Immunisation targets in Europe and Britain

As part of the policy for achieving health for all by the year 2000 the World Health Organisation European Regional Committee has adopted the goal of eliminating indigenous measles, poliomyelitis, neonatal tetanus, diphtheria, and congenital rubella. That policy set the background for the Second World Health Organisation Conference on Immunisation Policies in Europe, held in Karlovy Vary, Czechoslovakia, last year, which discussed the targets in detail.

Concern was expressed that the variation between countries both in vaccination schedules and in the collection of data on uptake and on the incidence of disease made comparisons almost impossible. One of the main recommendations adopted by the conference was that by 1985 all countries should report target diseases in a standardised format, using agreed definitions, and that the methods used in calculating immunisation uptake rates should be stated. The target was set of a 90% primary immunisation rate for all children under 2 years of age in the region by the year 1990 together with the establishment by 1986 of a system to monitor suspected adverse effects of immunisation.

Secondly, with morbidity and mortality from diphtheria, polio, and neonatal tetanus at an all time low the discussion on target diseases was dominated by measles and congenital rubella. To eliminate measles from Europe by 1995 will require all countries to attain an uptake of 95% in children before the age of 2 by 1990, and this level should be maintained subsequently. The conference recommended that all countries should have an effective measles surveillance and investigation system developed by 1988 so that by 1990 all suspected cases of measles could be investigated and outbreak control measures taken.

Congenital rubella presents more problems, for two approaches have been adopted within the European region: elimination of the disease by mass immunisation of all children or protecting girls of 10-14 years and women of childbearing age, as in Britain. For those countries adopting the former approach an uptake rate of 95% by 1995 was the target. The British approach requires virtually a 100% uptake rate in the target population to eliminate congenital rubella. As with measles, the conference urged all countries to develop effective systems for the surveillance and investigation of all suspected cases of congenital rubella.

Other diseases of public health importance that were discussed included pertussis and hepatitis B. The benefit of pertussis immunisation with currently available whole cell vaccines outweighs any possible risk of vaccine induced disease, and the conference recommended that all countries should use these vaccines. They should be withheld only after careful consideration of the consequences to the child and the community. Nevertheless, the development and clinical testing of new acellular vaccines should be encouraged. All countries were also urged to begin vaccination with hepatitis B vaccine for at risk groups (although these groups were not defined) and to establish a surveillance system for the different forms of viral hepatitis.

Without doubt the conference was valuable in reinforcing the commitment of member countries to the goals and activities of the Extended Programme on Immunisation, but some of the targets it set may prove unrealistic. In Britain, however, it should be possible by 1990 for 90% of all children to be immunised with the basic series of vaccines for all the target diseases (except possibly pertussis).

The use of standard definitions for reporting the targets may not be appropriate in England and Wales as the goal to be attained by 1985. Though our notification system (and other sources of data on commoner infectious diseases such as measles and whooping cough) is incomplete and lacks "standard definitions," it does provide reasonably accurate measures of trends to allow assessment of progress in these containment.5 Any change at this time might make these trends difficult to interpret. Standard definitions will become important when the incidence of these diseases becomes so low that every case is investigated, as is done at present with poliomyelitis.6

The stated target for measles is to eliminate the disease by 1995 by reaching a 95% uptake of vaccine in children by 1990. Assuming that elimination of measles is a worthwhile goal (a truth not universally acknowledged)7 this may also not be feasible. For example, the United States has not yet succeeded in eliminating measles despite achieving very high vaccine uptake rates in children and of enforcing immunisation at school entry of those considered susceptible. The Joint Committee on Vaccination and Immunisation has set a target of a level of uptake of measles immunisation in children in the second year of life of 90% by 1990—"from which level efforts to eliminate measles should be made."8 By 1990 the feasibility of eliminating measles should be more apparent, and a realistic final target could then be set. Notifications of measles would have to be extremely low by 1990 to make it cost effective to investigate all suspected cases of measles and to take measures to control infection spreading from each reported case.

Finally, the (perhaps somewhat academic) point should be made that it is not theoretically possible to eradicate congenital rubella by using a selective vaccination programme unless 100% coverage of the target group is achieved with a vaccine that is 100% effective.7 Nevertheless, congenital rubella should become extremely rare with this type of programme, and inability to eradicate it should not be used as a prime consideration in the choice of an appropriate rubella vaccine strategy. More important is the appropriateness of the chosen strategy for the country concerned.

