with a view to determining any possible differences in prognosis and treatment.

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SULPHONAMIDE ALLERGY

BY

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Sensitization to sulphonamide drugs may arise after internal or external administration. In the latter case the reaction is an eczematous dermatitis, and in the former a syndrome consisting of drug fever, skin eruption, leucocytosis, and—more uncommonly—joint effusions, conjunctivitis, jaundice, agranulocytosis, or other features.

When a patient develops any of these types of allergy, oral administration of the drug causes sharp reactions which render future sulphonamide therapy unpleasant or dangerous. In these cases the question which naturally arises is whether such reactions will occur if other drugs of the sulphonamide series are given. This is a point which has received little attention up till now. Moeschlin (1942) reported six cases sensitized to sulphathiazole, of which two reacted to other sulphonamides. Haviland and Long (1940) exposed two sulphathiazole-sensitive patients to sulphapyridine and obtained reactions. Cases of both single and multiple sensitivities have been described by Erskine (1938), Goodman and Arthur (1941), Bloom (1942), Costello (1943), and Swartz and Lever (1943).

All these cases followed internal administration. That the eczematous form of allergy can also exist to single or multiple sulphonamides was shown in a previous report (Park and Platts, 1942). The investigation reported here was undertaken to determine the frequency of these two types of allergy.

Methods Used

Forty cases of both internal and eczematous allergy have been investigated by skin tests and oral medication with various sulphonamides and the related compounds, sulphanilic acid and procaine.

For oral testing, a mixture was used which disguised the slightly bitter taste of the sulphonamide and in which different drugs could be given without the patient being aware of any change. The first dose was usually 0.5 g., and was worked up in the absence of a reaction to 1 g. four-hourly for 48 hours. Reactions in the eczematous cases consisted of a local flare-up plus a general

dermatitis, starting in about six hours, and, in the internal cases, of pyrexia starting in about two hours.

Skin tests were used in the eczematous cases only. Since ordinary patch tests are unreliable in sulphonamide eczema, a modified scratch technique was used, with 50% pastes of powdered sulphonamides in hydrous lanolin and a 2% lanolin paste of procaine. These were either rubbed repeatedly into the scratch or applied over it as a patch. The final method evolved was to apply four different test materials to one long scratch on pieces of cloth about an inch apart, and cover with adhesive for 48 hours. The positive reaction was seen on that part of the scratch in contact with the offending substance only.

Results

The results of the tests are shown in the following table:

Reaction	Sulphanilamide		Sulphapyridine		Sulphaguanidine		S'thi-azole	Others
	Skin Test	Oral	Skin Test	Oral	Skin Test	Oral	Oral	
Eczema ..	+	+	+	+	+	+	+	
" ..	+	+	0	0	0	0	0	
" ..	+	+	?	?	0	0	0	
" ..	+	+	+	+	+	+	+	Procaine skin test +
" ..	+	+	+	+	0	0	0	
Fever, rash, neutropenia ..	0	0	+	+				
Eczema ..	+	+			0	0	0	Procaine 0
" ..	+	+	0	0	0	0	0	
" ..	+	+	0	0	0	0	0	Procaine +
" ..	+	+	0	0	0	0	0	Procaine 0
" ..	+	+	0	0	0	0	0	
" ..	+	+	0	0	0	0	0	
" ..	+	+	0	0	0	0	0	
" ..	+	+	0	0	0	0	0	Sulphanilic acid + ; proc. +
" ..	+	+	0	0	0	0	0	Procaine 0
Fever, rash ..	0	0	+	+	+	+	+	
Eczema ..	+	+	+	+	+	+	+	S. acid + proc. 0
Photo-sensitivity ..	+	+	0	0				
Eczema ..	+	+	+	+	+	+	+	S. acid and proc. +
" ..	+	+	0	0	?	?	?	S. acid and proc. +
" ..	+	+	0	0	0	0	0	S. acid and proc. 0
" ..	+	+	0	0	0	0	0	S. acid 0
Fever, rash ..	+	+	+	+	+	+	+	Procaine +
Eczema ..	+	+	+	+	+	+	+	S. acid + ; proc. 0
" ..	+	+	0	0	0	0	0	S. acid 0
Fever, rash ..	+	+	+	+	+	+	+	S. acid 0
oedema ..	+	+	+	+	+	+	+	S. acid + ; proc. 0
Eczema ..	+	+	+	+	+	+	+	S. acid +
Fever, rash ..	+	+	+	+	+	+	+	
Eczema ..	+	+	0	0	0	0	0	Sulphadiazine 0
Fever, rash ..	0	0	0	0	0	0	0	Sulphamezathine +

Discussion

All drugs of the sulphonamide series consist chemically of the para-amino-phenyl-sulphonil radical ($\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2 -$), linked to various side chains, thus:

In the case of sulphanilamide the side chain is NH_2 , and in the case of sulphanilic acid is OH .

Of these 40 cases 24 reacted only to the individual drug by which they were initially sensitized, thus being allergic to the sulphonamide group plus all or part of the side chain. The last case (see table) shows how highly specific this allergy can be, being insensitive to sulphadiazine but sensitive to the same compound with two methyl groups added (sulphamezathine).

Allergy to Multiple Sulphonamides.—It was found that no case was allergic to more than one of the series without being allergic to them all and to sulphanilic acid. The group common to all

these is the sulphonamide or para-amino-phenyl-sulphonic radical, $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\cdot$. Of the 40 cases 16 were of this type. Two cases not included in this group, however, behaved in a peculiar manner. They were both eczemas, highly sensitive to small doses of sulphanilamide but not to small doses of other sulphonamides. Each of them reacted to other sulphonamides in heavy dosage, with mild eruptions only. This reaction included a selective flare-up of the sites of previously positive sulphanilamide skin tests, but not of the negative tests to other sulphonamides. Had they been allergic to the sulphonamide group they should have reacted to all these in roughly equal amounts (1 g. of sulphanilamide or sulphanilic acid is equivalent to about 1.5 g. of sulphapyridine or sulphathiazole). The marked difference suggests that a small quantity of sulphanilamide or closely related compound may be formed in the body from the other sulphonamide drugs.

