A Method of Desensitization of Allergy
Due to Streptomycin with Prednisone

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Lowell1 gave the incidence of allergy to streptomycin as 10 per cent. This high incidence is due to administration of the drug for long periods in tuberculosis. Most of the allergic reactions were not serious. There was no way of knowing whether a patient allergic to streptomycin could react again on re-administration. It might be assumed that he would. Houghton2 in England and Chakravarty3 in this country described two individual methods of desensitizing streptomycin allergy by ACTH and cortisone.

This presentation discusses the method by which four patients who were allergic to streptomycin could tolerate this drug after desensitization with prednisone.

When streptomycin with paraaminosalicylic acid (PAS) and/or isoniazid were given it was difficult to determine which of the drugs was causing allergy. For this purpose, an intradermal skin test with 10 mg. of streptomycin in 0.1 ml. of normal saline was given in one forearm. If there was induration of 5 to 10 mm. in diameter, the reaction was read as 1+, if 11 to 20 mm., it was 2+ and if more than 20 mm. or necrosis, it was 3+. If induration was less than 5 mm., it was read as doubtful and if no induration, but only erythema, it was considered negative.

The skin test generally became positive within 12 to 24 (occasionally 48) hours.

Simultaneously, with the streptomycin skin test in one forearm, purified protein derivative (PPD) No. 1 was given in the other.

Generally, both streptomycin skin test and PPD tests were positive in allergic cases. Prednisone was started after the skin tests were known. The dosage varied in some cases, but the following dosage schedule was followed:

For one week 50 mg. of prednisone was given orally each day. This was given in three divided doses. Then streptomycin skin test and the first dose of purified protein derivative No. 1 were repeated. Usually either the streptomycin skin test was negative or the reaction was much less than before. In cases with the streptomycin skin test still positive, prednisone was given for another week before streptomycin was started.

When the skin reactions were diminished at the end of one week, with prednisone, streptomycin was started intramuscularly, 10 mg. on the first day and doubled every day until it reached 800 mg. Then 1.0 gm. twice weekly. Patients reached 1.0 gm. of streptomycin on the ninth day.

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After 1.0 gm. of streptomycin was administered twice weekly for four weeks, prednisone was tapered off and stopped in about two weeks.

Before stopping prednisone, every patient was given 20 units of ACTH intramuscularly daily. This was gradually tapered off and stopped in eight days. ACTH was given to stimulate the adrenal cortex. The last four days of prednisone was combined with ACTH. This was given so that the adrenals had sufficient time to be stimulated and if there was any infection, in the meantime, prednisone would help, as the adrenal cortex was probably not stimulated fully in the first four days.

In this series, 150 patients were tested with streptomycin skin test of whom 12 were allergic clinically. Eleven allergic cases reacted to streptomycin skin test but one did not. The 138 who were getting streptomycin but were not allergic clinically were negative to streptomycin skin test.

During prednisone therapy these allergic patients were negative both to streptomycin skin test and PPD No. 1. When desensitization was done, reaction to PPD No. 1 gradually became positive but streptomycin skin test remained negative. This showed that desensitization was complete.

Unlike penicillin reaction, which was immediate, streptomycin skin test gave a delayed reaction, like tuberculin. This could be seen also from allergic rashes due to streptomycin. These rashes were of erythema and induration type. This type of reaction was due to the specific necrotising antibody factor or cellular sensitizing antibody. In this type of reaction sensitivity to the agent could not be transferred by serum as in immediate type of reaction, but could be transferred by certain cells from the sensitized subject. In immediate type, it was the release of histamine that caused the allergic reaction. The type of antibody was Reagin.

Case 1: This 47 year old white man was admitted with bilateral pulmonary tuberculosis, on October 25, 1955. He was treated with streptomycin 1.0 gm. twice weekly and PAS 12 gm. daily from October 28, 1955. On November 6, he had maculopapular rash and pruritus all over the body. On November 8, he had severe angioneurotic edema.

Haughton's method of desensitization was tried and 80 units of ACTH was given intramuscularly daily until all edema and rashes cleared. Benadryl, 50 mg. intramuscularly thrice daily was also given. After six days, all edema and rashes subsided.

Haughton recommended for desensitization: 80 units of ACTH intramuscularly. It should be given in divided doses with the full dose of the drug the patient was receiving prior to allergic manifestation, after all rashes and pruritus subsided.

