

however, raise the question of when to temporize and when to operate when inguinal hernia is a complication of late pregnancy. A strangulated hernia of bowel might present a far more serious problem than was found in this unusual case. Should it occur in conjunction with labour it might well be disastrous.

The pathological examination of the specimen was made by Dr. H. H. Pitts, of St. Paul's Hospital, Vancouver, B.C. I am indebted to him for this report.

ANAPHYLACTIC SHOCK FOLLOWING PROCAINE PENICILLIN INJECTION*

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WITH THE PUBLICATION of 6 cases treated with penicillin from February to August 1941,¹ a new drug appeared which brought some hope in the treatment of infection. Further trials showed the high value of the new drug. But, later on, some shadows appeared in the picture and the miraculous antibiotic was found to be capable of harming the one it was supposed to help. Reactions of different types and gravity were observed: local irritation, urticaria, angioneurotic oedema, erythema multiforme, serum-sickness, mental disorder and, rarely, anaphylactic shock.^{2, 4} Duemling reported an incidence of reactions of 10%, including Herxheimer's reactions, in 17,879 patients.⁵

The first case of anaphylactic death from penicillin was reported by Waldbott⁶ in 1949. A 39-year-old female with a history of asthma had received three courses of penicillin in the past. Following the third one, she developed severe urticaria, aggravation of her asthma, joint pains and a slight fever about one week after the administration of penicillin. Suffering again an aggravation of her chest condition, she reported to her doctor who recommended crystalline penicillin. Soon after the injection, she felt a strange taste in her mouth and experienced a feeling of swelling and tightness of her throat and nose. Her face became flushed. She became extremely cyanotic and felt itchy "all over". While leaning

over the kitchen table and asking for a glass of water, she collapsed and died.

About one year later, Burleson⁷ reported a second case. A 40-year-old male had had, in the past, 3 injections of penicillin. 15 minutes after the intramuscular injection of 200,000 units of crystalline penicillin, he went into shock. This patient recovered after the intravenous injection of 30 to 40 mgm. of diphenhydramine hydrochloride.

More recently, other similar reactions have been observed. In January 1952, Yuval⁸ reported the case of a 53-year-old mechanic who, after he was given 300,000 units of procaine penicillin intramuscularly, immediately felt dizzy and was forced to lie down. His respiration became stertorous and he could not respond to questioning. His radial pulse and apical beat were impalpable. No heart sounds could be heard. After 2½ minutes, his heart beat returned and he recovered completely, without any treatment, one hour later.

Thomson⁹ reported the case of a 67-year-old male admitted to hospital to have a bougie passed for a urethral stricture. He had had one reaction before with procaine-penicillin. As this first reaction was thought to be due to procaine, it was decided to use crystalline penicillin. Following the intramuscular injection of 300,000 units, he developed nausea, started to retch and produced a little amount of vomitus. He became increasingly cyanotic with shallow gasping respirations and entered into a stage of collapse. His pulse could not be felt. Although he was given adrenalin and nikethamide he died.

At a meeting of the New York Allergy Society, Siegal and Shepard¹⁰ reported three cases of anaphylactic shock following penicillin injections. The rest of the 60 members had personal knowledge of 3 other cases not reported.

Harpman¹¹ reported the case of a 3½-year-old child who died 3½ hours after the intramuscular injection of procaine penicillin. He had had one injection the day before without any reaction. One hour after the second one, he lost consciousness, became dyspnoeic and died.

Higgins and Rothchild¹² reported the case of a 57-year-old labourer admitted to the hospital on April 1952 for the removal of a nodule of the right breast. 300,000 units of penicillin were injected intramuscularly, after withdrawal of the syringe plunger, ensuring that the needle was not in a vein. A minute and a half later, the pa-

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tient suddenly became cyanotic and coughed. A tonic muscular spasm developed. No blood pressure or pulse could be obtained. He died 10 minutes after the injection. In his past history, he had had a local anæsthetic with procaine in 1949 and had received procaine penicillin in 1950 without any reaction. No family or personal history of any kind of allergic phenomena was elicited.

Mr. C.L., a 58-year-old white male gave a history of chronic bronchitis of 5 years' duration. He was given penicillin on 5 occasions for this condition without any reaction. His condition became worse in the fall of 1951 and he reported to this hospital for investigation in February 1952. A diagnosis of bronchiectasis of the right lower and middle lobes was confirmed by bronchogram.

