings is passed into the stomach, either through the nostril or by the mouth while the patient drinks a glass of water. The stomach is then emptied with a 50-ml. syringe. The material so obtained represents the first specimen. Then 100-200 ml. of saline or Ringer solution is injected through the tube under pressure, the fluid being partially withdrawn and re injected several times. After clamping of the tube the patient is asked to assume varying positions to allow close contact of the fluid with as large an area of gastric mucosa as possible. The fluid is finally aspirated as completely as possible, and represents the second specimen. These specimens are sent to the laboratory immediately after they have been obtained. They are centrifuged at 2,000 r.p.m. The sediment is spread on four to six slides, fixed in alcohol-ether, and stained by Papanicolaou's method.

The smears may contain exfoliated squames from the upper digestive tract and gastric mucosal fragments as well as inflammatory cells. Aspirated sputum may be mixed with gastric material; therefore bronchial epithelium and

*Read to the Section of Surgery at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.