Accordingly, on November 18, along with 80 units of ACTH intramuscularly, 1.0 gm. streptomycin and 300 mg. isoniazid were given. Para-aminosalicylic acid was not given as it was thought he might also be allergic to PAS, so the treatment was modified. After one day, he broke down again in macular rashes and angioneurotic edema followed by exfoliative dermatitis. So all drugs were stopped except ACTH and 80 mg. daily of oral prednisone in divided doses was added. This was continued until November 24, when ACTH was stopped and only 80 mg. of prednisone orally was given. Streptomycin skin test and PPD No. 1 were done on December 1955. Both were negative. On December 6, he was started with streptomycin intramuscularly as described above.

After Haughton's method failed to desensitize the allergy due to streptomycin, our method was tried.

Prednisone was given until February 6, 1956. After that, he was given ACTH to stimulate the adrenal cortex. He has tolerated streptomycin even without prednisone, since February 6, 1956. This patient is an example of severe allergic reaction and he was given high doses of prednisone for ninety days which is longer than usual.

Case 2: This 57 year old colored man had been treated with streptomycin 1.0 gm. twice weekly and isoniazid—300 mg. daily since August 18, 1955 for far advanced pulmonary tuberculosis. On January 8, 1956, he had pruritis and erythematous popular eruptions all over the trunk of his body.
Both streptomycin and isoniazid were stopped. When all rashes subsided isoniazid was started and the full dose, 300 mg. daily was tolerated. On February 13, 1956 he was restarted on streptomycin, 1.0 gm. but he broke into generalized rashes and itching. When all rashes subsided, it was decided to start para-aminosalicylic acid, 12 gms. daily, so he would be treated with INH and PAS. On February 18, 1956, he was started on 12 gm. of PAS but he had a rise in temperature to 104° F. and rashes all over the body. After all rashes subsided, he tolerated isoniazid well.

At this time it was decided to desensitize. He was skin tested on March 12, 1956. Streptomycin skin test was negative but PPD No. 1 was 1+.

He was desensitized with prednisone, but began itching when the dose was reduced to 10 mg. daily. This was controlled with pyribenzamine 100 mg. thrice daily.

He received prednisone for 50 days and was given ACTH after prednisone, as described in the method. He has tolerated streptomycin 1.0 gm. twice weekly for about four weeks after both prednisone and ACTH were stopped.

Cases 3 and 4 were desensitized by the same method as was used in Case 2.

SUMMARY

1. In the treatment of tuberculosis, allergy due to streptomycin is found in 10 per cent of cases.

2. To identify such allergy, intradermal skin test with 10 milligram streptomycin in 0.1 ml. normal saline is done. Among 150 patients 12 were allergic clinically. Of these 12 patients, 11 (90.7 per cent) reacted to streptomycin skin test. The rest of 138 patients who were not allergic clinically to streptomycin gave negative reactions to skin test.

3. The streptomycin skin test is a delayed type of reaction, which becomes positive in 12 to 24 hours.

4. To desensitize, 50 milligrams of prednisone is given orally daily for one week. After a week, along with 50 mg. prednisone daily streptomycin is given intramuscularly, starting with 10 mg. on the first day and doubled daily up to 800 milligrams. Then 1.0 gram of streptomycin is administered twice weekly. After 1.0 gram has been given twice weekly for four weeks, prednisone is tapered off and stopped, in about two weeks.

5. Before stopping prednisone 20 units of ACTH is given daily intramuscularly. ACTH is gradually tapered off and stopped in eight days.

6. Among four patients allergic to streptomycin and desensitized, three were positive to the first dose of purified protein derivative, one could not be tested due to angioneurotic edema. During prednisone administration all were negative to the same dose of PPD. Four weeks after prednisone was stopped, all were again positive to PPD.

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RESUMEN

1. Se encuentra la alergia a la estreptomicina en 10 por ciento de los casos.

2. Para reconocer tal alergia se hace la reacción intradérmica con 10 ml. de estreptomicina en 0.1 ml. de solución salina isotónica. Entre 150 enfermos, 12 eran alérgicos clínicamente.

De estos 12 enfermos, 11 (90.7 por ciento) reaccionaron al a prueba cutánea. El resto, 138 enfermos que no eran clínicamente alérgicos dieron reacciones cutáneas negativas.
3. La reacción cutánea a la estreptomicina es retardada y se hace positiva a las 12 o 24 horas. 

