

would be a great step ahead in a contribution which will increase the respect for the allergist by his fellow practitioner.

In the final analysis, we are inclined to agree with Dr. Josephson when he hesitates to draw conclusions on the practical significance of a skin test without supporting information from the history and from actual provocation studies. Our point was that, in the absence of these confirmatory findings, the skin test is not to be relied on for making the diagnosis of specific clinical hypersensitivity.

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Questions Regarding Alum-Precipitated Pyridine Complex

TO THE EDITOR:

Miss Margaret Strauss, Director, Allergen Laboratories, Dome Chemicals, Inc., has informed me there has been issued a license (Patent Pending) for the manufacture and sale of antigens described as alum-precipitated pyridine complex trade-named Allpyral, some of which will be available in the next weeks. Certain questions regarding the "complex" have been on my mind. I had hoped that, with time, discussion of papers presenting the use of such material, or consideration by the appropriate committee of the Academy, would have resolved these questions. Since allergists will soon be faced with queries by those who are not allergists and patients regarding this new preparation, I think it may be well to present these matters for consideration now. Furthermore, implications regarding basic factors should be discussed.

The alum-precipitated pyridine complex of pollen depends on the extraction of undefatted pollen with 50 per cent pyridine in water to dissolve the oil fraction as well as water-soluble antigens, essentially a simultaneous defatting and extracting process. It is implied that all fractions are then precipitated from solution by alum, as suggested by the name Allpyral. The questions which arise concerning this preparation involve 2 main points, namely:

1. Is there an actual complex or combination of pyridine with the pollen antigen which could help in any way to improve its effectiveness and safety?

2. Are oil fractions present in the final product and, if they are, are they desirable?

Pyridine, which contains 17.7 per cent N and is miscible with water, ether, oils, and many other organic liquids, is a good solvent. The use of the word complex suggests some combination of pyridine with the antigen rather than a simple solution. There is no indication of any such complexing at any time, and in the final steps, all pyridine is simply washed out with saline. The suggestion that pyridine contributes something significant to the final product is further carried out in the trade name "Allpyral."

It is stated that eye symptoms in pollenosis seem to be relieved more by the use of the whole pollen complex than by conventional antigens. The oily fraction of pollen is known to cause "delayed" contact dermatitis comparatively rarely. The typical manifestations of pollen sensitivity including the eye symptoms are specific "immediate" reactions to water-soluble, nonoily antigens. There is no published evidence that oil fractions are actually present in the final "pyridine complex," but, if they are, whatever we know of the matter suggests they could serve no useful purpose in the treatment of pollenosis, and therefore should not be injected. However, when the sediment of ragweed Allpyral 20000 μ per milliliter was extracted with ether, there was no evidence of an oil fraction in the ether.

It seems to me that no real changes are brought about by the use of pyridine in making the original extract and that the final product is not significantly different from the alum-precipitated pollen antigen reported by Zoss in 1937. It is of interest that Talmage and Dixon

in 1953 reported alum-precipitated radioactive water-soluble antigen had no or only very slight repository effect. It should be recognized that such alum precipitates consist of active antigen presumably adsorbed on alum particles and thus after injection freely available to immediate reaction with specific antibody. This is shown by the observation that after injection of the "complex" the maximum local reaction is reached in $\frac{1}{2}$ to 4 hours. The same precautions should be observed, therefore, as in the use of conventional solutions.

In conclusion, the phrase "alum-precipitated pyridine complex" of an antigen is misleading; a more accurate description would be alum-precipitated water-pyridine extract of an antigen. Since no oil fractions may be present and the producers state in the literature accompanying the package that "the low molecular, highly reactive fractions" are not present, the suggestion in the name Allpyral that all the fractions of the whole pollen are in the final product is misleading, as is the suggestion that pyridine is present when there is known to be none.

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Reply

TO THE EDITOR:

For the past 50 years allergists have been attempting to identify and improve allergenic extracts. The alum-precipitated pyridine extracts, made from nondefatted antigens, were developed in an attempt to produce an extract which would be simple to administer, maintain stability, have delayed action, and contain fractions from the native antigenic material not generally available in aqueous pollen extracts.

The name Allpyral is a registered trade name and is an abbreviation of *allergens pyridine alum* precipitated. As a matter of fact, a trade name need have no special reference to product composition.

The report referred to by Dr. Naterman, "The Alum Precipitate: Preparation and Clinical Investigation," reported by Zoss and associates,¹ concluded that "local and systemic reactions from intracutaneous and subcutaneous injections of alum-ragweed precipitate in ragweed-sensitive patients are similar to those produced by equal protein nitrogen concentrations of aqueous ragweed extracts." Alum-precipitated pyridine extracts can be administered in doses many times larger than those attainable with aqueous extracts and with many less local and systemic reactions.²⁻¹⁰ This shows the difference between the simple alum precipitate from aqueous pollen extract of Zoss and the alum-precipitated pyridine extracts—Allpyral. The pyridine extraction accounts for this difference between these two alum precipitates. In like manner, the Allpyral extracts cannot be compared to the I¹³¹-labeled alum-precipitated albumin and globulin of Talmage and Dixon¹¹ which was prepared in a similar manner as that of Zoss, i.e., an alum precipitate from an aqueous extract.

The alum-aqueous ragweed has also never had general acceptance because it became gummy and sticky on standing and so was difficult to administer. The Allpyral antigens are flocculent—never clump and are easy to resuspend with simple shaking.

Zoss and associates¹ stated: "In a series of ragweed-sensitive patients, the activity of alum-ragweed precipitate and aqueous ragweed extract was compared by intracutaneous tests. The two extracts were of the same protein nitrogen concentration and the intracutaneous injections were made in parallel rows on the upper arm with serial dilutions containing 1, 10, 100, 1000 P.N.U./c.c. No differences between the two extracts were demonstrated." This is a more critical difference between these two alum extracts. The Allpyral extracts cannot be used for an intracutaneous skin test, since with this new antigenic product an immediate response is not obtained in the above testing concentrations. Therefore, there is a very great difference between the immediate skin test reactivity of the antigen, alum precipitated from a pyridine extract, and that from an aqueous solution. The difference between these two alum extracts shows the importance of the pyridine processing. Alcohol, acetone, or other water-miscible organic solvents do not produce this type of product.