nitrogen-free preparation of dextran kindly furnished by Prof. H. Hibbert of McGill University.[4]

That adsorption to inorganic particles may increase the activity of poor antigens was shown in immunization experiments with albumose preparations.[5] Rabbits were injected with a fraction consisting largely of heteroalbumose resulting from peptic digestion of coagulated sheep serum and fractionation with alcohol. Three batches of 5 animals received repeated intraperitoneal injections of 25 mg. each of the preparation, one group receiving the substance without admixture, and the 2 others the same quantity mixed with charcoal and aluminum hydroxide respectively. Whereas in the first batch only one rabbit produced a weakly precipitating antiserum the injection of the material adsorbed either to charcoal or aluminum hydroxide was followed by the appearance of distinctly active precipitins in most of the animals.

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Enhanced Action of Morphine in Experimental Nephrosis after Oral Ingestion of Magnesium Sulphate.

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We have shown[1, 2, 3] that the oral administration of magnesium sulphate raises the plasma magnesium of animals and men with damaged kidneys, but not that of normal individuals.

In view of the old-time clinical teaching that one should exercise caution in the administration of morphine to severe nephritics and to old persons, we have tested the effects of morphine sulphate injections on rabbits whose kidneys were injured by the subcutaneous administration of 10 mg. $HgCl_2$/K. The plasma magnesium of these animals ranged from 1.89 to 2.17 mg. Mg. per 100 cc. and rose

[4] *c. f.* Zozaya, J., *J. Exp. Med.*, 1932, **55**, 325; 1933, **57**, 21.

[5] Landsteiner, K., and van der Scheer, J., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 983.

[1] Hirschfelder, A. D., and Serles, E. R., *J. Clin. Invest.*, 1932, **11**, 841.

[2] Hirschfelder, A. D., and Serles, E. R., *J. Pharmacol. and Exp. Therap.*, 1932, **45**, 264.

[3] Hirschfelder, A. D., (with the technical assistance of V. G. Haury), PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 996.

to 6.90 to 8.98 mg. Mg. Two hours after the oral administration of 2 gm. per kg. $MgSO_4$, $7H_2O$, 30 mg. morphine sulphate per kilo was administered subcutaneously to 8 of these nephrotic rabbits. In 3 of these narcosis lasted 9 to 11 hours (av. 9⅔ hours) and 5 animals died in deep narcosis in ½ to 5 hours after the injection. The 4 control animals receiving the same dose recovered from the narcosis after 3 to 4 hours. The narcosis of the controls was less intense than that of the nephrotic animals.

These results indicate that animals, whose plasma magnesium is only moderately elevated (7.0 to 8.70 mg. per 100 cc.) (as in the case in nephrotic patients who have received a single purgative oral dose of Epsom salts), are much more sensitive to morphine than are normal animals. These results are in striking contrast to the results obtained by MacKay and MacKay,[4] who found that "uraemic" (nephrectomized) rats are less sensitive to morphine than are normal rats. The level of the plasma magnesium is most probably the determining factor.

It is therefore evident that morphine should be administered only with the greatest caution to nephritic patients who have received Epsom salts as a purgative. From the results reported with barbitals in the paper to follow it is probable that the same should apply to nephritic patients who have received barbital or phenobarbital.*

[4] MacKay, E. M., and MacKay, L. L., *J. Pharmacol. and Exp. Therap.*, 1930, **40**, 207.

* This is the more probable because Barbour and Taylor[5] have shown that the administration of $MgCl_2$ subcutaneously increases the rapidity and intensity of barbital narcosis. Although in the doses used by them in normal animals the magnesium salt shortened the duration of narcosis and decreased the toxicity of the barbital it is probable that these latter effects would be somewhat different in nephritic patients where the magnesium could be excreted very slowly.

[5] Barbour, H. G., and Taylor W. F., *J. Pharmacol. and Exp. Therap.*, 1931, **42**, 321.