

- <sup>2</sup> Storie, V J, *The Role of Alcohol and Human Factors in Road Accidents*. Paper read at the 5th International Conference of the International Association for Accident and Traffic Medicine, London, 1-5 September, 1975.
- <sup>3</sup> Michon, J A, *Compensation of Defects in High-Risk Road-Users*, Working Paper ICP/SHS 041/7a. Conference on the Epidemiology of Road Traffic Accidents, Vienna 4-7 November 1975. Proceedings to be published by the World Health Organisation Regional Office for Europe, Copenhagen.

## Autoantibodies in breast cancer

Sera from patients with cancer often react against their own tumour cells. These so-called tumour-specific antibodies have been shown to occur in a diversity of malignant conditions by means of cytotoxic techniques or immunofluorescence.<sup>1</sup> Apparently the surface of the cancer cell contains antigens that are normal fetal or adult components but which become exposed to a greater degree or in a higher concentration than in normal cells and so induce the formation of these antibodies.

In 1971 Whitehouse and Holborow<sup>2</sup> showed that some other autoantibodies—those directed against smooth muscle (SMA)—may occur in various types of cancer; and, as they pointed out, their presence may further confound the detection of tumour-specific antigens. SMA in high and persistent titres occur mainly in the autoimmune type of chronic active hepatitis, but these antibodies may also be produced for one to seven weeks by non-predisposed subjects with viral hepatitis, infectious mononucleosis, or *Mycoplasma pneumoniae* infections.<sup>3</sup> Some of these antibodies react with the actin microfilaments<sup>4 5</sup> present in many cells,<sup>6</sup> and certain viruses may incorporate the antigen into their membrane, thus making it more immunogenic.<sup>7</sup> Farrow *et al*<sup>8</sup> suggested that the conversion of a normal cell to a malignant form may lead to the exposure of this antigen, and Gabbiani *et al*<sup>4</sup> showed that breast cancer cells contain more actin filaments than normal tissues, in keeping with the greater mobility of malignant growths. Subsequently, a higher frequency of antinuclear antibodies (ANA)<sup>9 10</sup> was also shown to occur in malignant disease. A dissident report, however, came from Tannenbergs *et al*,<sup>11</sup> who failed to observe any change in the incidence of these autoantibodies among 250 patients suffering from various types of cancer.

More recently these "non-tumour specific" antibodies have been studied in detail in patients with breast cancer by two groups of workers with somewhat conflicting results. Wasserman and his colleagues<sup>12</sup> observed a higher incidence of SMA and ANA in breast cancer patients at mastectomy than in matched controls. They noted that the patients who later had recurrence of their disease showed a significantly higher incidence of multiple antibodies compared with those who remained well. They proposed that in patients with breast cancer the increased incidence of autoantibodies might reflect not only a change in the cell membrane but also tissue damage due to the presence of cancer or disordered immunological reactivity associated with deficient tumour surveillance. These theories might also explain the prognostic significance of the autoantibodies.

The suggestion by Wasserman *et al* that autoantibodies in breast cancer may have prognostic implications could not be substantiated in the study reported by Mitra, Perrin, and Kumaoka at p 257. Though the patients were not followed prospectively, there was no difference in the incidence of

multiple antibodies in those with metastatic breast cancer and those with primary disease only. Their results apply to patients with breast cancer and normal women from both Britain and Japan; the Japanese are known to have a lower incidence of breast cancer and a better prognosis<sup>13</sup>. Further carefully conducted prospective studies are warranted in view of the implications the results may have in the practical management of breast cancer.

Another aspect of the investigation by Mitra *et al* was the study of thyroid autoantibodies. They observed a higher incidence of these antibodies in British women than in Japanese, possibly indicating a higher incidence of autoimmune thyroiditis in the British. This fits with the suggestion of Mitra *et al*<sup>14-17</sup> that mild thyroid deficiency may be a risk factor in breast cancer, the incidence of which is higher in Britain than in Japan. They propose that thyroid deficiency may initiate malignant transformation by sensitising the mammary epithelial cells to the action of prolactin. In support, workers from Japan have reported<sup>18</sup> a higher than expected incidence of breast cancer in a large series of patients with Hashimoto's thyroiditis. Nevertheless, it remains to be explained why women with established breast cancer did not show a higher prevalence of thyroid antibodies than their healthy counterparts. Possibly in these women the thyroid abnormality occurred during the early years critical for the initiation of breast cancer.