Allergy to Other Drugs.—Rogers (1938) described a case in which the administration of sulphanilamide caused a flare-up of the sites of several previous reactions to procaine. Procaine has the formula $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{COO}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{N}(\text{C}_2\text{H}_5)_2$. It therefore has in common with the sulphonamides the amino-phenyl radical, $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot$. Skin tests with procaine were made on 14 of the above cases allergic to multiple sulphonamides. Seven gave positive reactions. Four of these were tested with full oral doses of phenazone, which carries the radical $\text{NH}\cdot\text{C}_6\text{H}_4\cdot$, but none gave any reaction.

A possible case of sensitivity common to both sulphathiazole and arspenamine, which also contains the amino-phenyl radical, has been reported by Weinstein and Domm (1941).

Summary

The specificity of the sensitivity in 40 cases allergic to sulphonamide drugs has been investigated.

In 60% the allergy was confined to one sulphonamide drug. In 40% it occurred to multiple sulphonamides and to sulphanilic acid.

In about half of the latter allergy was to the sulphonamide radical, $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\cdot$. In the other half it was to the amino-phenyl radical, $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot$, reactions also occurring to procaine.

No cases were seen in which the sensitization was to still smaller groups than these.

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TREATMENT OF PULP INFECTION OF THE FINGERS IN THE FIELD

BY

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The following is based on observations made after three years in casualty clearing stations, during which time a large number of these cases have been treated. The main object of treatment was to avoid evacuation to the base, and to return the patient as soon as possible to his unit.

There is little need to labour the disability caused by a stiff and painful finger, especially if it be the index finger of the right hand. The finger may be merely useless or, as often happens, an actual hindrance, interfering with the use of the whole hand. It is not proposed to discuss the aetiology at length. Septic cuts, scratches, and unnoticed pricks are probably the chief precipitating causes. Contributory are the difficulties of ensuring asepsis by reason of water shortage,

dust, and the nature of the man's work; this is particularly so in the case of small parties.

Pathologically the lesion is at first a simple pulp infection, though lymphangitis, lymphadenitis, and general symptoms are not slow in supervening; untreated or inadequately treated bone necrosis follows with depressing frequency, with its consequent increase in the period of disability. The symptoms of the established case need little description. Severe and throbbing pain and complete loss of function are the salient features. General symptoms may be fairly severe, with headache and pyrexia; the finger is tense, red, and extremely tender. Here it may not be out of place to emphasize that the utmost gentleness in examination is essential. The patient will have to be re-educated in the use of the finger and hand: the more pain he suffers, the longer this is going to take.

Management of Cases in Detail

The successful management of these cases calls for attention to detail: a man may be off duty longer with a whitlow than after appendicectomy. In my experience, conservative methods are unavailing; the sulphonamide drugs are useful, but they will not cure the patient without surgical treatment. The primary stage in the treatment is the establishment of adequate relief of tension, and that as soon as possible. "Waiting for pus to form" is mentioned only to be condemned.

The operation is simplicity itself, and I have done many in field ambulance dressing stations with entirely satisfactory results. The anaesthetic of choice is pentothal sodium or some other intravenous barbiturate. If possible, this is preceded by morphine gr. 1/4 and hyoscine gr. 1/150. Adequate drainage is secured by laterally placed bilateral incisions, the pulp space is freely opened with fine Spencer Wells forceps, and a piece of glove rubber drain put across. The incision should not, and need not, traverse the flexure creases of the finger. For infections in the terminal phalangeal area it is, I think, not necessary to carry the incision in an acute case right across the tip of the finger. The drain is taken out after 48 hours; gauze and thick rubber drain are inferior to glove rubber in every way.

The incision of the whitlow is by no means the end of the case from a surgical standpoint. Morphine should, I consider, not be withheld for the first two nights, as a transient increase in the swelling may follow the incision. The incision is dressed once daily with hypertonic saline: Lieut.-Col. P. D. Johnson has suggested the use of sterile 12% sodium sulphate, and in my personal experience this is excellent. Every three hours warm sterile solution is poured over the dressing, which is undisturbed. Heat by means of a hot bottle or, if available, an electrically heated blanket is applied continuously for the first three or four days. I am not convinced that the sulphonamides greatly influence the condition, for after drainage the lymphatic and general conditions rapidly subside.

As soon as the incisions are clean, and swelling is subsiding, the encouragement of active movements should be begun. At no time should any attempt to force movement be made: it merely brings home to the patient that his finger is painful and useless. Progress is neither rapid nor spectacular. When incisions are healed the whole hand is placed in warm water and active movements persisted in. Passive movement is the worst form of interference. The man must be given to understand that further progress depends upon himself. This is the most difficult and trying part of all: it may take up to three months to secure full return of function. This time can be spent usually in the man's unit, supervised by his medical officer.

Summary

This paper on pulp infection of the fingers has been written largely from the military standpoint.

Emphasis has been laid on early, adequate, but not mutilating incisions to secure relief of tension.

Incisions are not to be made primarily to "find pus" but to prevent phalangeal necrosis by relieving pulp-space tension. Reliance should not be placed on the sulphonamide drugs as substitutes for incision.

Prolonged soaking of the finger should be avoided, and a method of avoiding this is suggested.