Because of his age and the condition of the remainder of his lungs, it was decided to treat him conservatively. He came back periodically to the out-patient department for follow-up and medication.

On July 11, 1952, he came to the clinic, complaining of increased cough, shortness of breath, chest pains, abundant muco-purulent sputum and loss of strength. On physical examination, both lungs were resonant and the expiration was prolonged. Coarsely vesicular râles were noticed at the right base anteriorly and posteriorly. Rhonchi were observed all through both lung fields. It was decided to give the patient 600,000 units of procaine penicillin daily for three days.

The first injection was given from a 5 c.c. vial of procaine penicillin, containing 300,000 units per c.c. at about 12.00 noon, on that day. The rest of the vial was used on other patients who did not show any reaction.

As the patient was leaving the hospital, approximately 5 minutes after the injection, he experienced swelling and itchiness of his hands and fingers. Rapidly, this sensation extended to his face and he felt "bad all over". His chest became "tight".

He came back to report the abnormal sensation and was told to lie down. A doctor was called and he found the patient lying in bed, unconscious, without palpable radial pulse or audible blood pressure sounds. He was somewhat cyanotic and his respirations were shallow. He was taken to the ward where adrenalin was given subcutaneously and the foot of the bed elevated. This medication was repeated 15 minutes later and about 10 to 15 minutes after the second injection, the pulse could be felt and his blood pressure was 70/30. The patient started to talk but was still very confused. He was then given 50 mgm. of diphen-hydramine hydrochloride orally every 6 hours for two days. His blood pressure returned to its normal level of 110/70 in the next 12 hours.

The next morning, the patient could describe the early sensations he had experienced immediately after the injection of procaine penicillin; remembered being told to lie down but did not recall anything from then until the time he became conscious during the night. He remained unconscious for about 12 hours.

To determine whether the reaction was due to penicillin or to procaine, it was decided, two weeks later, to perform intracutaneous injections of diluted solutions of procaine, penicillin and procaine penicillin. The solutions used were: (1) procaine 0.1%; (2) crystalline penicillin, 3,000 units per c.c.; (3) procaine penicillin, 3,000 units per c.c. All dilutions were prepared with saline.

1/20 c.c. of each solution was injected as follows: (1) procaine solution and crystalline penicillin into separate sites in the right forearm; (2) procaine penicillin into the left. The patient showed no reaction to procaine or crystalline penicillin but to procaine penicillin he showed an extensive local reaction with pseudopodia and some of the early symptoms of the previous reaction, *i.e.*, itchiness, sensation of swelling of the arm, etc. To prevent a more serious reaction, a tourniquet was applied and adrenalin given. Attempts to show the presence of antibodies by the Prausnitz-Küstner technique were unsuccessful.

DISCUSSION

If one considers the amount of penicillin injected daily throughout the world, the number of the severe reactions described above is very small. Nevertheless, it seems worthwhile to bring them to the attention of the medical profession because they can be prevented in some cases.

Lepper *et al.*¹³ and Mark, Lepper, Dowling *et al.*¹⁴ have demonstrated a higher incidence of reactions with penicillin in oil and beeswax than with crystalline aqueous penicillin of procaine penicillin in oil. These authors claim that the preparation in oil and beeswax is confined to one site for a longer period and, because of the local irritation, there are probably present many damaged proteins which may be conjugated with penicillin and render it antigenic. Waldo¹⁵ demonstrated in rabbits that penicillin must be bound to human albumen to become antigenic.

From the higher incidence of more severe reactions in the last two years, one may postulate that the sensitizing properties of penicillin are increasing with the widespread use of the drug. This is in agreement with Risman's¹⁶ findings.

There is also some evidence that people with a past history of penicillin reaction or other types of allergic phenomena are more likely to develop penicillin reactions of greater severity than individuals with no such history. Trichophyton infections or any fungus infection in the organism may predispose to penicillin reactions. Sanchez-Cuenca¹⁷ desensitized a patient who had developed a giant urticaria after penicillin by using increasing doses of penicillium extracts. He also studied the stools of eight persons, two of whom were sensitive to penicillin. He found penicillium to be present in the stools of the two sensitive persons and in one who was not sensitive. Ris-

man¹⁶ demonstrated a higher incidence of positive skin tests in people with a history of trichophyton infection. It is possible that both penicillin and trichophyton have a common nucleus responsible for cross-sensitization.

