considered together and second in the community-acquired infections. As with wounds, Staph aureus greatly outnumbers other pathogens at this site, but it is then followed by streptococci ahead of Gram-negative bacilli. The danger of bacterial dispersal from skin lesions as an often inapparent source of cross-infection requires constant vigilance.[6]

The principal site of infections already present on admission to hospital is the lower respiratory tract. When all types of community-acquired infections are considered together Staph aureus and E coli each account for one-fifth of cases, followed among the bacteria, rather startlingly, by Mycobacterium tuberculosis (8·4%), which is rivalled only by viruses (9·6%). Candida species and miscellaneous fungi account for only 4·1% and 0·3% respectively; but once in hospital the danger to immunocompromised patients posed by infection with these organisms—as with herpesviruses—is much greater than implied by their general prevalence rates.

The 1981 report mentions in a mere 11 words that it "reflects something of the added cost infection imposes on a hospital." In 1960 the cost of surgical sepsis alone in England and Wales was estimated at 1 000 000 days of excess hospital stay a year, with 5000 patients remaining in hospital for a month or more longer than expected and 500 or so dying from sepsis.

Things now seem better in relation to surgical sepsis, but most other forms of hospital-acquired infection appear to be at least as prevalent as they were 20 years ago. This is perhaps not surprising in our older and more debilitated hospital population. Many of these infections can and should be prevented, however, by rational measures based on adequately controlled trials. The recent survey points the way, but future investigations will require a more detailed and critical evaluation of the factors likely to be responsible and the effects of control procedures.

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[1] Selwyn S. Sir John Pringle: hospital reformer, moral philosopher and pioneer of antiseptics. Med Hist 1966;10:266-74.
[2] Selwyn S. Sir James Simpson and hospital cross-infection. Med Hist 1965; 9:241-8.
[3] Meers PD, Ayliffe GAJ, Emmerson AM, et al. Report on the National Survey of Infection in Hospitals, 1980. Journal of Hospital Infection 1981;2, suppl:1-51.
[4] Public Health Laboratory Service. Incidence of surgical wound infection in England and Wales. Lancet 1960;ii:659-63.
[5] Public Health Laboratory Service. Infections acquired in medical wards. J Hyg Camb 1965;63:457-77.
[6] Selwyn S, Chalmers D. Dispersal of bacteria from skin lesions: a hospital hazard. Br J Dermatol 1965;77:349-56.

Bronchoalveolar lavage

For more than 20 years lavage of the bronchial tree through a rigid bronchoscope has been used in the management of severe asthma[1] and of alveolar proteinosis.[2] Once Myrvik et al[3] had shown that in rabbits lavage could yield alveolar macrophages the technique formed the basis of the new topic of pulmonary cell biology, now rapidly developing and advancing our understanding of a wide variety of pulmonary diseases. The methods used for sampling the cells of the pulmonary inflammatory and immune systems of man have progressed through lavage via the rigid bronchoscope,[4] or via a large balloon-tipped catheter wedged into a primary or secondary branch of the bronchial tree,[5][6] to the present-day bronchoalveolar lavage

via the fibreoptic bronchoscope—which was developed in the early 1970s[7-9] with only minor modifications since then.

Briefly, the fibreoptic bronchoscope is wedged in a subsegmental bronchus and small quantities (20-60 ml) of warmed, sterile, physiological saline are instilled through the biopsy channel of the bronchoscope and immediately aspirated into a sterile trap.[10][11] This procedure is repeated until a total of 100-300 ml of saline has been instilled. Usually between 40% and 70% of the infused volume is recovered, but in patients with destructive lung disease and airflow obstruction the proportion is smaller; recovery correlates inversely with the severity of the airflow obstruction.[12]

Complications of bronchoalveolar lavage are rare. Transient respiratory distress and syncope have been reported,[11] but these are also seen in patients undergoing fibreoptic bronchoscopy without bronchoalveolar lavage. The most frequent complication is fever, but even this is seen in fewer than 3% of patients and rapidly responds to antibiotic treatment.

What are the present applications of bronchoalveolar lavage ? Clinically, it helps stage and monitor the progress of certain interstitial lung diseases. Untreated fibrosing alveolitis is characterised by the recovery of raised numbers of neutrophils[13] and eosinophils at bronchoalveolar lavage. These changes reflect the altered cellular populations found in specimens obtained by open-lung biopsy.[14][15] Thus serial bronchoalveolar lavage may be used to assess progress of the disease. Repeat open-lung biopsy, in contrast, is impracticable, transbronchial biopsy has a substantial sampling error,[16] and the standard pulmonary function tests or chest radiographs are less than adequate for monitoring progress[17]; so bronchoalveolar lavage opens a prospect of better control of treatment. Even if serial bronchoalveolar lavages are not performed studies (as yet to be independently confirmed) suggest that a single estimate of differential cell counts may be a useful prognostic indicator.[16][18] With pulmonary sarcoidosis, too, bronchoalveolar lavage appears to be helpful in assessing the activity of the disease. Sarcoidosis is characterised by recovery of increased percentages of lymphocytes at bronchoalveolar lavage,[19] and counts of the proportion of T lymphocytes, in conjunction with gallium-67 scanning, may predict which patients are likely to deteriorate and so need treatment.[20]

