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.

REFERENCES

Agius-Ferrante, T. J. (1955). *Brit. med. J.,* 2, 654.
—— (1957). Personal communication.
Angevine, D. M., Hamilton, T. R., Wallace, F. G., and Hazard, J. B. (1945). *Amer. J. med. Sci.,* 210, 33.
Ash, J. E., and Spitz, S. (1945). *Pathology of Tropical Diseases.* Saunders, Philadelphia.
Cochran, S. (1912). *J. trop. Med. Hyg.,* 15, 9.
Chung, H. L. (1944). *Chin. med. J.,* 62, 284.
Debono, J. E. (1957). Personal communication.
Hu, C. H. (1933). *Chin. med. J.,* 47, 1112.
—— (1936). *Ibid., Suppl.* 1, p. 1.
Kirk, R., and Sati, M. H. (1940). *Trans. roy. Soc. trop. Med. Hyg.,* 33, 501.
Lipscomb, F. E., and Gibson, M. O. J. (1944). *Brit. med. J.,* 1, 492.
Meleney, H. E. (1925). *Amer. J. Path.,* 1, 147.
Rigg, A. (1957). *Med. J. Aust.,* 1, 389.

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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 reinjected 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

carbon-laden phagocytes may be found. Undigested particles of food and a variety of organisms are seen according to the pathological changes in the stomach.

Normal mucosa (Special Plate, Fig. 1) is characterized by the regularity of its structure. The columnar cells that line the stomach are clearly seen. The cells are equally spaced, their cellular outlines being well defined. The nuclear chromatin shows no abnormal clumping and there is no variation in size and shape of nuclei.

In contrast to the normal epithelial cells the malignant cell groups show the following characteristics : (1) The tumour cells appear very frequently as clumps in which the nuclei are more closely approximated to each other—often there is overlapping of nuclei ; (2) the nuclei show irregular chromatin structure ; (3) the nucleoli within the nuclei may be large and are often present in increased numbers ; (4) the nuclear membrane stains intensively ; (5) the nuclei may show hyperchromasia ; (6) the nucleo-cytoplasmic ratio is changed in favour of the nucleus ; (7) there is a great variation in cell size ; and (8) the cytoplasmic outline may be indistinct. Some of these features are seen in Figs. 2 and 3 on the Special Plate. Malignant cell groups rarely show mitoses.

Besides these cytological criteria we look for the following features in the smears, as they are often found in the presence of carcinoma—namely, large numbers of polymorphs, plasma cells, fresh, diffusely distributed erythrocytes, and an abnormal bacterial flora which is an indicator for the presence of achlorhydria.

Results

So far, about 2,500 gastric cytological examinations have been made. Twenty-five cases of carcinoma have been discovered by cytology where other investigations (radiology and gastroscopy) have been negative. Whenever an operation specimen has been received the cytological findings have been carefully correlated with the morbid anatomical changes found in the stomach, which has been opened along the lesser curvature, pinned out flat, and fixed immediately after excision. One important conclusion to be drawn from our experience is that the best material for cytology was obtained from those cases in which the malignant lesion was subsequently found to be small, often confined to the mucosa. Paradoxically, the material most difficult to interpret comes from those cases in which the tumours are large and widely ulcerated. The lavage fluid of these cases contains much debris and many organisms and inflammatory cells which make cytodiagnosis difficult or impossible.

As a result of cytological investigation we have seen a number of cases in which the tumour was as yet entirely confined to the mucosal layers and no lymph-node metastases could be found. The following are two illustrative cases.

Case 1.—A woman aged 72 had complained of dyspeptic symptoms and loss of weight for three years. A barium-meal examination in 1955 showed no abnormality. On readmission in January, 1957, her test meal showed an achlorhydria; the barium-meal report stated: "The radiological features of abnormality in this stomach are not very .convincing." Gastric cytology showed undoubted malignant cells. At laparotomy no palpable tumour was found, but the wall of the pyloric antrum was oedematous. A partial gastrectomy was performed. Macroscopically, the pyloric antrum was the seat of a surface carcinoma, 7 cm. in diameter, which was covered by an inflammatory exudate. Histologically, it proved to be a typical mucoid carcinoma (Special Plate, Fig. 4) confined to the mucosa and nowhere infiltrating the muscularis. The remaining gastric mucosa showed chronic atrophic gastritis with widespread intestinal metaplasia. Large areas of the body mucosa were the seat of severe gastritic changes. No lymph-node metastases were found. Three months after the operation the patient was symptom-free and had gained 10 lb. (4.5 kg.) in weight.

Case 2.—A man aged 44, admitted in 1952, complained of stomach pain and loss of weight. The test-meal examination revealed achlorhydria; the barium-meal examination was nega-

tive. After two years he was readmitted for gastroscopy and a barium-meal examination. The former showed a small ulcer in the lesser curve, but the latter was again negative. Cytology of this case indicated the presence of malignant cells. Carcinoma was confirmed by the appearances of the operation specimen, the pyloric antrum showing chronic atrophic gastritis and a flat superficially ulcerated carcinoma (5 cm. in diameter) which infiltrated the submucosa at only one point. No lymph-node metastases were found.

