contraindications to pneumonectomy. The most important is the presence of contralateral secondary deposits. This is, in fact, not a very common finding and may be suggested if one or several 3 to 30 mm. circular shadows are seen. An isolated circular shadow may, of course, be due to a tuberculous caseous area or even an old healed infarct, and such lesions cannot always be excluded unless previous radiographs show they are of recent origin. Secondary deposits in ribs, clavicles, vertebrae, etc., will be very discouraging. On the other hand, local rib erosion by direct extension of the tumour mass is only a relative contraindication; and on some occasions the neoplasm and eroded rib have been removed at the same operation with apparent success.

Restriction of movement of one side of the diaphragm is unimportant, since it may be the result of distal inflammation. On the other hand, true paradoxical movement, often best seen when the patient sniffs, is very suggestive of phrenic nerve involvement by glandular secondary deposits. However, it may be possible to remove the offending gland if it is on the left side near the pericardium (Tubbs, 1951).

When pneumonectomy is under consideration for the treatment of a carcinoma of the bronchus the oesophagus should be examined radiologically by means of a 'barium swallow.' A fairly thick paste of barium sulphate is made up with water and its passage down the oesophagus is observed by fluoroscopy, the patient being rotated so that it can be seen from several angles. Any abnormal indentations or local deviation should be observed and radiographed. Deviation or indentation unassociated with the atelectasis or the bulk of the neoplasm itself will suggest the presence of mediastinal secondary deposits. Local irregular filling defects, or localized alterations in the mucosal pattern, will strongly suggest invasion of the oesophageal wall by the carcinomatous deposits and will preclude successful resection. The finding of such changes is, fortunately, not common, but this is no reason for neglecting the simple procedure.

BIBLIOGRAPHY

- BROCK, R. C. (1950), *Thorax*, 5, 5.
DAVIDSON, M. (1951), 'The Diagnosis and Treatment of Intrathoracic New Growths,' London & Oxford University Press.
LIVINGSTONE (1952), 'Modern Trends in Tuberculosis,' Butterworth, London.
TUBBS, O. S. (1951), 'The Diagnosis and Treatment of Intrathoracic New Growths,' London & Oxford University Press.

CYTOLOGICAL EXAMINATION OF THE SPUTUM AND PLEURAL EFFUSION IN CARCINOMA OF THE BRONCHUS

By J. L. PINNIGER, M.A., D.M., M.R.C.P.

Physician-in-Charge of Clinical Laboratories, St. Thomas's Hospital, London

Introduction

Cytological and histological procedures are the most precise pathological methods available to the clinician in his attempt to make a diagnosis of carcinoma of the bronchus. The former have the advantage that surgery is not required in order to obtain the specimens and on this score alone there is a strong case for developing the specialized technique that is required in their use.

Historically the method has been evolved along two independent channels, one in England having Dudgeon as the fount and inspiration and the other in the United States with Papanicolaou as the pioneer. Sporadic reports of the presence of neoplastic cells in sputum appeared in the Continental literature early in the century (von Hoesslin, 1921),

but Dudgeon and his co-workers (Dudgeon and Wrigley, 1935; Barrett, 1938) and his successor Bamforth (1946) were the first to make this diagnostic method the subject of intensive study. They gained their initial experience by making scrapings from solid tissues such as the breast (Dudgeon and Patrick, 1927; Dudgeon and Barrett, 1934). Papanicolaou's prime interest was in the cytology of the female genital tract (Papanicolaou, 1933), and his studies were the stimulus for the release, a decade or so after Dudgeon's original publication, of a flood of papers in America on the application of cytological technique to malignant conditions all over the body, culminating in a thorough and well illustrated monograph by Graham and her co-workers (Graham, 1950).

Indications for Use

Sputum. Early diagnosis of bronchial carcinoma is essential if the remote chance of radical cure is to be achieved. However, a positive cytological diagnosis is so rare before clinical suspicion is aroused that there is no place for making use of the technique as part of a routine screening procedure in all people of middle age having chronic coughs. In the group of patients with clinical signs and symptoms sputum examination should not be undertaken in preference to bronchoscopy unless the clinical state of the patient renders the latter a dangerous procedure. It has, however, an important place in those patients who have positive radiological signs, and in whom the tumour is beyond the range of bronchoscopic vision. In such cases investigation of many specimens is warranted if no positive findings are at first obtained. For those patients who have a bronchial carcinoma which is clearly inoperable on clinical grounds, positive cytological confirmation is often valuable. Objective evidence is always more satisfactory than inference and, if palliative radiotherapy is being considered, is usually required by the radiotherapist before treatment is started.