CONCLUSIONS

From these facts, it is evident that one must be careful in the use of penicillin therapy. Also, one must condemn the dispensing of penicillin tablets, lozenges, chewing gum, tooth paste and candy over the drug store counter for sore throat or common cold. When penicillin therapy is indicated, the physician should never fail to ask the patient these questions: has he ever received penicillin in the past? Has he ever had reactions, even mild ones, to the drug in the past? Has he had any fungus infections? One should give penicillin no longer than is clearly indicated. If a mild reaction occurs, the nature of which might possibly suggest sensitivity to penicillin, one should pause and consider before continuing therapy.

SUMMARY

1. The literature on anaphylactic shock following penicillin injections has been reviewed.
2. One case is presented who survived. The antigen appeared to be the procaine-penicillin compound.
3. Predisposing factors to penicillin reactions are discussed.
4. The need for careful evaluation of any patient prior to the administration of penicillin is stressed.

REFERENCES

1. FLOREY, H. W. AND ABRAHAM, E. P.: *J. Hist. Med. & Allied Sc.*, 6: 302, 1951.
2. MORGINSON, W. J.: *J. A. M. A.*, 132: 915, 1946.
3. GORDON, E. J.: *J. A. M. A.*, 131: 727, 1946.
4. BATCHELLOR, HORNE, ROGESON: *Lancet*, 261: 195, 1951.
5. DUEMLING: *Ann. New York Acad. Sc.*, 48: 201, 1946.
6. WALDBOTT, G. L.: *J. A. M. A.*, 139: 526, 1949.
7. BURLESON, R. J.: *J. A. M. A.*, 142: 562, 1950.
8. YUVAL, A.: *Lancet*, 262: 163, 1952.
9. THOMSON, W. O.: *Brit. M. J.*, 4775: 70, 1952.
10. Editorial: *J. Allergy*, 23: 383, 1952.
11. HARPMAN: *Brit. M. J.*, 4780: 392, 1952.
12. HIGGINS AND ROTHCHILD: *New England J. Med.*, 247: 644, 1952.
13. LEPPER, M. H. et al.: *J. Clin. Invest.*, 27: 546, 1948.
14. MARK, LEPPER, DOWLING et al.: *J. Clin. Investigation*, 28: 826, 1949.
15. WALDO, J. F.: *J. Clin. Investigation*, 28: 1039, 1949.
16. RISMAN, G. et al.: *J. Allergy*, 21: 425, 1950.
17. SANCHEZ-CUENCA, B.: *J. Allergy*, 21: 176, 1950.

ACTINOMYCOSIS OF FOREARM

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THIS MAN was first seen by me in March, 1952 with the following history:

He came to Canada from the Treviso province of Northern Italy a year previously. He had noticed a vague swelling in the upper part of the right forearm before he left Italy. During the next year the forearm gradually became painful, the swelling increased, and a second swelling appeared below the first.

When I saw him the upper swelling appeared to be attached to the flexor belly of the muscles, and about 2" in diameter. The lower swelling was a little smaller though more prominent, and deep fluctuation could be detected. The skin moved freely over both areas and was not thickened or reddened. X-ray was negative.

He was operated on by Dr. O'Callaghan ten days later, and both masses were dissected free from the flexor muscles and tendons. The lower mass was cystic, and contained yellowish milky fluid; no "sulphur granules" were noted.

Pathology report was as follows:

A granulomatous type of reaction composed of tubercle-like formations containing sulphur granules characteristic of actinomycosis or ray fungus. These will be identified by the use of special stains but there is very little doubt of their nature in the H and E sections. The granulomatous reaction is rather heavy and occasional foreign body giant cells identified. There is marked peripheral fibrosis. Portions of the granuloma appear to be present in the small amount of striated muscle tissue which is found in most of the sections. Diagnosis: Actinomycosis of forearm.

He was given 800,000 units of penicillin daily for seven doses in the postoperative period, and when a small collection of fluid formed at the lower end of the incision this was aspirated (culture negative) and replaced by a solution of crystalline penicillin. The fluid did not reform, and the wound healed firmly by first intention, and the man was back at work within three weeks.

A month after operation he was started on a six weeks' course of penicillin 1.2 million units daily, and this we believe will complete the cure.

This patient appeared to be in excellent health apart from this focus of infection. Chest x-ray was negative. Barium x-ray showed a normal cæcum. He had a small discharging sinus in his upper jaw which was negative for fungus on culture.