These and similar cases, diagnosed by cytology, presented morbid anatomical appearances which were entirely new to us. Never before had I observed a gastric carcinoma limited to the mucosa, and only a few such cases—found accidentally at necropsy or in operation specimens—are described in the literature. It therefore appears that cytology can discover gastric carcinoma at a very early stage, even at a time when the operating surgeon may not be able to feel the lesion, as the tumour is entirely confined to the mucosa.

It is of great interest that these carcinomata arise in stomachs the mucosa of which has undergone a profound structural alteration. Some form of chronic atrophic gastritis is invariably present, often with widespread intestinal metaplasia, a condition which is regarded by some pathologists as a precancerous lesion. Our findings seem to lend some support to this conception. In addition, chronic atrophic gastritis is clinically associated with an achlorhydria, and achlorhydria is present in most cases of gastric carcinoma.

It has often been stated that chronic gastritis is a lesion which develops secondarily to carcinoma, possibly as a result of obstruction. The small carcinomata seen in our specimens do not support this assumption.

Study of the case histories of the patients with " surface carcinoma " has taught us that this type of carcinoma develops very slowly, and it may take from two to three years before the surface carcinoma develops into the carcinomatous tumour we are more familiar with.

Therefore it must be our aim to detect the tumours while they are still confined to the mucosa.

Conclusion

I would like to express the opinion that patients with an achlorhydria which is always associated with structural mucosal changes such as a diffuse chronic atrophic gastritis should be investigated until it has been proved that there is no evidence of carcinoma. Cytological examination, to which few patients object, is an easy method for screening and following up. Finally, the gastric cellular material reflects better than any other method the pathological processes of the entire gastric mucosa, and can provide satisfactory diagnostic results which compare favourably with radiological and gastroscopical findings.

BIBLIOGRAPHY

Ayre, J. E., and Oren. B. G. (1953). *Cancer*, 6, 1177.
Konjetzny, G. E. (1938). *Der Magenkrebs*. Enke, Stuttgart.
Panico, F. G., Papanicolaou, G. N., and Cooper, W. A. (1950). *J. Amer. med. Ass.*, 143, 1308.
Reineboth (1896). *Dtsch. Arch. klin. Med.*, 58, 62.
Rosenthal, M., and Traut, H. F. (1951). *Cancer*, 4, 147.
Rubin, C. B., and Benditt, E. P. (1955). Ibid., 8, 1137.
Vincent Memorial Hospital (1950). *The Cytologic Diagnosis of Cancer*. Saunders, Philadelphia.

A conference on cerebral palsy was held at the Duchess of York Hospital for Babies, Manchester, on February 15 under Professor W. GAISFORD'S chairmanship. Paediatricians, orthopaedic surgeons, medical officers of health, and physiotherapists attended. In the morning papers were read, and during the afternoon session Mrs. BOBATH gave a demonstration of her methods of physiotherapy on a series of children whom she had never treated previously.

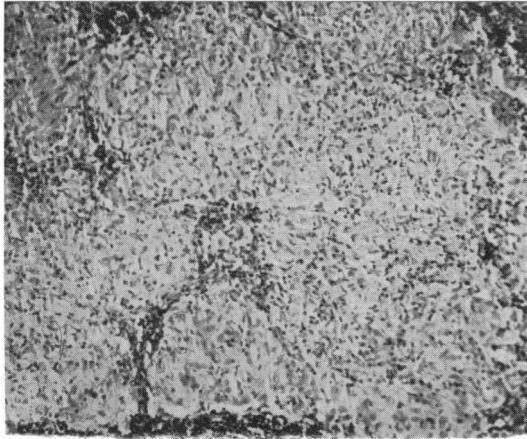## D. W. BELL *ET AL.*: LEISHMANIASIS OF LYMPH NODES

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

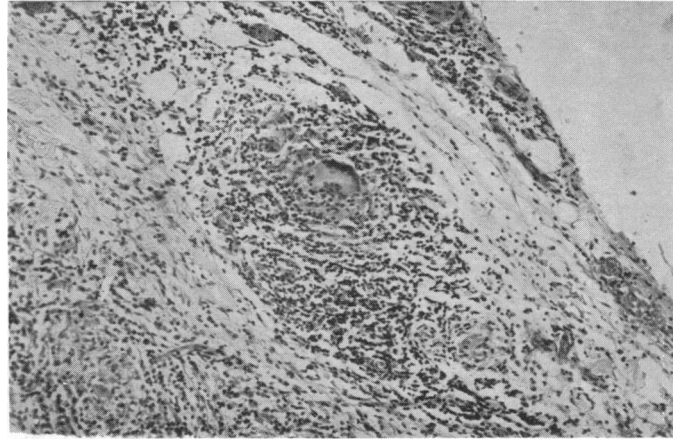FIG. 2.—Case 1. Lymph node: capsular and periadenoid reaction. (Haematoxylin and eosin. ×60.)
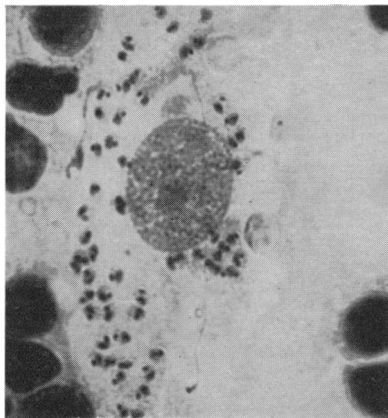
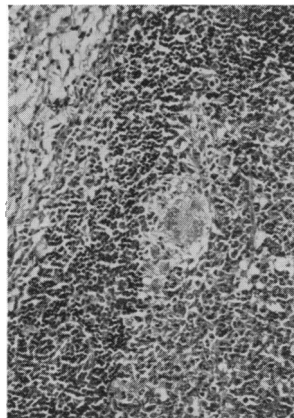FIG. 3.—Case 2. Lymph-node puncture: L.D. bodies. (Leishman. ×750.)

