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DISCUSSIONS

CLARKE: Can you suggest any practical way under racing conditions for distinguishing between procaine and procaine penicillin? Obviously you cannot take a series of blood samples from a horse actually racing.

TOBIN: No, I know no way on a single sample.

BLAKE: It depends on how soon, following the administration of procaine penicillin, it is tested. We do have an electron capture method for penicillin G. and if procaine is present, we have to assume it was given as procaine penicillin, but the only realistic way is to take multiple blood samples, not realistic on a racetrack.

TOBIN: If Blake finds a positive he would ask for another sample from that horse immediately. If it was procaine penicillin we would still expect to find it in the plasma, if it was procaine HCl it should be undetectable.

MAYNARD: There are preparations which contain both procaine hydrochloride and procaine penicillin.

TOBIN: What is the procaine HCl in the preparation for? It would seem to be pharmacologically unnecessary.

ROBSON: The chief use of procaine in humans is that penicillin salts by themselves cause local pain that may be present for a period of several hours, and procaine was introduced as a local anaesthetic to prevent the injection mass being painful.

TOBIN: I understood the reason is to delay absorption.

JAGGARD: Have you done any work yet with azomycin? We have found that it will stay in the horse's urine for 3 to 4 days possibly because of buffers, lecithin and other ingredients in the formulation.

TOBIN: We find procaine penicillin, after intramuscular injection, in the urine for 2 weeks under experimental conditions.

MAYNARD: In British Columbia, they also extracted some degradation products of penicillin which were picked up on the GC mass spectrometer. They are investigating it at present.

TOBIN: Model 2 assumes a single site from which absorbtion of an intra-muscular injection occurs and there is a discrepancy. We can only account for about half the drug absorbed and we assume a single first order rate of absorption.

DEBACKERE: Is it a question of protein-binding?

TOBIN: I see no reason if it is a simple question of protein binding why the simple model should fit subcutaneous but not fit intramuscular administration, it is an event subsequent to absorption, protein-binding occurring in the central compartment. We have to assume binding in the tissue of some sort, this seems to be practised by the drug right through. The calculated half-life is a little slower than we observed for subcutaneous administration, the same, however, was much more marked for intramuscular and the same applied to procaine penicillin and intra-articular injections. There are also discrepancies between the urinary levels and the plasma levels. Some sort of binding seems to be a constant characteristic of the kinetics of this drug.

DEAN: Following a normal therapeutic dose of procaine penicillin injection, for how long could an anlytical chemist detect it in the urine?

TOBIN: It would depend on the analytical chemist! We reckon to find the drug for 2 weeks.

BLAKE: The GC derivative method that Tobin was referring to, detects about 1 to 2 picograms injected on the column, depending upon how large blank is.

LAMBERT: With the routine method used in Ireland, we are finding procaine penicillin after about 40 hours, but we wouldn't go on looking for it for 2 weeks.

JAGGARD: We cannot find procaine HCl after 24 hours by our routine procedure. With procaine penicillin we find it for maybe 48 hours, with azomycin, we cand find it for 3 or 4 days but that is our limit.

EXCRETION AND METABOLISM OF NIKETHAMIDE IN THE HORSE

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ABSTRACT

It is well known that nikethamide (N,N-diethylnicotinamide, Coramine^{R}) is metabolized very rapidly to nicotinamide. Hence, there is difficulty in proving that nikethamide has been used as a doping substance because nicotinamide is a normal physiological metabolite in the organism as well as a vitamin preparation. However, an intermediate metabolite (N-ethylnicotinamide) was found by us in the urine of horses treated with Coramine^{R}. This was characterized by gas chromatography/mass spectrometry, and synthesized and identified as being N-ethylnicotinamide.

The excretion and metabolism of nikethamide after intramuscular injection in the horse was followed using quantitative gas chromatography of urinary extracts over a period of several hours and the results of these experiments are reported.

Changes in urinary pH had no significant effect upon either the metabolism or rate of excretion of the drug.

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