Possibly of even greater importance than its direct clinical applications is the access that bronchoalveolar lavage provides to bronchoalveolar proteins and cells for research. For example, both pulmonary alpha$_1$-antitrypsin[21] and alveolar macrophages,[22] recovered by bronchoalveolar lavage, have been the subjects of recent studies of the development of emphysema in cigarette smokers. Similar applications of bronchoalveolar lavage to pulmonary biochemistry and cell biology should provide new insights into this and other inflammatory and immunological disorders of the lung.

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[1] Thompson HT, Pryor WJ. Bronchial lavage in the treatment of obstructive lung disease. Lancet 1964;ii:8-10.
[2] Ramirez-RJ. Bronchopulmonary lavage. New techniques and observations. Diseases of the Chest 1966;50:581-8.
[3] Myrvik Q, Leake ES, Fariss B. Studies on pulmonary alveolar macrophages from the normal rabbit: a technique to procure them in a high state of purity. J Immunol 1961;86:128-32.
[4] Keimowitz RI. Immunoglobulins in normal human tracheobronchial washings: a qualitative and quantitative study. J Lab Clin Med 1964; 63:54-9.
[5] Finley TN, Swenson EW, Curran WS, Huber GL, Ladman AJ. Bronchopulmonary lavage in normal subjects and patients with obstructive lung disease. Ann Intern Med 1967;66:651-8.

[6] Harris JO, Swenson EW, Johnson JE 3rd. Human alveolar macrophages: comparison of phagocytic ability, glucose utilization, and ultrastructure in smokers and nonsmokers. J Clin Invest 1970;49:2086-96.

[7] Warr GA, Martin RR. In vitro migration of human alveolar macrophages: effects of cigarette smoking. Infect Immun 1973;8:222-7.

[8] Yeager H Jr, Zimmet SM, Schwartz SL. Pinocytosis by human alveolar macrophages. Comparison of smokers and nonsmokers. J Clin Invest 1974;54:247-51.

[9] Reynolds HY, Newball HH. Analysis of proteins and respiratory cells obtained from lungs by bronchial lavage. J Lab Clin Med 1974;84:559-73.

[10] Hunninghake GW, Gadek JE, Kawanami O, Ferrans VJ, Crystal RG. Inflammatory and immune processes in the human lung in health and disease: evaluation by bronchoalveolar lavage. Am J Pathol 1979;97: 149-205.

[11] Cole P, Turton C, Lanyon H, Collins J. Bronchoalveolar lavage for the preparation of free lung cells: technique and complications. Br J Dis Chest 1980;74:273-8.

[12] Greening AP, Lowrie DB, Poole GW. Bronchoalveolar lavage in pulmonary diseases including sarcoidosis. Br J Dis Chest 1981;75:321.

[13] Reynolds HY, Fulmer JD, Kazmierowski JA, Roberts WC, Frank MM, Crystal RG. Analysis of cellular and protein content of broncho-alveolar lavage fluid from patients with idiopathic pulmonary fibrosis and chronic hypersensitivity pneumonitis. J Clin Invest 1977;59:165-75.

[14] Haslam PL, Turton CWG, Heard B, et al. Bronchoalveolar lavage in pulmonary fibrosis: comparison of cells obtained with lung biopsy and clinical features. Thorax 1980;35:9-18.

[15] Hunninghake GW, Kawanami O, Ferrans VJ, Young RC Jr, Roberts WC, Crystal RG. Characterization of the inflammatory and immune effector cells in the lung parenchyma of patients with interstitial lung disease. Am Rev Respir Dis 1981;123:407-12.

[16] Crystal RG, Gadek JE, Ferrans VJ, Fulmer JD, Line BR, Hunninghake GW. Interstitial lung disease: current concepts of pathogenesis, staging and therapy. Am J Med 1981;70:542-68.

[17] Crystal RG, Fulmer JD, Roberts WC, Moss ML, Line BR, Reynolds HY. Idiopathic pulmonary fibrosis: clinical, histologic, radiographic, physio-logic, scintigraphic, cytologic, and biochemical aspects. Ann Intern Med 1976;85:769-86.

[18] Rudd RM, Haslam PL, Turner-Warwick M. Cryptogenic fibrosing alveo-litis. Relationships of pulmonary physiology and bronchoalveolar lavage to response to treatment and prognosis. Am Rev Respir Dis 1981;124: 1-8.

