

melanomas occur less frequently; and rare varieties include lymphosarcomas and other sarcomas, gliomas, plasmacytomas, and mucoepidermoid carcinomas. The most common malignant tumour seen in the nose is a late secondary extension of carcinoma of the maxillary sinuses, the treatment being that of the primary tumour.

Both innocent and malignant neoplasms may cause a purulent nasal discharge. Pain or bleeding will also occur if a tumour of either type destroys bone by pressure absorption. In general, tumours confined to the nasal passages produce nasal obstruction and epistaxis rapidly while those that invade the nasal cavity secondarily (such as carcinomas of the paranasal sinuses) produce symptoms late in the course of the disease; often the diagnosis is not apparent until the tumour has penetrated the surrounding bony walls, causing swelling of the face, proptosis, and epistaxis. Swelling of the palate, pain, or loosening of the teeth may send the patient to a dental surgeon, and proptosis or unilateral epiphora to an ophthalmologist. Since the clinical differentiation between a simple and a malignant neoplasm of the nose may be difficult, all such cases should be referred promptly to a rhinologist, whose investigations are likely to include anterior and posterior rhinoscopy, x-ray examination of the nose and paranasal sinuses, and biopsy of the swelling—absolutely essential for accurate diagnosis.

Simple tumours are removed intranasally under general anaesthesia, preferably augmented by instillation of a cocaine solution to control haemorrhage. If a haemangioma is present the base is cauterised to prevent recurrence. Squamous cell papillomas of the nasal vestibule are quite common; again the base of the tumour should be cauterised, otherwise a squamous carcinoma may develop at the site of repeated excisions.

The pleomorphic adenoma or mixed tumour is rare and until the series recently reported by Compagno and Wong⁷ no single investigator had been able to collect enough cases for evaluation. Compagno and Wong have studied 40 cases and have follow-up data on 34 of these for over seven years. Most of these neoplasms originate from the mucous membrane of the bony or cartilaginous septum but they may also occur on the lateral nasal wall. They are seen in all age groups but are most common in white people in the third to sixth decade. The symptoms are of nasal obstruction and a mass in the nasal cavity and the lesions are seen as polypoid, broad-based swellings.

Local but adequate excision is the treatment of choice, and most patients in the American series were treated by local or wide excision in the form of septectomy, turbinectomy via a lateral rhinotomy, or a Caldwell Luc procedure. Thirty-one of the 34 patients followed up did not have a recurrence of the tumour. Those that did recur either had not been completely removed or recurred locally and were removed again without further recurrence.

Squamous carcinoma of the skin of the nose may extend into the vestibule or nasal septum and may be treated by excision or radiotherapy. Basal-cell carcinoma may affect both the nose and the paranasal sinuses. Early lesions respond well to radiotherapy, but wide surgical excision is necessary if the tumour has reached the underlying bone. Malignant melanoma of the nasal passages is uncommon; bleeding occurs early in the disease and the tumour may metastasise to cervical lymph nodes. Wide surgical excision is essential—the response to radiotherapy is poor—and chemotherapy combined with surgery is the most successful form of treatment.

² Macbeth, R, *Journal of Laryngology*, 1965, **79**, 592.

³ Willis, R A, *Pathology of Tumours*, 3rd edn. London, Butterworths, 1960.

⁴ Black, B K, and Smith, D E, *Archives of Neurosurgery and Psychiatry*, 1950, **64**, 614.

⁵ Wadsworth, P, *Journal of Laryngology*, 1969, **83**, 87.

⁶ Harrison, D F N, *Proceedings of the Royal Society of Medicine*, 1968, **61**, 13.

⁷ Compagno, J, and Wong, R T, *American Journal of Clinical Pathology*, 1977, **68**, 213.

Non-bacterial thrombotic endocarditis

Non-bacterial thrombotic endocarditis is the term applied to bland vegetations of platelets and fibrin on a virtually normal heart valve. Sometimes there is minor degeneration of the collagen framework, but no appreciable inflammatory reaction occurs apart from an occasional macrophage infiltration.^{1 2} The condition normally comes to light as a coincidental postmortem finding—usually in about 0.5% of consecutive necropsies—in patients who have died of other conditions, notably cancer; thus it used to be regarded as an agonal phenomenon and was called terminal endocarditis.

