

of the drug alone or other drugs may lead to pseudolupus or that an idiopathic form of the disease exists is expected from retrospective analysis of the other cases known so far. According to the latest report from Germany⁴ all fifteen pseudolupus patients described had venous disease.

In all our patients the symptoms regressed or subsided 4-6 months after withdrawal of the drug and have not so far reappeared. Treatment with corticosteroids often seemed beneficial. More prolonged follow-up is needed to decide whether chronic disease—as described in some cases^{1,4}—can always be avoided by complete withdrawal of the drug.

We can only speculate as to how the drug leads to disease. Since pseudolupus developed after 5-14 months on the drug, a chronic toxic effect may be postulated. However, since the illness continues after withdrawal for months with symptom-free intervals, other factors may play a role. In the seven patients investigated immunologically, signs of an immunological imbalance were found, such as anergy, lymphopenia, and raised IgM and C₃ levels. Leucocytosis, the increase of young neutrophils, and the granulocyte-rich pleuritic exudates point to further alterations of neutrophil function. However, all these abnormalities may be a consequence of the disease rather than the cause. The glycoside component of venocuran and sera from patients on this drug depressed in-vitro lymphocyte reactivity to P.H.A. Similar effects have been described with various other glycosides and also with salicylates, drugs which are considered safe for long-term treatment and which are not known to have serious side-effects of this nature.^{11,12} Therefore, this in-vitro finding, though noteworthy, may be irrelevant to the disease.

Our data strongly suggest a link between a drug and a distinct disease, but are not conclusive. They are reported in this form because of their grave implications. It seems amazing that it should take 15 years for such a serious and not uncommon side-effect of a widely used drug to be recognised. Yet only a chain of fortuitous events led to its discovery, the most important being the presence of a serological marker of the disease. It is now up to physicians as well as to the drug manufacturers (who collaborated in our investigation) to take the necessary steps should further evaluations confirm that pseudolupus is indeed an iatrogenic disease.

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LOCAL PRODUCTION OF SPECIFIC IgE ANTIBODIES IN ALLERGIC-RHINITIS PATIENTS WITH NEGATIVE SKIN TESTS

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Summary A group of patients with allergic rhinitis had a clinical history strongly suggestive of house-dust-mite (*Dermatophagoides pteronyssinus*) allergy but negative skin reactions when prick tested with *D. pteronyssinus* extracts. These patients were proved to be clinically allergic by nasal provocation with this allergen. Although radioallergosorbent tests showed that these patients lacked specific IgE antibodies in their serum, they did have specific antibodies in their nasal secretions. These findings indicate that these patients had allergic rhinitis mediated by the local production of IgE antibodies.

Introduction

THE diagnosis of allergic rhinitis due to house-dust mite is dependent upon two major factors—a positive clinical history and a positive immediate weal-and-flare skin reaction with the relevant allergen. The immunological mechanisms are type I, immediate hypersensitivity.¹ Patients can present with a history strongly suggestive of house-dust-mite allergy yet fail to give this positive weal-and-flare reaction on skin testing.^{2,3} The mast cells in the skin of these patients can mediate a type-I reaction since a skin response is obtained with other allergens to which the patient may also be sensitive (e.g., grass pollen).

We have investigated patients with a history of house-dust-mite allergy which has been confirmed by nasal provocation tests. Nevertheless, these patients were negative on skin testing, and we suspected that local and not systemic production of allergen-specific IgE might explain these observations. We looked therefore in the nasal secretion and serum for IgE antibodies directed against the house-dust mite in this group of patients and compared them with a group who were similarly allergic but who did give positive skin tests.

Patients, Materials, and Methods

Patients

Patients were selected from those attending an allergy clinic who presented with a history suggestive of allergic

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rhinitis due to the house-dust mite. Fourteen patients were skin-test negative to *Dermatophagoides pteronyssinus* (five male, nine female, average age 27.2 years). Six males who were skin-test positive (average age 26.2 years) and five controls (four male, one female, average 28.4 years) were also studied. The same batch of allergen extract was used in all test systems in this study (Dome Laboratories, batch no. 9106042).

Nasal Provocation Test

The allergen extracts were diluted in 50% glycerol-saline to 40, 200, and 1000 protein nitrogen units per ml. The diluted extract was administered as an aerosol to a single nasal airway, beginning with the lowest dose. In the absence of a reaction the procedure was repeated after 20 minutes with a higher concentration of allergen. A positive reaction was recorded when the patient sneezed or reported itching and nasal obstruction.

Radioallergosorbent Test (R.A.S.T.)

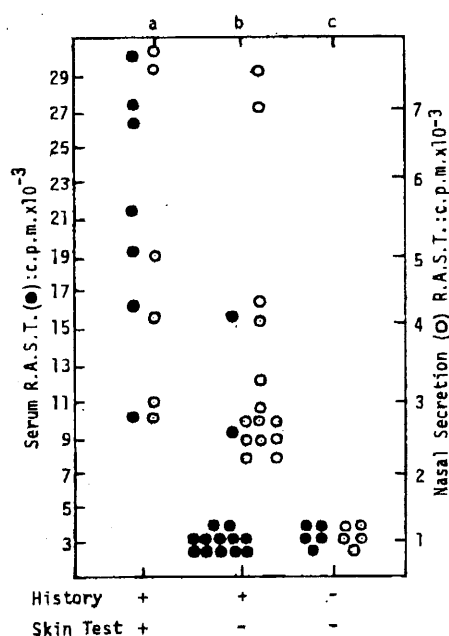
R.A.S.T. assays were performed using the procedure of Ceska.⁴ Allergen extracts were chemically bound to paper discs (Whatman no. 54) by reaction with cyanogen bromide (Fluka A.G.). Goat anti-human IgE (Miles Research Division) was purified by affinity chromatography⁵ and the pure antibody was labelled with iodine-125.⁶ R.A.S.T. assays were performed on both nasal secretion and serum.

