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Pre-exposure prophylaxis of rabies

The risk of developing rabies after a bite by a rabid animal can be reduced to about a tenth by cleaning the wound vigorously and by active together with passive immunisation.[1 2] The immunological mechanisms are poorly understood,[3] but there are three major defects in this regimen. Firstly, the antibody response to conventional vaccines is unpredictable and is rarely evident unti 6-10 days after the first injection:[4] by then rabies virus may have invaded the central nervous system and become inaccessible to humoral antibody. Secondly, the use of rabies antiserum to inactivate virus during this vulnerable period suppresses the response to vaccine.[3 5 6] Thirdly, the nervous tissue vaccines and equine antisera that are most widely used throughout the world may cause dangerous reactions. Though the introduction of purer and more potent vaccines and human rabies immune globulin will improve postexposure prophylaxis, this will never be a completely certain way of preventing rabies.

Pre-exposure vaccination is a more reliable means of protection: it has been claimed that no case of rabies has occurred in a person known to have had rabies antibodies in their serum at the time of exposure.[7] The protective value of rabies vaccines in man is inferred from the serum neutralising antibody titre which they induce, but in the words of one authority:[8] "no particular humoral or cellular immune response to rabies virus antigens has ever been correlated specifically with resistance to the disease." Duck embryo vaccine (DEV) was the first vaccine considered safe enough to be used before exposure: neuroparalytic complications occurred in only 1 in 32 000 of those vaccinated compared with an incidence of 1 in 1630 in those given nervous tissue vaccines.[7] But DEV is a disappointingly unreliable antigen,[9] failing to produce detectable antibody levels in between 5% and 20% of cases given the usual three or four dose pre-exposure course.[10] Over two-thirds of those vaccinated develop mild local symptoms; 10% have 'flu-like systemic symptoms; and 0·5% suffer anaphylactic reactions.[11] Serious neurological complications have, however, been rare.[11-13]

The most promising recent development is human diploid cell vaccine (HDCV), which is derived from fixed virus grown in the Wi-38 strain of human diploid fibroblasts and subsequently inactivated.[14] This produces an earlier, greater, and more certain neutralising antibody response than DEV or nervous tissue vaccines. Two to four 1-ml doses of HDCV, given by intramuscular injection over 2-4 weeks, produce high levels of antibody, perhaps 20 times greater than those resulting from a comparable course of DEV, in all those vaccinated.[15-20] A tenth of the dose is equally effective if given intradermally,[21] and the most economical pre-exposure course is two 0·1 ml intradermal doses given four weeks apart.[16] In individuals given other rabies vaccines a single dose of HDCV has had a remarkable booster effect.[22]

So far the protective value of HDCV has been proved only in animals,[23] but it is now being evaluated in the post exposure prophylaxis of human patients bitten by rabid animals. Local and febrile systemic reactions to HDCV are no more frequent than with DEV, no neurological complications have been reported, and none would be expected since the culture medium is human, non-neural tissue.[19] HDCV will soon be licensed for production and use in Britain, and will become the vaccine of choice for protecting people with a high risk of exposure to rabies in animals or in man—namely, anyone likely to be in contact with imported animals before or during their quarantine period, those who work with these animals or with the rabies virus in laboratories and zoos, and medical staff caring for patients suffering from rabies. Unfortunately, the high cost of HDCV (estimated at £10 or more per 1 ml dose) may make its use impracticable in developing countries, where rabies is so important.

Another possible application of pre-exposure vaccination has recently been investigated. The present European epizootic of fox rabies threatens to reintroduce the disease to Britain. Attempts to reduce the fox population within the endemic zone have failed,[24] but captive foxes have been immunised against the disease by using an oral rabies vaccine in sausage baits.[25] Many practical and ecological problems have to be solved, however, before mass immunisation of foxes can be contemplated.

