PENICILLIN SENSITIVITY : A CASE REPORT

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Case Report.

"Mrs. X aged 28 years came for consultation to the M. I. Room at 10.30 hours on 2nd March 1954 for upper respiratory catarrh.

Pervious history: Cervical Adenitis treated with 28 gms of Streptomycin about one year ago. No history of allergic constitution. She had four injections of Penicillin in the past without any reactions. Exact date and type of drug used could not be ascertained. General health good, physical examination except for signs and symptoms of Naso-Pharyngitis was essentially negative.

Intra-muscular injection of Procaine Penicillin ("Distaquaine") (400,000 units) was given in the gluteal region at 10. 45 hours. Soon after patient got up from the bed and after walking two yards to a chair, began to sneeze, followed by coughing and dyspnoea; also brought up a large amount of sputum. She was put in a recumbent position and given 1 cc of 1/1000 Adrenalin hypo-dermically. Patient become unconscious soon after, pulse feeble, respiration stertorous and cyanosed. 2 cc Coramine was given intra-venously, air passages were cleaned, artificial respiration was started. She was removed to the Military Hospital.

At 11. 10 hours, no heart sounds or respiratory sounds could be heard. Coramine was given intra-cardiacly, oxygen under pressure, and as a last resort cardiac massage. All attempts failed to resuscitate the patient. P. M. was refused."

The tragic case reported above shows you the seriousness of Penicillin anaphylaxis. It must be admitted that in our enthusiasm, of the benefits of Penicillin, we have neglected its diverse, serious and frequent reactions. In many cases this sensitivity has been produced unnecessarily by the widespread misuse of Penicillin. The purpose of this article is to stress methods to prevent reactions of this valuable, in many cases, life-saving drug. It must be stated that Penicillin still retains its pride of place in the therapeutic armentarium when used with discretion. It is not the intention to denounce its efficacy, or its importance.

Penicillin Reactions.

The sensitiveness is due to the presence of cellular as well as humoral anti-bodies in the system as a result of allergic constitution and previous sensitization. Because of such wide spread antigen-antibody reactions, it is no wonder that the manifestations range from mild headache and pruritis to fatal anaphylaxis at the other extreme. Males are noted to be more susceptible than females. All children show low sensitivity.

General Symptoms.

Drug fever, headache, giddiness, nausea, chills, faints, and generalised muscular pains.

Skin Reactions.

Urticaria is a common symptom. It may occur at once or after few days of treatment. It is easily controlled by anti-histamines. Normally it lasts for a few days, but some cases of chronic urticaria have been reported especially following use of depot Penicillins (Penicillin with oil or Procaine Penicillin).

Sterile Abscesses. Usually follow use of oily suspensions when given subcutaneously instead of in the muscle. Local heat and massage are usually sufficient and surgical treatment is rarely required.

Drug Rashes. A common reaction of fleeting nature induced by Penicillin in any form and given by any route. It may consist of erythematous patches, punctate or macular eruption.

Contact Dermatitis. Severity and extent depend on exposure. It is caused by local applications and also from handling of the drug by doctors and nurses.

Local Lesions Local lesions occur at the site of administration and include:

Glossitis, Stomatitis, gastric symptoms, black hairy tongue and infections by saprophytic fungie when given orally. Oedema, erythema and pruritus at the site of injection. Local reactions when used as spray, ointment or drops: Erythema Nodosum, Erythema multiforme, Bullous dermatitis and Exfoliative dermatitis have all been reported, the last often with fatal outcome.

Reactions in the Blood. Eosinophilia, purpuric lesions and Agranulocytosis have been reported.

Reactions of Cardiovascular System 'Faints', shock and vasomotor collapse are quite common. Dyspnoea, palpitation and tachycardia may be encountered. But the most serious and fatal form of reaction in this group is Periarteritis-nodosa.

Serum Sickness Reactions.

This is the commonest reaction and may follow any form of administration. Symptoms usually appear a week after administration and include prutitus, urticaria, joint pains, irregular fever, wheezing and cosinophilia. Duration of symptoms is usually a week to 10 days.

Anaphylaxis.

Anaphylactic shock caused by Penicillin differs in no way from that induced by

other causes. It is most dramatic in onset and may be precipitated by small quantities of drug in any form. Shorter the interval between the onset and administration, the more dangerous the reactions. Fatal cases usually develop symptoms in less then 15 minutes after the drug is given. The case reported above is the seventeenth in literature and there must be several others which remain unreported.

Miscellaneous reactions.

Convulsion after intra-thecal use, peripheral neuritis (especially in nerves near the site of injection), precipitation of asthmatic attacks, laryngeal oedema, exacerbation of existing fungus lesions; Jarisch-Herxheimer type of reaction with grave consequences in leuties have all been known to occur. Extreme nervousness and fear of death have also been reported.

We cannot overlook the serious consequences that may result when giving Procaine Penicillin as a result of neglect of simple precaution of withdrawing the piston to ensure that the needle is not in a vein. Neglect of this simple technique when giving injections, may result in accidental intra-venous injection which can prove fatal.

Discussion.

Penicillin reactions seldom occur with the first injection or administration of the drug. In overwhelming majority of cases there is history of previous medication, often repeatedly and in large doses. Present increase in reactions from this drug is due to its uncontrolled and widespread misuse on account of the low toxicity of Penicillin. A large proportion of sensitive individuals have a previous history of allergic conditions *e. g.* asthma, urticaria, serum sickness, hay fever, eczema and allergic rhinitis. Depot Penicillin is more likely to produce sensitivity as the ingredients in combination increase the possibility of two or more substances having a synergistic, sensitizing effect. It is also possible that reaction in such cases is not due to penicillin itself, but other allergens *e. g.* procaine. In such cases, the real sensitivity to Penicillin 'G' can be determined by skin tests.