Pleural fluid. The question of early diagnosis of malignant disease does not arise here, but in those patients in whom there is uncertainty as to whether an effusion is tuberculous or malignant, an early decision in favour of tuberculosis is obviously of benefit to the patient. As in the case of sputum examination, a positive cytological diagnosis provides satisfactory objective evidence of the correct diagnosis in patients with clinically malignant pleural effusions. It is perhaps more important here in view of the greater difficulty in obtaining biopsy evidence.

Other material. Cytological diagnostic methods have been applied to examination of other material in patients suspected of bronchial carcinoma. Perhaps the most useful application is in the examination of tissue aspirated at lung puncture for a peripherally situated radio-opaque pulmonary nodule. Examination of bronchial aspirations taken at the time of bronchoscopy has proved disappointing and misleading in our hands having, except in isolated cases, no advantage over sputum preparations from the same patient (Bamforth, 1953; Wetherley-Mein, 1953). Scrapings taken from lymph nodes or skin nodules removed at biopsy can often lead to a confident diagnosis of carcinoma within half an hour of operative removal. This may occasionally be desirable when an answer is required clinically before a histological preparation is ready. The tissue from which the scrapings are made should still be in the fresh, and not formalin fixed, state.

Technique

The techniques used by most authors are basically similar, differing only as to the fixatives and stains used. In order to get good preparations it is of cardinal importance to obtain fresh specimens. Sputa must be genuine expectorations—so often saliva is uselessly presented for examination—and care must be taken in spreading samples on to the slide, streaky white and especially bloodstained areas being the most likely sources of tumour cells. With pleural fluids the centrifuged deposit is used for preparing the slides. Technical details of preparation can be found elsewhere (Dudgeon and Wrigley, 1935; Barrett, 1938; Graham, 1950). Briefly, the slides are placed while wet into a fixative such as Schaudinn's mercuric chloride solution, stained with haemalum and eosin or corresponding dyes and finally mounted. At least three slides should be prepared from each sample, and these are examined microscopically, using low and high power dry objectives, with the oil immersion lens for detail.

Histology

The identification of malignant cells by this method requires not only an understanding of histological criteria for malignancy but also a sound knowledge of the varied cytology of the particular material examined (Barrett, 1938; Graham, 1950). The latter needs many hours of often tedious microscopic study, but this is the only sure way of giving reliable reports as to the presence of malignant cells. In the sputum the common carcinoma cells seen are the small anaplastic, or 'oat,' cells and squamous cells. On occasions the neoplastic cells may show considerable morphological variation in a single specimen. 'Oat' cells are characteristically in small clusters or streaks, appearing as naked nuclei with fine irregular chromatin stippling (Fig. 1), whereas squamous cells may be identified either as small clumps or isolated atypical cells, often having the characteristic 'bird's-eye' feature (Fig. 2). Mucus secreting (columnar cell) carcinoma is rare here, but in contrast it is the common form seen in the pleural fluid (Figs. 3 and 4). Carcinoma cells when seen in the sputum nearly always come from a primary tumour of bronchus, whereas in the pleural fluid secondary carcinoma cells are as frequent as those of primary carcinoma of the bronchus. In the latter group mucus secreting (columnar) cells are most common, oat cells are much less frequent and squamous cells are rare (Bamforth, 1946).

Results

It is reasonable to give one of three reports on the examination of prepared slides—that carcinoma

FIG. 1.—Oat cell carcinoma in sputum showing the characteristic lack of cytoplasm and stippling of nucleus. $\times 500$.

FIG. 2.—Squamous cell carcinoma in sputum showing a 'birds-eye' cell lying at the top left hand corner separate from the main mass. $\times 500$.

FIG. 3.—Low power view of sediment from pleural fluid showing the characteristic clumps of mucus secreting (columnar cell) carcinoma. $\times 120$.

FIG. 4.—High power view of one of the clumps taken from Fig. 3. $\times 500$.

cells either are, or are not, present or that some atypical cells, which defy precise classification, are observed. This last report must in no way be taken as indicating carcinoma, but implies that a search of further specimens is warranted. In good hands a positive report is as definite as a positive histologic finding. False positives decrease with increasing experience, but even in expert hands are not entirely unknown, owing to the occasional atypical cellular proliferation which occurs in inflammatory states such as bronchiectasis (Dudgeon and Wrigley, 1935; Bamforth, 1946; Woolner and McDonald, 1949). It is easier to be certain of a positive diagnosis in sputum than in pleural fluid, for in the latter case endothelial cell proliferation can at times be so marked in some non-malignant states that cellular clumps, closely simulating carcinoma, are produced in the fluid. The cells in Fig. 5 are taken from an effusion following a pulmonary infarct. Errors in pleural fluid will be minimized if positive diagnoses are limited to those which show a number of large

clumps of hyperchromatic and atypical cells in the centrifuged deposit, as in Figs. 3 and 4. Indeed it is a good working rule both for sputum and pleural fluid, in view of the seriousness of a false positive report, that carcinoma should never be diagnosed unless the findings are unequivocal. If any element of doubt exists a report should indicate that atypical cells have been observed, inviting the submission of further specimens for examination.