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Infiltrating lobular carcinoma of the breast

The nosological entities identified by pathologists should have clinical relevance. For a primary malignant tumour the clinician would ideally like the pathologist to predict the probability and pattern of secondary spread and the chances of response to treatment. Recent reports on the behaviour of infiltrating lobular carcinoma—the second most common carcinoma (at least 8% of invasive breast carcinomas) after infiltrating duct carcinoma—suggest that progress is being made towards this ideal.

Infiltrating lobular carcinoma is distinguished from infiltrating duct carcinoma histologically by its small cells, diffusely infiltrative pattern, and the formation of characteristic linear arrays or "Indian files" of tumour cells that sometimes form targetoid patterns around non-neoplastic ducts. Three variants of this classical pattern have been described and designated solid, alveolar, and mixed, according to the histological picture. A further variant, signet ring cell carcinoma of the breast, is characterised by large and frequent intracytoplasmic lumina; this form of infiltrating lobular carcinoma should be distinguished from the rare signet ring type of mucoid carcinoma, which is a form of duct carcinoma.

What does the diagnosis of infiltrating lobular carcinoma tell the clinician? Taken overall, infiltrating lobular carcinoma appears to have the same likelihood of axillary node infiltration and distant metastases and the same survival rates as infiltrating duct carcinoma. Classical infiltrating lobular carcinoma has a better prognosis and the solid variant a poorer prognosis than infiltrating duct carcinoma. Furthermore, there appear to be differences in the distribution of metastases and in oestrogen receptor status between infiltrating lobular carcinoma and infiltrating duct carcinoma.

The differences in metastatic pattern between the two types of tumour which have been reported may influence clinical presentation and management. Infiltrating lobular carcinoma tends to produce diffuse or finely nodular infiltration of the peritoneum and retroperitoneum, which is often associated with diffuse infiltration of the stomach wall, ovaries, and uterus. Metastatic infiltrating duct carcinoma spreads to these sites much less frequently, and, when it does, tends to form large nodules, contrasting with the diffuse pattern of infiltrating lobular carcinoma. Retroperitoneal infiltration may also spread to the walls of the ureters and cause a functional block of urinary flow. Hydronephrosis is a common accompaniment of this finding and the patient may rarely present with the sudden onset of loin pain and perinephric extravasation of urine. Usually, however, the hydronephrosis is silent and not associated with an increased incidence of urinary tract infection.

The retroperitoneum may be the site where metastases are first detected in patients who undergo mastectomy and are followed up with serial bone scans. In a recent report of patients who developed metastatic infiltrating lobular carcinoma half showed a gradual increase in retention of isotope within the pelvis of the kidney, indicating progressive hydronephrosis. This was not seen in patients with metastatic infiltrating duct carcinoma who were followed up in the same way.

When infiltrating lobular carcinoma metastasises to the central nervous system it almost always produces symptoms and signs of carcinomatous meningitis. The cerebrospinal fluid contains malignant cells, protein concentration is raised, and glucose concentration reduced. By contrast, infiltrating duct carcinoma is almost always associated with parenchymal deposits; thus the presentation of metastases in the central nervous system in the two tumour types is quite different.

Widespread infiltration of organs with infiltrating lobular carcinoma cells may lead to the serendipitous diagnosis of carcinoma of the breast. We have made the diagnosis of primary infiltrating lobular carcinoma after seeing characteristic cells in biopsy specimens from the cervix, bladder, endometrium, gall bladder, and stomach. In the latter it may be misdiagnosed as limitis plastica.

Several studies, though not all, have shown that the proportion of oestrogen receptor positive tumours is higher in infiltrating lobular carcinoma than in infiltrating duct carcinoma. In our own series the proportion of breast carcinomas with detectable oestrogen receptors was 82% for infiltrating lobular carcinoma (compared with 63% for infiltrating duct carcinoma), and this is associated with a higher probability of response to endocrine treatment in patients who go on to develop metastatic disease.

The findings outlined above show the distinctive nature of infiltrating lobular carcinoma. This may reflect an origin of these tumours from a different cell type within the breast than infiltrating duct carcinomas or, more probably, from a single cell type that may differentiate along separate pathways into either infiltrating lobular carcinoma or infiltrating duct carcinoma. The distinctive pattern of spread of infiltrating lobular carcinomas may be associated with determinants on the cell surface—as yet not identified—that are not shared by infiltrating duct carcinomas.

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