[19] Weinberger SE, Kelman JA, Elson NA, et al. Bronchoalveolar lavage in interstitial lung disease. Ann Intern Med 1978;89:459-66.

[20] Crystal RG. Skin testing, blood studies, and bronchoalveolar lavage to assess activity of pulmonary sarcoidosis, pp 81-3. In: Crystal RG, mod-erator. Pulmonary sarcoidosis: a disease characterized and perpetuated by activated lung T-lymphocytes. Ann Intern Med 1981;94:73-94.

[21] Gadek JE, Fells GA, Crystal RG. Cigarette smoking induces functional antiprotease deficiency in the lower respiratory tract of humans. Science 1979;206:1315-6.

[22] Hoidal JR, Fox RB, LeMarbe PA, Perri R, Repine JE. Altered oxidative metabolic responses in vitro of alveolar macrophages from asymptomatic cigarette smokers. Am Rev Respir Dis 1981;123:85-9.

Electron microscopy: an essential tool for morphological diagnosis?

The importance of the electron microscope in medical research has been well recognised and universally accepted for at least three decades. What, perhaps, has not been widely recognised so far is the part the instrument can play in routine pathology laboratories. One well-known text on general pathology, for example, stated in 1977 in its section on the interpretation of needle biopsy specimens of the liver that electron microscopy was not yet used in routine laboratories.[1] Since then the need to examine tissue electronmicroscopically has become more generally acknowledged, since such studies can be of direct value in the management of patients.[2]

The value of electron microscopy is shown by a recent report of its use in 49 neoplasms including poorly differentiated carcinomas and sarcomas, lymphomas, and amelanotic melanomas. The diagnosis achieved by light microscopy was compared with the ultrastructural changes. The results showed that in 40 of the 49 cases (82%) electronmicroscopical examina-

tion confirmed the tentative diagnosis made at light micro-scopical level. In 11 of the 40 cases more specific diagnosis was possible. In 6% (three cases) the original light micro-scopical diagnosis had to be corrected. In two patients even electronmicroscopical examination failed to resolve the problem.

Kuzela et al[2] considered the more precise histogenetic diagnosis clinically helpful in 56% of cases studied. They inquired about the value of the instrument in the eyes of a surgeon, a radiotherapist, and a medical oncologist. In 38% of cases all three clinicians agreed that electron microscopy would influence patient management. In an additional 18% one of the three clinicians considered electronmicroscopical examina-tion to be of practical significance. In the remaining 44% this form of investigation was considered irrelevant. The authors concluded that electronmicroscopical evaluation forms a beneficial adjunct to the correct diagnosis in selected tumours, permitting more specific features to be examined in identifying the cell of origin in poorly differentiated neoplasms.

The electron microscope is not only useful in the context of patient management in evaluation of the pathological features of tumours. The instrument has also proved of great value in certain other fields: examination of renal biopsy specimens, for example, has not only led to a more precise diagnosis but has also permitted evaluation of tissue not possible on conventional light microscopical examination. This also applies to tissue from other organs including the heart.

Though needle biopsies of the heart have been undertaken,[3] the bioptome,[4,5] an instrument which is essentially a catheter with a cutting device at one end and an operating handle at the other, has been used with increasing frequency in evaluating endomyocardial tissue.[6] This is another area where electron-microscopical examination in combination with light micro-scopy is important and contributes substantially to more precise morphological diagnosis and thus to patient manage-ment.

Several examples spring readily to mind. Despite many staining techniques available for the detection of amyloid in the heart (and other organs) at light microscopical level, electron microscopy affords the most accurate assessment. Another example where electron microscopy has proved to be of inestimable value is in the accurate diagnosis of conditions such as Fabry-Anderson disease.[7]

One of the best-recognised applications of electron micro-scopy in patient management is in the administration of agents such as Adriamycin, or doxorubicin, which have been used for their antineoplastic effect on a broad spectrum of malignant diseases. Unfortunately patients may develop cardiotoxicity with long-term repeated treatment, particularly if the cumulative dose of 500 mg/m^2 is exceeded or if the drug is administered in combination with radiation therapy. By means of endomyocardial biopsy the cardiotoxic changes can be accurately assessed and doses of the cytotoxic agents can be monitored, permitting the maximum amount of drug to be administered with the minimum risk of heart failure.[8]

More accurate evaluation can also be made of possible degenerative changes in patients diagnosed clinically and at light microscopical level as suffering from myocarditis.[9] Preliminary results of sequential biopsies on these patients have shown the beneficial effect of administration of cortico-steroids or immunosuppressive agents or both.

One field of cardiological pathology where electron micro-scopy has proved to be a major diagnostic tool is in the evalua-tion of eosinophils in patients with suspected endomyocardial disease associated with eosinophilia. It has become recognised