to those with the AA genotype. The groups were not, however, matched by socioeconomic and other factors that might have contributed to the observed difference, and the selection of subjects from twin studies may have further complicated assessment. A study from Jamaica (p 1371) appears to reach different conclusions. Both investigations concerned small numbers of people, and clearly more extensive studies are required; but the prevalence of the trait and the far-reaching implications of any possible pathogenicity demand that these should be based on impeccable diagnostic and epidemiological criteria.

Radiotherapy and the heart in Hodgkin's disease

Many treatments in medicine and surgery are not totally safe. To put a risk into perspective we need to study its incidence in various circumstances and, in the case of drugs or radiation, at various dosage levels. Every risk and every hope of benefit must be weighed against the hazards and benefits of alternative courses of action (or inaction). If we are too complacent, patients may be put at risk before the danger is fully appreciated. If we are too alarmist, those who would benefit from a treatment may be denied it because of exaggerated fears of its effects.

A recent report in the American Journal of Medicine has described two fairly young men who had coronary attacks some years after successful treatment for Hodgkin's disease, and one of them died. Was mediastinal radiotherapy responsible? While agreeing that other factors may have played a part (one of them had smoked 40 cigarettes a day), the American authors argued that it probably was. They had found four other reports of young men who had died in similar circumstances, necropsy confirming that coronary disease, not recurrent Hodgkin's disease, had caused death.

Isolated reports of this kind serve a useful purpose but may easily give a false impression of the size of the problem. Reviews of all the experimental and clinical evidence, undertaken over the last 50 years, have concluded that the heart stands up surprisingly well to radiation, often showing not the slightest electrocardiographic or histological abnormality even after absorbing large doses. When electrocardiographic changes have occurred they have been mostly trivial and transient and sometimes due to other causes. Many thousands of patients with breast cancer have survived in good health for many years after quite intensive radiation to part of the heart in the course of radiotherapy to the parasternal lymph glands. No evidence has been found of any increased incidence of heart disease in these women.

When the mediastinal glands are irradiated in Hodgkin's disease the dose absorbed by the heart (or a portion of it) will vary considerably, not only with the dose chosen for the target lymph glands but also according to the technique. For this reason the incidence of cardiac effects reported from one centre (for example, 6% at Stanford University) may not apply to another. Many centres seem to avoid these complications completely, perhaps partly by giving a dose which others might regard as less than optimal. At the other extreme, Byhardt et al recently reported no fewer than 24 cases of pericardial effusion in 83 patients given mediastinal radiation. Nevertheless, 10 out of the 24 were symptomless; Hodgkin's disease itself occasionally affects the pericardium; and radiation was given mainly by a single anterior beam giving an average pericardial dose of 5325 rads. This was more than the mediastinal glands themselves received and is considerably above the dose received by the heart when treated by some of the techniques commonly used in other centres.

Patients with existing heart disease might be thought to be especially at risk, but there is no evidence that this is so. Indeed, controlled experiments in dogs have actually shown a beneficial effect, radiated animals showing a higher survival rate after coronary artery ligation.

Hence probably there is no good evidence that heart muscle and its blood supply are any more susceptible to radiation than any other muscle. Most radiotherapy centres use a dose technique for mediastinal Hodgkin's disease which probably carries only a small risk of contributing to future heart disease. But vigilance and further study are required, preferably always with expert assessment of the dose received at different points in the heart and mediastinum.

Boys who are too tall

Being too short or too tall may be a social or psychological disability—and sometimes both. Yet it is easier to find a consensus of opinion on a height that is too short for psychological comfort than to determine what would be considered excessive. Last year we reviewed attempts to limit the height of healthy girls whose growth promised to make them excessively tall. More recently Zachmann et al have attempted to limit the growth of boys whose predicted height was over 198 cm.

Clearly the success of attempts to limit children's growth must depend on the accuracy with which eventual height can be predicted. The work of Tanner and his associates does allow a usefully accurate prediction for normal children. Pathological causes of excess height, such as an over-secretion of growth hormone or cerebral gigantism, have to be excluded. For boys from 4 to 12 years the prediction of eventual height is accurate within ±7 cm. Using this method, Zachmann's group found that the best results from treatment with testosterone came in boys at the onset of puberty whose bone age was about 12 years; they calculated that eventual height was curtailed by 8 cm. As they point out, their treatment was completely
unphysiological: massive doses of testosterone injected every two or three weeks for over one year. This inevitably suppressed gonadotrophin secretion, and in some instances testicular growth took a long time to recover. They also warn that such large doses of androgen should not be given in the form of 17-alkylated compounds because of the danger of cholestasis and possible hepatoma formation.

The number of boys that might be considered for such cosmetic endocrinology must be few. Judgment is necessarily subjective, and the doctor has to assess the validity of the parent's request for treatment in terms of the degree of disability, if any, to be suffered by the tall male.