Recently, however, it has become increasingly evident that non-bacterial thrombotic endocarditis is not always a silent, terminal condition. The sterile, rather friable vegetations have a tendency to embolise, and occasionally the systemic embolism may produce clinical syndromes due to infarction of the brain, kidney, or spleen. The endocardial lesion may be the dominant feature of an illness due to an adenocarcinoma of the pancreas, stomach, or lung that has remained completely silent. The condition should therefore always be suspected in a patient with known malignant disease who suddenly develops symptoms due to occlusion of one or more arteries. Sometimes there is also migratory thrombophlebitis—long known to complicate carcinoma of the pancreas, stomach, colon, and lung—and this association of intravascular clotting disorders suggests that the conditions are related to some disturbance of the coagulation mechanism. Among the clotting abnormalities that have been found are hyperfibrinogenaemia, hypofibrinogenaemia, thrombocytopenia, and decreased concentrations of factors V, VIII, and XIII.³ Circulating fibrin degradation products have also been found. Many of these findings are compatible with disseminated intravascular coagulation, and some cases of non-bacterial thrombotic endocarditis may well be associated with this widespread disorder of clotting.

Interestingly, non-bacterial thrombotic endocarditis has been reported in the adult type of respiratory distress syndrome precipitated by poisoning with the tricyclic anti-depressant drug amitriptyline.⁴ One factor in the pathogenesis of this type of respiratory distress syndrome appears to be the embolism of microthrombi from the peripheral circulation to the capillaries of the lungs. The factors that predispose to the development of microthrombi in the peripheral vasculature may also operate in some cases of non-bacterial thrombotic endocarditis.

Apart from its regional embolic features non-bacterial thrombotic endocarditis is usually silent clinically. Evidence of cardiac dysfunction is seldom present, as there is no valvular destruction. Coronary embolism, however, sometimes occurs. Fayemi and Deppisch⁵ have recently reviewed six cases of non-bacterial thrombotic endocarditis with coronary embolism and myocardial infarction—part of a series of 65 cases of non-bacterial thrombotic endocarditis encountered during 10 years

¹ Linsell, C A, and Martyn, R, *East African Medical Journal*, 1962, **39**, 642.

of necropsy examinations. All six patients had malignant disease—abdominal adenocarcinoma in four cases, bladder cancer in one, and Hodgkin's disease in one. Only one patient had symptoms referable to the heart; in the remainder neurological phenomena, shock, or recurrent pulmonary embolism predominated. The neurological component would in any case tend to dull the awareness of chest pain that is typical of coronary-artery occlusion. Nevertheless, myocardial infarction was the cause of death in three patients. Only one patient had clinical and laboratory evidence of disseminated intravascular coagulation.

This fresh series of cases once again emphasises the clinical concomitants of this thrombotic valve disease, the sometimes widespread embolic phenomena, and the relation to distant carcinomas of secretory tissue. The aetiology and pathogenesis of non-bacterial thrombotic endocarditis are still obscure, but the evidence points to some degree of intravascular coagulation. The significance of the condition depends on the primary cause; where this is deep-seated abdominal cancer the prognosis is very poor and the condition is little more than a clinical curiosity. Study of non-bacterial thrombotic endocarditis may, however, be important in shedding light on the clotting abnormalities found in malignant disease.

¹ *British Medical Journal*, 1967, **3**, 812.

² *British Medical Journal*, 1971, **3**, 5.

³ Goodnight, S H, *Annals of the New York Academy of Sciences*, 1974, **230**, 271.

⁴ Lindström, F D, Flodmark, O, and Gustafsson, B, *Acta Medica Scandinavica*, 1977, **202**, 203.

⁵ Fayemi, A O, Deppisch, L M, *American Journal of Clinical Pathology*, 1977, **68**, 393.

Epidemiology of ovarian cancer

Cancer of the ovary causes more deaths than any other gynaecological disorder—about 4000 in Britain each year. The death rate has steadily increased during this century and is still rising among older women.¹ Scrutiny of the rates shows that women born during this century have experienced fairly steady death rates (adjusted for age), but that these are higher than for women born towards the end of last century, and much higher than for those born earlier still. These changes may be partly due to better diagnosis, but perhaps they also reflect changes in life-style that occurred many years ago. Firmer evidence for an environmental cause comes from comparison of the current incidence of ovarian cancer in different countries with similar diagnostic facilities. Thus these neoplasms are common in most Western countries but rare in Japan,² though when Japanese migrate to the United States their mortality begins to approach that of the host country.^{3 4}

Attempts to discover the causes of ovarian cancer have been hampered by the large variety of histological types and the inability of pathologists to agree on their classification. It would be surprising if all the different kinds of ovarian cancer had the same aetiology. Nevertheless, the results of the US Third National Cancer Survey show that the common epithelial tumours do share some epidemiological features.^{5 6} Their incidence increases appreciably with age, and they are commoner among whites than blacks. They are also commoner among women who have never married.

