

morphine with the same order of potency as did reserpine. This shortening of reaction time may well be another manifestation of 'stimulant' effects of reserpine, reflected as a lowering of electroshock threshold(7) and prolongation of rhinencephalic seizures(8) and would suggest that neither SU-5171 nor syrosingopine have these properties to the degree that reserpine does.

That syrosingopine, with a potency of 1/20 that of reserpine in causing sedation, produces the same degree of antagonism to morphine analgesia, rules out the possibility that the sedative effect *per se* is a causal factor in producing this phenomenon.

*Summary.* The sedative properties of reserpine or esters or reserpine seems to bear no relationship to ability of these compounds to antagonize morphine analgesia since one such agent (syrosingopine) possesses 1/20

the sedative properties of reserpine yet is equally potent in its ability to antagonize morphine analgesia.

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### Effect of Molybdenum on Fluoride Retention in the Rat.\* (24948)

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Adler(1) has shown that 0.1  $\mu\text{g}$  Mo/ml (as ammonium molybdenate) reduces the incidence of dental caries in the rat. His studies were prompted by the observation that 2 communities in Hungary had low dental caries rates and low fluoride levels, thus suggesting that low caries incidence was not the result of fluoride in water. Spectrographic analysis of these waters showed that molybdenum was present in excess of that found in similar communities in which the incidence of dental caries was higher. Since these data have considerable practical importance it was of interest to learn more about the relationship between skeletal retention of fluoride in presence of molybdenum.

*Methods.* 24 weanling Sprague-Dawley strain rats, bred and raised in our laboratory, were divided into 4 groups according to initial body weight. Group 1 received fluoride-low

drinking water ( $\text{F} = 0.01 \mu\text{g}/\text{ml}$ ) *ad lib*. Group 2 received 50  $\mu\text{g}/\text{ml}$  Mo (as  $\text{NH}_4)_6\text{Mo}_7\text{O}_{24} \cdot 4\text{H}_2\text{O}$ ) in drinking water. Group 3 received 50  $\mu\text{g}/\text{ml}$  F (as NaF) in drinking water, and group 4 received Mo and F at same concentration as animals in Groups 2 and 3. All animals received the same fluoride low stock corn diet ( $\text{F} = 0.5 \mu\text{g}/\text{g}$ ). Animals were housed individually in raised screen cages in temperature controlled room. After 30 days the animals were sacrificed, the femur removed from each animal and the carcass prepared for fluoride analysis by methods previously described(2).

*Results.* The data obtained are in Table I. During the 30 day experimental period animals receiving fluoride-low drinking water and 50 ppm Mo gained on the average of 87 g. Those which received 50 ppm F gained less weight (70 g), but those receiving both Mo and F gained (98 g). No animals died during experimental period.

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TABLE I. Effect of Molybdenum on Fluoride Retention in the Rat.

| Group              | Mean wt gain (g) | Carcass fluoride |                    | Femur fluoride   |                    |
|--------------------|------------------|------------------|--------------------|------------------|--------------------|
|                    |                  | Total ( $\mu$ g) | Cone. ( $\mu$ g/g) | Total ( $\mu$ g) | Cone. ( $\mu$ g/g) |
| Control            | 87               | 145 $\pm$ 21     | 26.4 $\pm$ 3.1     | 6.37 $\pm$ 1.03  | 35.5 $\pm$ 5.9     |
| 50 ppm Mo          | 87               | 212 $\pm$ 12     | 39.9 $\pm$ 3.7     | 15.37 $\pm$ 1.48 | 88.3 $\pm$ 7.0     |
| 50 " F             | 70               | 8200 $\pm$ 550   | 1640 $\pm$ 65      | 392 $\pm$ 23     | 2340 $\pm$ 165     |
| 50 " Mo + 50 ppm F | 98               | 9820 $\pm$ 390   | 1830 $\pm$ 66      | 464 $\pm$ 24     | 2560 $\pm$ 115     |

Values include stand. dev.

When the carcass was used to evaluate fluoride retention, 145  $\mu$ g of F was present in control animals, while animals receiving 50 ppm Mo had 212  $\mu$ g of F. When animals received 50 ppm F, 8200  $\mu$ g of F was found in the carcass, and when both Mo and F was fed 9820  $\mu$ g was found. Similar ratios are evident when the femur is used as index of skeletal fluoride retention.

*Discussion.* The presence of Mo seems definitely associated with increasing retention of fluoride in the rat. This is demonstrated by 2 types of evidence. (1) It increases retention by apparently increasing availability of both fluoride present, as a constituent of the diet and also that small fraction present in drinking water; and (2), it increases retention of that available fluoride added directly to drinking water as sodium fluoride. When total fluoride in the carcass is used to evaluate fluoride retention, a 32% increase is

found when 50 ppm Mo is added to low-fluoride drinking water as compared to group receiving no Mo. When both Mo and F are added to drinking water there is approximately 17% more fluoride in the carcass than when only F is present. Both of these differences have probabilities in excess of 0.01. These data suggest that one of the functions of Mo is to increase the availability of the fluoride ion.

*Conclusions.* The presence of 50 ppm Mo as ammonium molybdenate is associated with significantly more fluoride retention in skeletal and carcass of the rat, than when Mo is absent from drinking water. These data suggest that Mo may act metabolically to increase availability of fluoride ion.

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## Spatial Summation of Pain. (24949)

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An old textbook concept, probably largely based on Hardy's work(1) maintains that pain does not show spatial summation. Recently however, Green(2) has shown that pain summation occurs for small areas at pain threshold. The present investigation is an attempt to resolve this problem. The approach used is crude. However it allows a comparative evaluation over a wide range of experimental conditions, practically impossible to

obtain with more refined technics. A constant heat stimulus was applied and the elapsed time determined until the subject reported the first pricking pain (threshold). Then the size of the stimulation area was changed and threshold time was again determined. This was done for 3 different sizes of stimulation area. The entire procedure was repeated with the subject reporting the maximum bearable pain (supra-threshold pain). All the above procedures were then repeated for 2 other levels of heat stimulation. The heat stimulus

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