The first consideration must be the accuracy of diagnosis. Having proved that the tall boy is normal, the doctor has to calculate the likely diminution of height to be achieved by treatment as accurately as possible, and this diminution has to be accepted by all parties as well worthwhile for the patient's future contentment. For, while it is of scientific interest that the normal growth pattern can be distorted in this way, the mere fact that that treatment is feasible does not necessarily justify its use.


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**Exposure to asbestos dust**

Occupational exposure to all commercial types of asbestos may lead to the development of pulmonary fibrosis and carcinoma of the lung, particularly in cigarette smokers. The carcinomata occur in the lungs of asbestos workers who have had sufficient exposure to have at least a moderate pulmonary fibrosis. In recent years, at least 60% of those workers who have been accepted by the pneumoconiosis panels as being disabled by asbestososis have subsequently developed cancer of the lung. These are people who had an excessive exposure to asbestos dust more than 20 years ago.

Diffuse mesothelioma of the pleura appears to be much more frequently associated with exposure to crocidolite (blue) asbestos dust than the other varieties of fibre. As yet there has been no case in Britain in which conclusive evidence implicating another type of asbestos alone has been established. Mesotheliomas may occur without any features of asbestososis, and there is no suggestion that the incidence of the tumours is affected by cigarette smoking. Nevertheless, there is evidence of a dose-response relationship among cases occurring in industry. The question of the occurrence of these tumours among the general public was considered in detail in 1972 by the Advisory Committee on Asbestos Cancers to the Director of the International Agency for Research on Cancer (IARC). The committee examined the possibility of an increased risk of mesothelial cancers at low levels of exposure to asbestos, such as may have been encountered by the general population in urban areas. The answer was that there was evidence of an association of mesothelial tumours with air pollution in the neighbourhood of crocidolite mines and of factories using mixtures of asbestos fibre types. These findings related to conditions many years ago. There was no evidence of an excess risk of mesotheliomas from asbestos air pollution in the neighbourhood of chrysotile and amosite mines. Differences were reported in the incidence of mesothelioma between urban and rural areas, the causes of which had not been established; but from the information available there was no indication of a risk to the general public.

Since then no further evidence has been produced to alter the conclusions of the advisory committee.

There are difficulties in giving a precise answer to possible risks from exposure to crocidolite asbestos dust. Everyone living in our urban society is likely to have some asbestos in their lungs. For 10–30%, of the proved cases of mesothelioma of the pleura no history of exposure to asbestos dust has been found. Nevertheless, if patients in this latter group, or their relatives, are repeatedly interrogated, some evidence of exposure to asbestos dust may emerge, usually trifling and not necessarily to blue fibre. With the thousands of uses of asbestos only very few people in an urban community can say that they have never seen or touched materials containing asbestos fibre.

To put the health hazard of asbestos to the general public into perspective, about 200 mesotheliomas are diagnosed per year in the United Kingdom, and of these at most 60 occur in people with no known exposure to asbestos. Even if it was assumed that all of these cases were due to environmental exposure to low levels of asbestos the risk would be small—for example, it is less than 1 in 100th of the chance of being killed on the roads.

Asbestos of various types, and particularly blue asbestos, has been highly effective in insulating and fire-proofing buildings and must have saved many lives. Much of the material used for these purposes was blue asbestos—before it became implicated in the development of the mesotheliomas. The use of blue asbestos was severely restricted in Britain in 1969, and the fibre has not been imported since 1970. The Health and Safety Executive has established stringent regulations for the alterations and demolition of buildings which have been insulated with material containing crocidolite asbestos and the disposal of the material. Clearly it is neither possible nor desirable to demolish every building containing this type of fibre. It is more important that the crocidolite should be removed and replaced where it has been used to insulate steam pipes and boilers. The insulation has to be removed from these tubes and cylinders at regular intervals for inspection, often in confined spaces. Whenever the fibre has been exposed and is flaking off the possible danger must be taken seriously, and precautions should be taken to prevent any leakage. However, even in populations with a history of high exposure to crocidolite asbestos dust the incidence of mesotheliomas is less than 7%. The relative safety of substitute materials is under study. Experiments on animals indicate that rigid or semi-rigid fibres with a diameter of less than 1 μm can be dangerous, but the tumour incidence with these other fibres is much less than with asbestos.

The Secretary of State for Employment has appointed a committee to inquire into the possible dangers of exposure to asbestos. Meanwhile, an attempt is being made to establish the actual amount, and type, of mineral dust in the lungs of all cases of mesotheliomas occurring in Britain over the period of one year. This will require collaboration by the coroners, pathologists, epidemiologists, and the Government departments concerned. The actual analysis of the material from the lungs depends on recent advanced techniques, but it should give a clearer indication of the relative hazards from occupational, immediate environmental, and general exposure to the different types of asbestos and mineral dusts.