- <sup>1</sup> Southam, C M, in *Immunological Disease*, ed M Samter, vol 1, p 743. Boston, Little, Brown and Co, 1975.
- <sup>2</sup> Whitehouse, J M A, and Holborow, E J, *British Medical Journal*, 1971, 4, 5 11.
- <sup>3</sup> Biberfeld, G, and Sterner, G, *Clinical and Experimental Immunology*, 1975, in press.
- <sup>4</sup> Gabbiani, G, Trenchev, P, and Holborow, E J, *Lancet*, 1975, 2, 796.
- <sup>5</sup> Norberg, R, Lidman, K, and Fagraeus, A, *Cell*, 1975, in press.
- <sup>6</sup> Pollard, T D, Weihing, R R, *Critical Reviews in Biochemistry*, 1974, 2, 1.
- <sup>7</sup> Fagraeus, A, *et al*, *Nature*, 1975, in press.
- <sup>8</sup> Farrow, L J, Holborow, E J, and Brighton, W D, *Nature New Biology*, 1971, 232, 186.
- <sup>9</sup> Burnham, T K, *Lancet*, 1972, 2, 436.
- <sup>10</sup> Zeromski, J O, Gorny, M K, and Jarczewska, K, *Lancet*, 1972 2, 1035.
- <sup>11</sup> Tannenbergs, A E G, *et al*, *Clinical and Experimental Immunology*, 1973, 15, 153.
- <sup>12</sup> Wasserman, J, Glas, U, and Blomgren, H, *Clinical and Experimental Immunology*, 1975, 19, 417.
- <sup>13</sup> Wynder, E L, in *Prognostic Factors in Breast Cancer*, eds A P M Forrest and P B Kunkler, p 32. Edinburgh, Livingstone, 1968.
- <sup>14</sup> Mitra, I, *Nature*, 1974, 248, 525.
- <sup>15</sup> Mitra, I, *Experientia*, 1975, 31, 1218.
- <sup>16</sup> Mitra, I, and Hayward, J L, *Lancet*, 1974, 1, 885.
- <sup>17</sup> Mitra, I, Hayward, J L, and McNeilly, A S, *Lancet*, 1974, 1, 889.
- <sup>18</sup> Itoh, K, and Maruchi, N, *Lancet*, 1975, 2, 1119.

## Segregated smokers

It is surprising how recently tobacco smoking has become acceptable in public places and mixed company. From James I's much quoted blast against it in the seventeenth century up to the outbreak of the first world war the practice was held to be impolite at best and in many circles offensive. The smoker took his solace in a "smoking room" or in the great outdoors or in public bars liberally provided with spittoons. But in the last 50 years this obnoxious practice has become the common-place norm in restaurants, offices, cinemas, shops, and many other public but enclosed places. The theatres in London's west end have successfully fought back and prohibited it in the auditorium. Some food shops have likewise done so. But smokers in general retain a remarkable liberty to inflict their offence on people who resent it—a liberty taken on

occasion even in public places despite "No smoking" notices.

Recently the Institution of Professional Civil Servants tried to get the employment side, the Civil Service Department, to take some action on this matter. The staff side put up three sensible proposals. They are worth setting out in full because other bodies representing employees may wish to take them up. The staff side asked the Civil Service Department to: (1) issue a general warning throughout the Civil Service on the health hazards of smoking; (2) separate non-smokers from smokers where practicable; and (3) institute no-smoking periods. Nobody familiar with the brainwashing induced by smoking will be surprised to learn that these proposals were rejected.

