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An Unusual Reaction to Procaine Penicillin G

On January 4, 1980, a Public Health Nurse informed our office of an unusual reaction following an intramuscular injection of 2.4 million units of aqueous procaine penicillin G (APPG) for the treatment of gonorrhea. Shortly after the injection the patient stated, "What strong medicine," then complained that her mouth felt numb. She slumped in her chair and fell to the floor where she began to have violent, uncontrolled thrashing and became cyanotic. Epinephrine was administered since anaphylaxis was suspected. This seemed to have little effect however, but the patient slowly ceased this activity. After this episode the patient became depressed. She stated that she had remained alert throughout the thrashing episode and could hear comments directed to her but could not react appropriately or control the thrashing about. She had received penicillin previously without difficulty.

In our opinion this episode most likely represented an acute reaction to procaine and not an allergic or anaphylactic response to penicillin. Several reports of similar reactions exist and Dr. Jack Armstrong of the CDC in Atlanta has reviewed these published reports for the information of CDC Public Health Advisors working with venereal diseases. The information provided here is a summary of his report.

The first such "neuropsychiatric" reaction to procaine penicillin was reported in 1952. Dr. Armstrong's literature search located 10 separate subsequent reports through 1974 documenting 122 cases. Prominent characteristics of the reactions were agitation, violence, and hysteria (43%), sensory hallucinations (53%), and a fear of impending death (41%). Grand mal seizures, cyanosis, and syncope were also reported but uncommon. A bounding pulse and normal to elevated blood pressure was also characteristic and in contrast to the hypotension and thready pulse characteristic of anaphylaxis.

An allergic mechanism seems unlikely in most instances since many cases admit prior penicillin injections without difficulty and subsequent injections infrequently lead to reaction. Furthermore allergic manifestations such as urticaria are unusual and in four cases skin testing for penicillin allergy was negative. The incidence of this type of reaction appears to be about 0.1 - 0.3% and without any proven racial or sex predominance. The only known sequelae are anxiety and/or depression and fatigue which occasionally have persisted for as long as three months.

Each 4.8 million units of APPG has 1.92 grams of procaine which in the free state has a serum half life in vitro of about one hour. Known toxicity of procaine is directly related to plasma concentration. Intravenous procaine is known to cause hypertension, dizziness, numbness, confusion, and convulsions. Plasma procaine levels have been recorded to be elevated following intravenous administration of APPG therefore suggesting procaine reactions are due to CNS procaine toxicity.

At present prevention is aimed at measures preventing inadvertent intravenous administration of APPG such as aspiration prior to injection. An alternative acceptable antibiotic can be used if a history suspicious of procaine reaction is elicited. Treatment of procaine reactions is supportive with reassurance, restraint, and observation. Oxygen is used as necessary.

Not all the reactions following APPG injections are penicillin allergy. Procaine reaction should be considered as treatment differs.