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Resistance to Morphine in Experimental Uremia.

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It is a common clinical observation that uremic individuals often tolerate very large amounts of morphine even in an initial dose. An increased resistance to morphine is also present in experimental uremia.

About 70 hours after being doubly nephrectomized, uremic rats become rigid, shiver, the body temperature drops and they soon die. Sixty hours after the operation they are lively, and, as a rule indistinguishable from their controls. At this time uremic rats show a much greater tolerance for morphine than controls which have undergone identical treatment except for the removal of the kidneys. Subcutaneously the minimum lethal dose for the uremic rats was increased 40 to 100 per cent over their controls. Several of the uremic rats recovered, after 2.0 mgm. morphine sulphate per gram body weight. The increased tolerance was evident whether the morphine was administered subcutaneously, intraperitoneally, intravenously, or by stomach tube.

A relation of the increased morphine tolerance to the adrenal cortex hypertrophy in uremic rats is suggested. Many findings point to a connection between non-specific resistance and the adrenal cortex. In so far as morphine is concerned, we have been able to confirm the observations of Lewis¹ and Scott² that tolerance to morphine is decreased following double adrenalectomy. In addition we have found that the adrenal cortex hypertrophies when a rat is given increasing doses of morphine. The hypertrophy is greater the larger the tolerance attained.

¹ Lewis, J. T., *Am. J. Physiol.*, 1923, lxiv, 506.

² Scott, W. J. M., *J. Exp. Med.*, 1923, xxxviii, 543.