But the battle of clean air is worth continuing, for the non-smokers as well as being right will probably win in the end. The grip that tobacco has obtained on a substantial minority of the population shows some signs of weakening. And the careless disregard that smokers too often show for both the sense and the sensibility of non-smokers runs counter to a growing concern in other ways to behave in a healthier fashion. Spitting in public, for instance, once so commonplace as to go unremarked, has diminished in the last 50 years so greatly as to evoke distaste and even remonstrance nowadays. Again, people take more care than formerly to guard against the spread of infections—"Coughs and sneezes spread diseases." So that it is against this improved attitude to public health that smokers continue to puff carcinogens into other people's lungs as well as their own.

There are already too many people around saying No. And in relation to smoking the railways and airlines set an unfortunate example. Instead of "No smoking" compartments there should be "Smoking" compartments. So that as well as education in schools and public places on the dangers of smoking to the smoker, its possible risks and undoubted offence to people who must associate with him, and its evil example to young people, some official encouragement to keep the smoker in his place would be welcome. That smokers will exist in the community for the foreseeable future is undoubted. Let them be segregated so far as is reasonably practicable in offices, restaurants, pubs, village halls, lecture theatres, committee rooms, cinemas, factory floors, and workshops, as well as in public transport vehicles, by notices showing where they may smoke, if they must, among fellow addicts.

## Early detection of growth hormone deficiency

When a child's short stature is due to lack of growth hormone, every year without treatment means a permanent loss of some inches in his final height. The indications for and the long-term effects of human growth hormone therapy are now well known. Only those children in whom the secretion of growth hormone is deficient will benefit from this treatment, but in such cases the regular injection of human growth hormone should be started at the earliest possible moment and continued until growth potential is exhausted with the closure of the epiphyses.

Growth hormone deficiency may be due to structural damage to the hypothalamus and pituitary—such as that due to craniopharyngioma—when it is usually associated with

defective secretion of other pituitary hormones. In practice, however, the most common disorder is an isolated deficiency due to a defect of either release or synthesis of growth hormone. This condition is not associated with any structural defect of the pituitary; it affects boys far more frequently than girls; and it may be familial. From birth onwards the rate of growth is very low, and the rate of bone maturation is much delayed. The absence of growth hormone makes the child relatively plump. Of all types of growth hormone deficiency this type responds the best to treatment with human growth hormone.

Early treatment is of paramount importance, for if left undiagnosed the child's height falls further and further below the norm, and later treatment can never compensate for all the height lost. Tanner has recently made an eloquent plea for early diagnosis,<sup>1</sup> pointing out that experience in the Medical Research Council trial had been that correct diagnosis often seemed to have been unduly delayed. Proper diagnosis of short stature should be possible by the time any child reaches the age of 5. By this age any sufferer from isolated growth hormone deficiency will have a body height that is at least three standard deviations below the mean. Doctors concerned with child care should ensure that all children as short as this have been referred to a paediatric or endocrine unit by the time they are due to start school. Although new methods of extraction have greatly improved the yield of growth hormone from human pituitaries, it will remain a scarce commodity. To ensure that the hormone is given to those who need it and that long-term treatment is monitored for success, the preparation and distribution of human growth hormone are still organised by the Medical Research Council, now with the co-operation of the DHSS.

<sup>1</sup> Tanner, J M, *Health Trends*, 1975, 7, 61.

## Nucleus hospitals

Early next month the Department of Health will be explaining its plans for nucleus hospitals to the Joint Consultants Committee and will justify yet another change in direction in the hospital building programme on the grounds of financial necessity. The nucleus concept provides standard designs for the units required in the first phase of a district general hospital and is based on a standard module, two storeys high, with variations in ward design kept to a minimum. The economic arguments for mass production are familiar and convincing, and to that extent the proposals will meet with a general welcome. But there are wider implications of this revision of Department policy which have been given too little attention.

Quite why it took the DHSS more than 20 years to realise the practical advantages of standardisation of some features of hospital design must remain a mystery. In the early years of the NHS it was assumed that, just as gentlemen always had their suits made to measure, hospitals should always be designed from the site upwards, taking into account all the personal idiosyncrasies of the hospital staff and local traditions. Need we be surprised that while half the schools in Britain are post second-world-war—and so are half the houses—less than a quarter of all NHS hospitals were built after 1948 and indeed half of them go back beyond the Kaiser's war? The tortoise pace of hospital rebuilding in Britain compared to