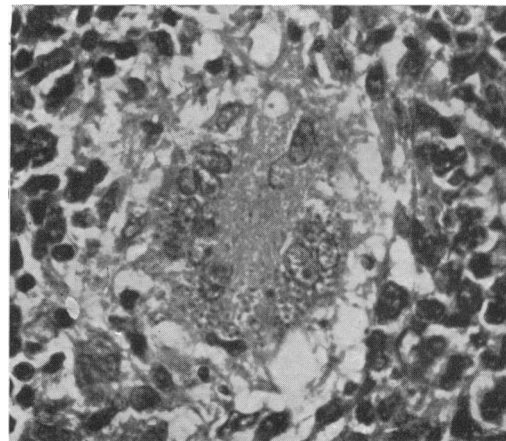FIG. 4.—Case 3. Lymph node: giant cell in follicle. (Haematoxylin and eosin. ×60.)

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

R. O. K. SCHADE. EXFOLIATIVE CYTOLOGY OF GASTRIC CARCINOMA
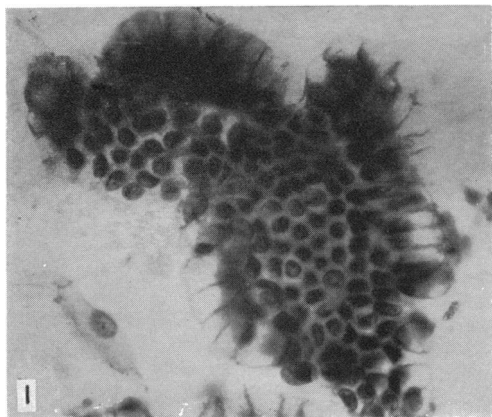
FIG. 1.—Clump of normal gastric epithelium with regular structure and nuclei of equal size. Cell boundaries are well defined. (×712.)
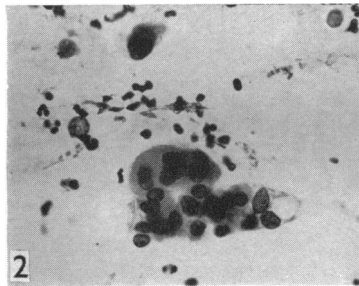
FIG. 2.—Clump of malignant cells showing overlapping and variation in size of nuclei. The background is formed by squamous cells, organisms, and polymorphs. (×475.)
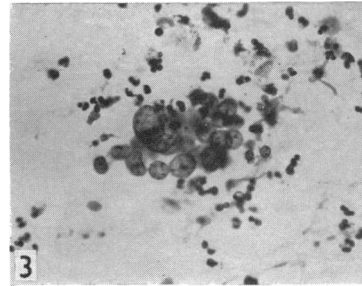
FIG. 3.—Group of malignant cells denuded of cytoplasm. Note variation in size of nuclei and prominence of nucleoli. Polymorphs and organisms form the background. (×475.)
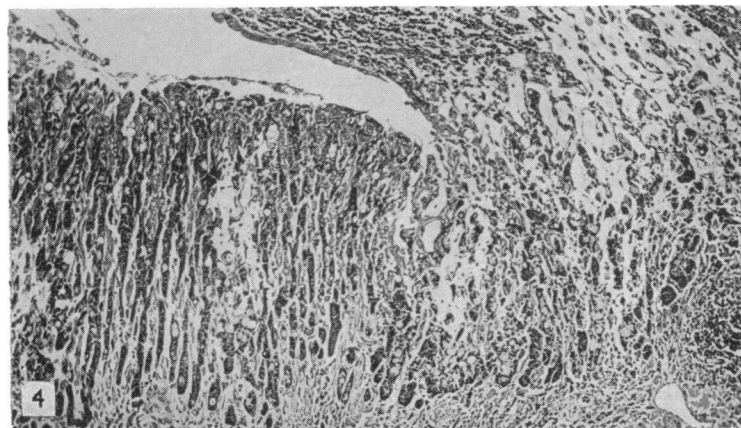
FIG. 4.—Typical mucoid carcinoma, entirely confined to the mucosa. (×165.)