4. Para obtener la desensibilización se dan 50 ml. de prednisona oralmente, diariamente por una semana. Después de una semana se da además, junto con la prednisona, estreptomicina intramuscular empezando con 10 mg. en el primer día y doblando la dosis diariamente hasta 800 ml. Desde entonces se da 1 gm. dos veces por semana. La prednisona se va disminuyendo y se suprime al cabo de dos semanas. 

5. Antes de suspender la prednisona se dan 20 unidades de ACTH diariamente intramuscularmente. La ACTH se disminuye gradualmente y se suspende al cabo de ocho días. 

6. Entre los enfermos alérgicos a la estreptomicina y desensibilizados, tres eran positivos a la primera dosis de PPD, uno no pudo ser probado debido a edema angioneurótico. 

Durante la administración de prednisona todos fueron negativos a la misma dosis de PPD. Cuatro semanas después de que la prednisona se suspendió todos volvieron a ser positivos a PPD. 

**RESUME**

1. Dans le traitement de las tuberculose, on trouve une allergie à la streptomycine dans 10% des cas. 

2. Pour indentifier une telle allergie, il convient de pratiquer un test cutané intradermique avec 10 ml. de streptomycine, dissous dans du sérum physiologique normal à 0,1 ml. Para 150 malades, 12 se montrèrent cliniquement allergiques Parmi ces 12 malades, II (90.7%) réagirent au test cutané à la streptomycine. Le reste des 138 malades qui n'eurent pas d'allergie clinique à la streptomycine eurent des réactions négatives au test cutané. 

3. Le test cutané à la streptomycine provoque une réaction retardée qui devient positive en 12 à 24 heures. 

4. Pour désensibiliser, on donne quotidiennement pendant une semaine, 50 ml. de "prednison" par la bouche. Après une semaine, on peut utiliser la streptomycine par voie intramusculaire, en commençant par 10 mg. le premier jour, puis la dose est doublée chaque jour jusqu'à atteindre 800 ml. Alors 1 gramme de streptomycine est administré deux fois par semaine. Après une période de ce traitement pendant quatre semaines, la prednisone est diminuée arrêtée au bout de deux semaines. 

5. Avant d'arrêter la "prednisone," on donne quotidiennement 20 unités d'ACTH par voie intramusculaire. L'ACTH est progressivement diminuée et arrêtée au bout de 8 jours. 

ZUSAMMENFASSUNG

1. Bei der Behandlung der Tuberkulose findet man eine Streptomycin-Allergie in 10% der Fälle.

2. Um solche Allergie zu erkennen, wird ein intrakutaner Hauttest mit 0,1 Streptomycin in 0,1 normaler Kochsalzlösung vorgenommen. Von 150 Patienten waren 12 klinisch allergisch, von diesen 12 Patienten reagierten 11 (90,7%) auf den Streptomycin-Haut-Test. Der Rest der 138 Patienten, die klinisch nicht allergisch auf Streptomycin waren, hatten negativen Reaktionen auf die Hautprobe.


4. Zwecks Desensibilisierung werden 0,5 Prednison oral täglich eine Woche lang gegeben. Nach einer Woche mit diesen 0,5 Prednison täglich wird Streptomycin intramuskulär gegeben beginnend mit 10 mg. am ersten Tag und täglicher Verdopplung bis zu 0,8. Dann wird 1 gr. Streptomycin 2 mal wöchentlich verabfolgt. Nachdem 1 gr. 2 mal wöchentlich 4 Wochen lang gegeben worden ist, wird das Prednison allmählich verringert und nach ungefähr 2 Wochen ganz gestoppt.

5. Ehe mit dem Prednison aufgehört wird, werden 20 Einheiten ACTH täglich intramuskulär gegeben. Das ACTH wird schrittweise vermindert und in 8 Tagen damit aufgehört.

6. Von 4 gegen Streptomycin allergischen und desensibilisierten Patienten reagierten 3 positiv auf die erste Dosis PPD und einer konnte nicht getestet werden infolge eines angioneurotischen Oedems. Während der Prednison-Behandlung reagierten alle auf die gleiche Dosis PPD negativ. 4 Wochen, nachdem das Prednison abgesetzt worden war, reagierten alle wieder positiv auf PPD.

REFERENCES