Penicillin by oral route is the safest. The only disadvantage is the increased cost of heavy dosage, but these days when the drug is relatively cheap, this is not really a valid objection. It may be stated that it is rare to get reaction on first administration and if first dose did not produce 'reaction, it is most unlikely that subsequent doses given at intervals of less than four days will produce any reactions.

Patients who have to be given Penicillin must be asked :

History of personal and family allergy (asthma, hay fever, urticaria, sneezing, drug or food reactions), previous use of Penicillin in any form and any reactions after such use, especially local swelling and itching at the site of injection, urticaria, wheezing, rashes or drug fever.

Patients who answer to the above in the affirmative should be suspected of sensitivity unless proved otherwise. They must be subjected to a cutaneous scratch

test. A drop of fresh solution of the drug to be used is brought in contact with a superficial cut in the skin, not deep enough to draw blood. A positive test which is a wheal and zone of redness around the scratch within 20 minutes indicates dangerous level of sensitivity. Those who give a negative skin reaction, but have a history of allergy should be tested by intra-cutaneous test with 0.02 cc of 5000 units per c.c. Penicillin solution. An immediate positive intra-cutaneous test debars the patient from use of Penicillin while a delayed reaction obtained after 24 to 48 hours is a possible risk, the gravity of which should be weighed against the infection under treatment (KERN & WIMBERLY).

Those who give negative reaction can be given Penicillin without any risk. Persons with allergic constitution (asthma, hay fever, urticaria, sneezing etc.) should not be given any Penicillin except in case of serious infection. In these cases skin test must be carried out before Penicillin is given and depot Penicillin should be avoided for obvious reasons. Local applications *e. g.* sprays, lozenges, ointments induce sensitivity without any therapeutic benefit. Use of such preparations should be discouraged. Injection of Penicillin in the arm, low enough, to allow use of tourniquet to prevent absorption in case of reaction has been advised (KERN & WIMBERLY)

We, doctors, must avoid unnecessary sensitization of patients by routine prescription of Penicillin preparations in every infection, however, minor it may be. It amounts to use of a modern bomber to destroy an ant hill. Finally, the best way to prevent reaction in Penicillin sensitive individuals is to use some other antibiotic.

Treatment of Penicillin Reaction

Anaphylactic shock: Death may follow so soon after the injection that all may be over before any treatment can be given. Adrenaline, coramine, aminophylline, ephedrine and calcium are the mainstays of treatment. Route of administration is selected according to situation and even intra-cardiac route may have to be resorted to. Oxygen must be started and artificial respiration is often necessary. Anti-histamines should be given by injection in full doses. General treatment is the same as for shock. Use of A. C. T. H. by intra-venous drip has also been reported to have proved useful.

Minor Reactions: Withdrawal of the drug; antihistamines; adrenaline; intravenous calcium and aminophylline; general symptomatic treatment and treatment of shock. If withdrawal of the drug is not feasible, Penicillin may be given together with anti-histamines to minimise the reactions, but these must be given in full dose at least one hour before Penicillin injection.

Serum Sickness Type of Reaction:

Administration of anti-histamines is the treatment of choice. It is effective against urticaria, pruritus and eosinophilia but for joint pains and fever, anti-pyretic and analgesics are required. Local heat and splinting are soothing to the joint conditions. Local use of anti-histamines also helps.

Fish, sea food, nuts and choclates must be excluded from the diet. Only cooked food which is nutritious and full of Vit. 'C', should be eaten.

Exfoliative Dermatitis and Peri-arteritis Nodosa

A. C. T. H. and Cortisone are the main stays of treatment.

Treatment of late Syphilis cases (Penicillin Sensitive) with Penicillin.

To avoid a Herxheimer type of reaction initially, very small doses of crystalline Penicillin are given at 3 hourly intervals as follows:

2500 units	8 doses
5000 units	8 doses
10,000 units	8 doses
15,000 units	8 doses
25,000 units	till completion of course of treatment.

Preliminary treatment with Iodides and small doses of Bismuth should be given for 3 weeks.

Desensitization:

It may be necessary in certain cases to continue Penicillin despite minor reactions. In that case patient should be given full doses of anti-histaminic drug and after 12 hours a small dose of 500 units of preferably Penicillin 'G', may be given intra-muscularly; provided injections of anti-histamine and adrenaline are at hand and the patient is under constant supervision (Beckman). If there is no reaction within 6 hours, dosage is gradually built up, in doubling doses, to full therapeutic level at intervals of 4 to 6 hours.

Further, a person can be desensitized. An initial injection of 400 units of crystalline Penicillin 'G' is given and repeated thrice a week in gradually increasing doses till normal dosage is reached without side effects (Peck Seigal and Bergamin). However, if a scratch test is strongly positive and there is history of violent reactions, it will be wiser not to try desensitization in out-patient practice. To sum up, before Penicillin is administered:

(1) Elicit history of allergic constitution *e. g.* asthma, Hay-fever, urticaria etc. Previous administration of Penicillin and any reactions in the past.

(2) Avoid giving Penicillin for minor ailments. Avoid local applications *e. g.* sprays, lozenges, ointment etc. and depot preparations, especially in persons of allergic constitution.

(3) Most dangerous reactions like anaphylactic shock can be avoided by carrying out simple skin tests described above.

(4) One must be able to recognise the earliest symptoms and be prepared to treat the most severe reactions.

(5) Anti-histamine drug must be kept at hand when Penicillin is being injected.

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