despite rapid renal clearance of the drug, the overall rate of elimination suggests that a substantial proportion of the injected dose leaves the body by alternative pathways.

The factor limiting the natriuretic effect of bumetanide in normal subjects appears to be the renal response rather than the availability of the compound at its site of action.

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Atropine sulphate absorption from an intramuscular injection of a mixture of the oxime, P2S, and atropine in exercising humans

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The accepted therapy for poisoning by some anticholinesterase compounds is atropine and pralidoxime mesylate (P2S). Holland & White (1971) have already shown that the absorption of atropine from an intramuscular injection was not significantly affected by mixing it with P2S. The subjects of their investigation were, however, at rest, whereas, in practical circumstances it is most likely that the therapeutic mixture would have to be injected in men undertaking heavy physical activity. The present study was, therefore, conducted with men exercising on a bicycle ergometer. The investigation was arranged to disclose the effects of atropine uptake on heart rate, rectal and epigastric skin temperature, and sweat loss in the following experimental conditions for each of nine healthy male volunteers following a set work/rest routine of 150 min:

(a) control i.e. no injection;
(b) 2·0 mg atropine in 2·5 ml water for injection B.P.;
(c) 750 mg P2S mixed with 2·0 mg atropine;
(d) 750 mg P2S in 2·5 ml water for injection B.P.

The work component of the routine was such that men attained heart rates between 110–130 beats/min in the control condition and was determined during the training period. The injection was given either into the buttock (5 men) or the outer thigh (4 men). At least four days separated any two tests with any one subject.

Tests were held in a room with an air temperature of 25° C and a relative humidity 65–75%. The men wore shorts, pants, socks and army boots.

No significant differences were found between the data obtained from the men following injections of either the atropine alone or the atropine/P2S mixture. Both sets of data were higher than the corresponding control values, becoming significant at 10 min post-injection for the heart rate ($P<0·02$), 32 min for skin temperature ($P<0·05$), and 60 min for rectal temperature ($P<0·01$). Maximum mean heart rates were 164 beats/min compared to the 122 in the control tests.

The mean total sweat loss of 620 ± 156 g (mean $\pm$ S.E.) following atropine alone, and 648 ± 170 g following atropine/P2S were not significantly different; both were, however, significantly less than the value of 992 ± 246 g obtained in the control tests ($P<0·01$).

Time to maximal effect on heart rate is difficult to measure as other factors, such as changes in body temperature, also influence the rate. Examination of the change in heart rate increase would suggest that this may occur 40 to 50 min after the injection.

All men experienced a dry mouth between 10 and 25 min following either injection. This symptom had almost disappeared by 130 min.

One man complained of fatigue for a short time 70 min after both injections.

The data for P2S alone were the same as that for the control. Its rate of absorption was not altered by mixing it with atropine.

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