Clinical action on a negative cytological report must take notice of the patient's symptoms and signs. If the latter indicate carcinoma as a likely diagnosis—and no other information is forthcoming, such as by the bronchoscope or by lymph node or other secondary biopsy—then, as stated earlier, repeated examination of many samples of sputum is warranted. In the case of pleural effusion, sputa should also always be examined and, of course, the same applies to any subsequent pleural fluids if further samples become available.

It is difficult to state precisely what percentage of negative reports are false ones, as the long term

FIG. 5.—High power view of endothelial cell clumps in a pleural fluid from a case of pulmonary infarction. $\times 500$.

follow-up of all such cases investigated is well-nigh impossible in a hospital having many out-patients. It is certain that such false negatives exist and form an appreciable percentage of the whole. There are various reasons for this. Specimens may be unsatisfactory because they are not fresh or because in the case of sputa they consist mainly of saliva. Some tumours desquamate less easily than others, figures given by some authors for sputum indicating that these form approximately 30 per cent. of the total (Dudgeon and Wrigley, 1935; Gower, 1943; Woolner and McDonald, 1949). When occasional exfoliated cells are present singly, they may not be sufficiently distinctive to warrant a positive diagnosis. Finally, not the least important factor in many laboratories is the falling off of acuity of observation if the microscopist is faced with a large number of slides requiring attention. In many centres in the United States cytological diagnostic procedures are undertaken by staffs devoting their whole time

to the study, and consequently screening of prepared slides can be a leisured and thorough process. In this country, by contrast, cytological diagnosis is but one of the many jobs that fall to a clinical pathologist, with the result that the care given to the individual specimen must vary inversely with the total number submitted.

Summary

It can be said that cytological examination of sputa and pleural fluids is a very useful tool in the diagnosis of carcinoma of the bronchus, and after a long trial period has come to stay. Considerable experience is necessary before reliable interpretation of results can be achieved, and the number of positive diagnoses will be increased by an intelligent selection of clinical material and by the submission of adequate freshly obtained specimens for cytological analysis, whether they be sputum, pleural fluid or biopsy tissue.

Acknowledgments

I wish to acknowledge the help I have received from Drs. J. Bamforth, D. S. Cadman and G. Wetherley-Mein in preparing this article. My thanks are also due to Mr. A. E. Clark for the photomicrographs.

BIBLIOGRAPHY

- BAMFORTH, J. (1946), *Thorax*, **1**, 118.
 BAMFORTH, J. (1953), *Practitioner*, in the press.
 BARRETT, N. R. (1938), *J. Thorac. Surg.*, **8**, 169.
 DUDGEON, L. S., and PATRICK, C. V. (1927), *Brit. J. Surg.*, **15**, 250.
 DUDGEON, L. S., and BARRETT, N. R. (1934), *Ibid.*, **22**, 4.
 DUDGEON, L. S., and WRIGLEY, C. H. (1935), *J. Laryng.*, **50**, 752.
 GOWER, F. J. S. (1943), *Brit. J. Surg.*, **30**, 193.
 GRAHAM, R. M., and other members of the Vincent Memorial Laboratory staff (1950), 'The Cytologic Diagnosis of Cancer,' W. B. Saunders Co., Philadelphia and London.
 VON HOESSLIN, H. (1921), 'Das Sputum,' Julius Springer, Berlin.
 PAPANICOLAOU, G. N. (1933), *Amer. J. Anat. Supplement*, **52**, 510.
 WETHERLEY-MEIN, G. (1953), Personal communication.
 WOOLNER, L. B., and McDONALD, J. R. (1949), *Amer. J. Clin. Path.*, **19**, 765.

RUTHIN CASTLE, NORTH WALES

A Clinic for the diagnosis and treatment of Internal Diseases (except Mental or Infectious Diseases). The Clinic is provided with a staff of doctors, technicians and nurses.

The surroundings are beautiful. The climate is mild. There is central heating throughout. The annual rainfall is 30.5 inches, that is, less than the average for England.

The Fees are inclusive and vary according to the room occupied.

For particulars apply to THE SECRETARY, Ruthin Castle, North Wales.

Telegrams: Castle, Ruthin.

Telephone: Ruthin 66