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Abnormalities of taste

On careful examination most patients who complain of loss of taste will be found to be suffering from loss of smell, and they interpret their failure to appreciate "flavour" as lack of taste. Recognition of this distinction is important from the diagnostic, therapeutic, and legal viewpoint.[1]

Actual abnormalities of taste exist, however, and are usually referred to as ageusia, hypogeusia, or dysgeusia according to the nature of the symptom. Electrical measurement of taste has produced valuable quantitative information,[2] but the qualitative investigations of taste remains the traditional testing with salt, sweet, sour, and bitter solutions.

Since the chorda tympani, which transmits the gustatory impulses, travels through the middle ear to join the facial nerve ear disease should be considered in all patients with abnormalities of taste. A common cause is damage to the chorda during stapes surgery, but if the operation was on one side only attenuation of the symptom can be predicted confidently even though complete recovery is unlikely. There is an important difference between those patients with chronic middle ear infection who have retained the sense of taste and those with the more serious erosive cholesteatoma, where taste is usually completely absent.[3] Abnormalities of taste occur when the facial nerve itself is affected by the disease. If in addition there are lesions of the auditory and vestibular pathways serious petrosal or cerebello-pontine lesions must be excluded.

There remain a group of patients with taste symptoms in whom no aural lesions are found; they are perhaps more numerous than is generally thought. Only recently, for instance, has the simple question been raised of why after surgical operations patients find hospital food tasteless. The complex metabolic changes affecting metallic ions which follow surgery and severe burns[4] have been overlooked because the hypogeusia recovers with the patient, though recovery may be delayed by severe anorexia. Henkin drew attention to the abnormalities of taste and smell which occur in endocrine disorders such as adrenal cortical insufficiency, chromatin-negative gonadal dysgenesis, and hypogonadotrophic hypogonadism. With others[5] he has recently noted these symptoms in untreated hypothyroidism. The importance of these findings may be considerable in the aged, where loss of taste is often accompanied by anorexia and an alteration of the quality of the food intake. There is a danger of unrecognised subclinical avitaminosis, which may produce a vicious circle—perceptual changes of taste and smell may be associated with pellagra. Medical training in Britain, resting on a generally well-fed and affluent population, has tended to decry the protective uses of vitamins, but it may be time to review this attitude in the context of the increasing numbers of aged patients and the rising price of food.

Thiol-containing drugs may reduce the acuity of taste, which may then be restored by zinc and copper ions.[6] Chelating agents such as penicillamine may produce dysgeusia, though treatment with copper has not proved successful. Griseofulvin, lincomycin, tranquillisers, and the tetracyclines may occasionally produce symptoms, but more sporadically. Loss of taste also occurs after the use of thiamazole and carbimazole; it returns to normal after the drug has been withdrawn.[7] The active thiocarbamine contains an SH group, which may possibly combine with metallic ions such as Zn^{++}.

Though these observations have provoked much interest, the obstacles in bringing theory closer to practice lie in the difficulty of measuring zinc in body tissues—and indeed in all zinc measurement techniques. Moreover, we still do not know how serum zinc concentrations correlate with those in the urine, and in the body itself. Nevertheless, there are strong indications for using non-toxic zinc salts in the management of patients with abnormalities of taste.

Bizarre gustatory symptoms in patients with mental illness should not be overlooked, as these may be a side effect of lithium carbonate.[8] Any patient who develops this symptom should be asked for a full list of the drugs he is taking.

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Early gastric cancer

Early gastric cancer is usually curable—in obvious distinction to the high mortality of the more usual clinical form of the disease. In common speech "early" signifies a relationship in time, but in this context it must be defined using other dimensions, for data are seldom available on how long stomach cancer has been in existence before it is removed.[1 2] In fact, the term has become synonymous with growths limited to the mucosa and without evidence of infiltration beyond the muscularis mucosae.[3] These neoplasms may metastasise to lymph nodes while remaining intramucosal, and they are distinct both from more deeply infiltrating growths and from carcinoma-in-situ. A diagnosis of carcinoma-in-situ or the less definite changes of dysplasia refers to cytological features confined to cells within the basement membrane of glands. A continuing difficulty is the distinction between regenerative hyperplastic epithelium, as may be seen in chronic gastritis or in association with healing gastric ulcers, and so-called dysplastic epithelium. Perhaps the term epithelial dysplasia