Nasal Secretion

The nasal secretions were collected by placing a 1×10 cm. strip of filter paper (Whatman no. 1) in the nose for 15 minutes (a non-traumatic procedure). The secretion is then eluted in saline for 5 minutes and concentrated by freeze drying before assaying the specific IgE.

Results

We divided our patients into two groups. The study group, with a history of house-dust-mite allergy but no positive skin test, and a positive control group who gave both a positive history and a positive skin



the importance of a good clinical history, especially since there is another group of individuals (not reported here) who give neither a suggestive history nor positive nasal provocation test, yet have positive skin tests and raised levels of IgE antibodies to specific allergens in their serum.

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INFUSION THROMBOPHLEBITIS AND INFECTION WITH VARIOUS CANNULAS

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Summary A prospective study was carried out of the frequency of thrombophlebitis and bacterial contamination of cannulas associated with four commonly used intravenous cannulas of differing length and chemical composition. For all cannulas the frequency of thrombophlebitis increased significantly with time. Long 'Teflon' cannulas were significantly more likely to be contaminated with bacteria and associated with thrombophlebitis than all other cannulas, while the low frequency of thrombophlebitis with butterfly stainless steel cannulas was shown to be due to their short duration of use. It is suggested that long teflon cannulas should be avoided and that infusion thrombophlebitis could be eliminated as a clinical problem by the use of intermittent short duration intravenous infusions.

Introduction

INTRAVENOUS infusion is associated with a small mortality from septicæmia¹ and a considerable morbidity from thrombophlebitis² at the infusion site. These problems have been considered by many workers and numerous recommendations have been made as to the means of reducing their frequency. These have involved the use of aseptic technique during cannula insertion,³ topical application of various antibiotics,^{4,5} Millipore filters,⁶ and recommendations to buffer the infusion fluids.⁷ The effect of the type of cannula used has received scant attention. Intravenous cannulas differ greatly both in their chemical composition and in the trauma associated with their insertion; however, there are few comparative data on their liability to produce thrombo-

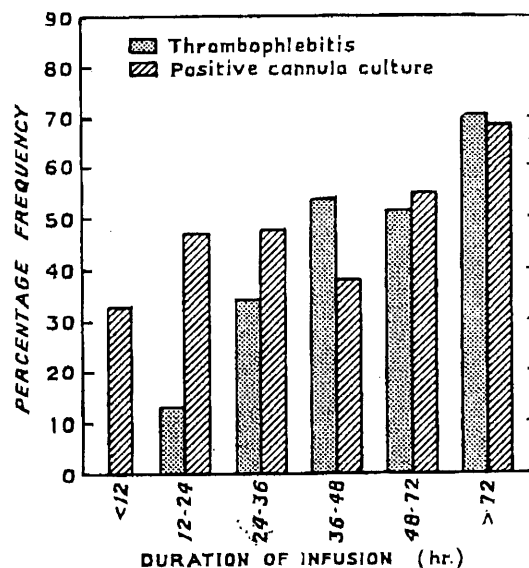
phlebitis or bacterial contamination. We compared the frequency of bacterial colonisation of the cannula and local thrombophlebitis associated with four different cannulas. These comprised three short cannulas—one of stainless steel (butterfly), one of polypropylene ('Medicut'), one of 'Teflon' ('Venflon')—and one 12-inch long cannula of 'Teflon' ('E-Z cath').

Materials and Methods

Patients requiring intravenous infusion were allocated randomly to one of four types of cannula—i.e., butterfly (stainless steel), E-Z cath (12-inch long flexible teflon), medicut (polypropylene), venflon (short rigid teflon). All cannulas were erected by one person (C. C.) who recorded the type of cannula used, its situation, the duration of the infusion, and the reason for discontinuing the infusion. At the end of the infusion the cannula was removed and flushed through with 2 ml. of Todd-Hewitt broth which was added directly to Robertson's meat medium and incubated at 37°C for up to 7 days. Sub-cultures were made and any organisms present identified. After discontinuing the infusion the site of cannula insertion was assessed for evidence of thrombophlebitis by an observer who was unaware of the type of cannula used. Initially an attempt was made to grade the thrombophlebitis according to its severity, but this was abandoned for two reasons: firstly, it was our practice to stop the infusion at the first sign of thrombophlebitis, and its severity therefore depended to a large extent on how early it was brought to our notice; and, secondly, the severity of thrombophlebitis often increased after the cannula was removed. For these reasons thrombophlebitis was simply recorded as being present if there was an area of inflammation along the course of the vein of 3 cm. or more from the point of cannula insertion.

Results

A total of two hundred and six infusions were studied, the cannulas used being forty-eight butterfly, forty-six E-Z cath, sixty-one medicut, and fifty-one venflon.



Frequency of thrombophlebitis and positive cannula cultures in infusions of differing duration.