The influences of marital status and parity have been disentangled in an elegant study by Joly *et al*,⁷ who showed that, while the risk was higher in single women, it was higher still among married women who had not borne children. Compared with controls, patients with ovarian cancer included more women who had tried to become pregnant but failed and more who had conceived only once or twice. The authors concluded that some factor was both depressing fertility and increasing the risk of ovarian cancer in these women.

The association with low parity has now been confirmed in another case-control study.⁸ One thought-provoking aspect of this study is that fewer of the patients with ovarian cancer reported using oral contraceptives. Unfortunately there were defects in the methods for selecting and interviewing controls, so that we are uncertain how much reliance we can place on this finding. If the difference is real it could be related to the lower fertility of women who develop cancer of the ovary: it would be helpful to know whether the patients with ovarian cancer also made less use of other contraceptive methods.

Another recent report from the United States suggested that treatment with stilboestrol for menopausal symptoms might increase the risk of ovarian cancer.⁹ This conclusion was based on small numbers, however, and a second study did not incriminate exogenous oestrogens.¹⁰

We still need more information about any effects of hormone preparations—before or after the menopause—on the risk of ovarian cancer. But drugs are unlikely to be the factor responsible for the apparent rise in incidence this century—or the large geographical variation. Graham and Graham¹¹ suggested that asbestos might be the culprit: a reasonable suspicion, since many ovarian tumours are ultimately of mesothelial origin,^{12 13} and the tendency of asbestos to cause peritoneal mesothelioma is well known.¹⁴ Nevertheless, there is little evidence to link asbestos with cancer of the ovary. Newhouse *et al*¹⁵ did find an excess of deaths from ovarian cancer among workers heavily exposed to asbestos, but the numbers were very small, and possibly peritoneal mesotheliomas could have been misdiagnosed as ovarian cancers (or vice versa).

Perhaps a more likely culprit is diet. Mortality from ovarian cancer in different countries correlates with several dietary variables,¹⁶ and dietary habits change when people migrate from Japan to the United States¹⁷ (and experience more ovarian cancer). Though dietary influences are difficult to assess, they certainly deserve attention in future studies.

¹ Office of Population Censuses and Surveys, *Cancer Mortality, England and Wales, 1911-1970*. London, HMSO, 1975.

² Waterhouse, J, *et al* (eds), *Cancer Incidence in Five Continents, Volume 3*. Lyon, International Agency for Research on Cancer, 1976.

³ Haenszel, W, and Kurihara, M, *Journal of the National Cancer Institute*, 1968, **40**, 43.

⁴ Dunn, J E, *Cancer Research*, 1975, **35**, 3240.

⁵ Weiss, N S, Homonchuk, T, and Young, J L, *Gynecologic Oncology*, 1977, **5**, 161.

⁶ Weiss, N S, Young, J L, and Roth, G J, *Journal of the National Cancer Institute*, 1977, **58**, 913.

⁷ Joly, D J, *et al*, *American Journal of Epidemiology*, 1974, **99**, 190.

⁸ Newhouse, M L, *et al*, *British Journal of Preventive and Social Medicine*, 1977, **31**, 148.

⁹ Hoover, R, Gray, L A, and Fraumeni, J F, *Lancet*, 1977, **2**, 533.

¹⁰ Annegers, J F, O'Fallon, W, and Kurland, L T, *Lancet*, 1977, **2**, 869.

¹¹ Graham, J, and Graham, R, *Environmental Research*, 1967, **1**, 115.

¹² Scully, R E, *American Journal of Pathology*, 1977, **87**, 686.

¹³ Parmley, T H, and Woodruff, J D, *American Journal of Obstetrics and Gynecology*, 1974, **120**, 234.

¹⁴ Greenberg, M, and Lloyd Davies, T A, *British Journal of Industrial Medicine*, 1974, **31**, 91.

¹⁵ Newhouse, M L, *et al*, *British Journal of Industrial Medicine*, 1972, **29**, 134.

¹⁶ Armstrong, B, and Doll, R, *International Journal of Cancer*, 1975, **15**, 617.

¹⁷ Tillotson, J L, *et al*, *American Journal of Clinical Nutrition*, 1973, **26**, 177.