CSM UPDATE

Desensitising vaccines

DESENSITISATION THERAPY (hyposensitisation or immunotherapy) has been used to treat allergic disorders since the early 1900s. It aims to reduce the susceptibility of patients to symptoms induced by specific environmental allergens to which they have been found to be sensitive. The two types of desensitising vaccines most commonly used in the United Kingdom are extracts of house dust mite and grass pollen. Extracts of a large variety of other allergens, including bee and wasp venoms, are also available and are given either singly or in combination. A confusing number of different units are used to express the allergen content of the products currently marketed. The absence of a standard unit means that products containing the same allergens are not interchangeable. Treatment entails serial subcutaneous injections of increasing concentrations of allergen(s). These are usually given at intervals of seven to 14 days before any likely natural exposure to the allergen(s), for seasonal allergic disorders, or at any time for perennial allergies. The number of injections in a course of treatment varies from three to 18, depending on the products used. In addition, maintenance injections of allergens, usually at monthly intervals, are advocated for perennial allergies.

There is convincing evidence of efficacy for some vaccines. These include the rag weed extracts used in the United States, where rag weed is a common cause of allergy; the vaccines used to protect against anaphylaxis induced by some antibiotics; and the bee and wasp venoms. The efficacy of other vaccines is more difficult to assess. In double blind placebo controlled studies carried out in patients with hay fever and asthma there is some evidence that by the end of a course of grass pollen extracts some patients will be less susceptible to symptoms induced by environmental grass pollens, but no follow up studies have been conducted to examine long term protection from such allergens. Evidence in support of the efficacy of short term courses of extracts of house dust mite is less convincing, and there is no evidence that these induce long term protection. In addition, few data exist on the effects of these extracts on objective measurements of lung function in asthmatic patients.

All desensitising agents have the potential to induce allergic type reactions, the most serious of which are bronchospasm and anaphylaxis. Since 1957, 26 patients in the United Kingdom have died from anaphylaxis induced by these products—11 of these since 1980 and five in the past 18 months (table I). In most of these cases adequate facilities for cardiorespiratory resuscitation were not available. Asthmatic patients seem to be particularly susceptible to severe adverse reactions.

Table II shows the number of reports of anaphylaxis and bronchospasm on the adverse reactions register of the Committee on Safety of Medicines for each desensitising vaccine. It also gives an estimate of the incidence of these reactions calculated from the number of reactions reported to the CSM and the number of courses of treatment sold over the same period. It is important to realise that this is probably the minimum incidence of such adverse reactions, as many reactions are not reported to either the CSM or the appropriate pharmaceutical company. The data suggest that some extracts are more likely to induce anaphylaxis or bronchospasm than others, but such conclusions may be misleading because of different usage and reporting rates for the different vaccines. In addition, for the products that include many different allergens it is often not clear from the adverse reaction reports which particular allergens were involved; thus these figures relate only to the product as a whole and do not give any idea of the adverse reactions to any particular allergen. Although anaphylaxis and bronchospasm seem more likely to occur when high concentrations of extracts are used, they have also been reported at the lowest concentrations recommended for treatment.

From the information available to the CSM anaphylaxis does not seem to be a problem when extracts of allergens are used as diagnostic skin tests.

Conclusions—Desensitising vaccines have the potential to induce severe bronchospasm and anaphylaxis, and these reactions have resulted in 26 deaths since 1957—5 in the past 18 months. The efficacy of the desensitising agents used in this country—apart from the bee and wasp venoms and the vaccines used to prevent anaphylactic reactions to some antibiotics—remains in doubt. At present there is no accurate information on the comparative efficacy and safety of these agents.

None of the desensitising vaccines should be considered to be free of risk. It is essential, therefore, that physicians carefully weigh the potential benefits of the vaccines against their known risks before embarking on treatment in any patient. In view of the appreciable risks incurred during treatment these agents should be used only where facilities for full cardiorespiratory resuscitation are immediately available, and patients should be kept under medical observation for at least two hours after treatment.

TABLE I—*Details of 26 patients* who died from anaphylaxis induced by desensitising agents†*

	No		No
Indication for treatment:		Adverse reactions reported to previous injections in final course of treatment:	
Asthma	16	Yes	6
Hay fever	1	No	20
Unknown	9		
Type of treatment:		Time of onset of reaction:	
Normal course	16‡	<10 minutes	14
Maintenance injections	4	<30 minutes	4
Unknown	6	<90 minutes	2
		Unknown	6

* 13 female, 12 male, one of unknown sex; mean age 31 (range 11-57) years.
† Specific Desensitising Vaccine in 16 cases, Migen in four, Norisen in three, Pollinex in two, and Alavac-S in one.
‡ Five had undergone previous courses without adverse reactions.

TABLE II—*Number of cases and incidence (per course of treatment) of serious adverse reactions to desensitising agents reported in the UK. Figures given in parentheses after each agent are number of courses sold during the stated period*

	Anaphylaxis	Bronchospasm	Anaphylaxis+ bronchospasm	Death
Extracts of house dust mite				
Norisen (24 000; 1978-86):				
No of cases	39	19	58	3
Estimated incidence	1/615	1/1263	1/413	1/8000
Migen (114 600; 1973-86):				
No of cases	19	33	52	4
Estimated incidence	1/6031	1/3472	1/2203	1/28 650
Pollen extracts				
Norisen Grass (43 500; 1978-86):				
No of cases	14	14	28	0
Estimated incidence	1/3107	1/3107	1/1553	
Pollinex (643 500; 1974-86):				
No of cases	30	27	57	2
Estimated incidence	1/21 450	1/23 833	1/11 289	1/321 750
Alavac-P (39 500; 1979-86):				
No of cases	3	7	10	0
Estimated incidence	1/13 166	1/5642	1/3950	
Spectralgen Pollen (500§; 1982-6):				
No of cases	1	7	8	0
Estimated incidence	1/500	1/71	1/62·5	
Extracts of many different allergens				
Norisen* (67 000; 1978-86):				
No of cases	17	8	25	0
Estimated incidence	1/3941	1/8375	1/2680	
Conjuvac (1830; 1981-6):				
No of cases	1	3	4	0
Estimated incidence	1/1830	1/610	1/457	
Allpyral (389 961; 1978-86):				
No of cases	14	12	26	0
Estimated incidence	1/27 854	1/32 496	1/14 998	
Alavac-S (65 300; 1979-86):				
No of cases	11	5	16	0†
Estimated incidence	1/5936	1/13 060	1/4081	
Specific Desensitising Vaccine (67 900; 1979-86):				
No of cases	39	29	68	5‡
Estimated incidence	1/1741	1/2341	1/998	1/13 580
Wasp and bee venoms				
Pharmalgen (1500§; 1980-6):				
No of cases	2	3	5	0
Estimated incidence	1/750	1/500	1/300	
Albay (182):				
No of cases	0	0	0	0
Estimated incidence				

*Excluding extracts of 100% house dust mite and grass pollen. §Numbers of patients. †One death in 1972; ‡eleven additional deaths during 1957-79 (data on number of courses of treatment sold unavailable).