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Tho elimination and toxicity of caffein in nephrectomized rabbits.

By **W. SALANT** and **J. B. RIEGER.**

[*Presented by permission of the Secretary of Agriculture.*]

In experiments on the elimination of caffein in rabbits and guinea pigs carried out by the writers[1] in this laboratory recently it was found that much larger amounts of caffein were recovered from the gastro-intestinal canal when these animals were fed oats than when carrots were given. Since greater quantities of urine are secreted on a diet of carrots than on one of oats, it seemed probable that the excretory function of the gastro-intestinal canal might be stimulated to greater activity in order to compensate for the diminished diuresis when oats were fed. The elimination of caffein into the gastro-intestinal canal after the removal of both kidneys ought to be greater, therefore, than in normal animals.

In experiments which were performed with caffein which was given subcutaneously to rabbits after double nephrectomy, the following results were obtained: The amounts recovered at the end of about 22 hours from the contents of the stomach and intestines varied between 7.7 per cent. and 11.78 per cent., which is two to three times greater than was found in normal rabbits, much larger amounts being present in the intestines than in the stomach. In one rabbit which died seven hours after caffein was injected subcutaneously, about $10\frac{1}{2}$ per cent. were recovered from the intestines and about half this amount was obtained from the contents of the stomach.

The total amount of caffein eliminated in nephrectomized rabbits in about 22 hours was approximately equal to that eliminated by the gastro-intestinal canal and kidneys combined of normal rabbits during an equal period of time, thus showing that the stomach and intestines acquire much greater power of elimination after the kidney is removed.

Observations were also made on the toxicity of caffein in nephrectomized rabbits. The results obtained showed that the resistance

[1] Bull. 157, Bur. of Chemistry.

is not less than in normal rabbits. In fact, it showed rather a tendency to greater resistance after the kidneys had been removed. Thus 100–150 milligrams of caffein per kilo failed to produce symptoms in nephrectomized rabbits. As was shown by the writers elsewhere,[1] 15 omilligrams per kilo injected subcutaneously into normal rabbits are usually toxic. A dose of 200 milligrams per kilo proved fatal to one rabbit, but two others survived with the manifestation of symptoms. It is interesting to recall in this connection that similar results were obtained several years ago by Meltzer and Salant[2] in experiments with strychnin in nephrectomized rabbits.

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A quantitative study of the pupil dilatation caused by adrenalin.

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In the normal rabbit, adrenalin given subcutaneously has no effect on the pupil; if given intravenously in fairly large doses there may be a dilatation lasting less than a minute. S. J. Meltzer and C. M. Auer have shown that after removal of a superior cervical sympathetic ganglion in rabbits, the pupil of the corresponding side dilates maximally upon the administration of adrenalin either subcutaneously, intravenously or by instillation. Their experiments were carried out from the qualitative point of view, that is, fairly large doses of adrenalin were used and a wide, long-lasting dilatation of the pupil on the gangliectomized side resulted.

I have recently made a quantitative study of the effects of intravenous injections of adrenalin on the pupil after removal of a superior cervical ganglion in rabbits. The object was to determine the minimal dose that will give a dilatation, and also the amount and duration of the dilatation produced by larger doses. The doses of adrenalin used per kilo animal, expressed in c.c. of the 1/1,000 commercial adrenalin solution, were 1/50, 1/30, 1/20, 1/10 and 2/10 c.c.

[1] Bull. 148, Bur. of Chemistry.

[2] *Jour. Exp. Med.*, 1901, Vol. 5, p. 643.