almost no contamination with other substances likely to interfere with the tests, it could be used directly for biological and colorimetric assays. The relative proportions of adrenalin and *nor*adrenalin were the same as in the crude extracts. For spleen and splenic nerves from cattle, the following ranges of figures may be regarded as representative.

Tissues (cattle)	*l*-adrenalin-HCl	*l*-arterenol-HCl	
Splenic nerves	0·2 – 0·5	10–20	μgm./gm.
Spleen	0·05–0·12	2–4	,,

U. S. v. Euler

Physiology Department,
Karolinska Institutet,
Stockholm.
Aug. 3.

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Alloxan Diabetes in Dogs with Renal Pedicles Clamped

Jiménez Díaz, Grande Covián and De Oya[1] have reported that in dogs in which the vessels of both kidneys were clamped, the intravenous injection of alloxan in doses of 80–100 mgm./kgm. failed to produce either the hyperglycæmia or uræmia observed in controls in which the clamping was omitted. They postulated that "contact between alloxan and the kidney is apparently necessary for the display of the full diabetogenic effect". However, diabetes was observed on injecting alloxan during clamping of both renal pedicles in rats[2,3] and rabbits[4]. Recently, Jiménez Díaz and Souto Candeira[5] postulated that "alloxan produces some kind of renal injury which accentuates diabetes. . . . In conclusion, the kidney is apparently not necessary for the production of alloxan diabetes, but renal injury produced by alloxan would contribute to accentuate it."

Experiments were performed on dogs anæsthetized with 'Nembutal' (33 mgm./kgm. intraperitoneally). Alloxan was injected intravenously (75 mgm./kgm.) in 25–45 sec. The fasting blood sugar-level was determined before and 24–48 hr. after the injection of alloxan. Some of the animals died before the end of 48 hr., so these have not been considered as valid. Out of fifteen controls thirteen developed diabetes after alloxan injection. The clamping of both renal pedicles followed by the alloxan injection had a clear protective effect since only two dogs out of eleven developed a full diabetic condition (see accompanying table).

Diabetes due to intravenous injection of alloxan (75 mgm./kgm.) in dogs anæsthetized with 'Nembutal' (33 mgm./kgm. intraperitoneally)

Procedure	Diabetic
Controls	13 out of 15
Renal pedicles clamped	2 ,, 11
Renal vessels clamped	3 ,, 8
Renal nerves clamped	2 ,, 9
Spleen vascular pedicle clamped	0 ,, 6
Renal denervation and clamping	1 ,, 7
Bilateral nephrectomy before alloxan	5 ,, 5
Bilateral nephrectomy 2–12 hr. after renal clamping and alloxan	7 ,, 11

When clamping was limited to the vessels (both renal arteries and veins), excluding nervous structures, only three out of eight dogs which were injected with alloxan developed diabetes. Likewise the clamping of both renal pedicles, excluding only the vessels, protected seven out of nine dogs so injected.

Alloxan injected immediately after denervation of both renal pedicles, leaving the renal arteries and veins intact (without clamping), also protected six out of seven dogs.

Alloxan injected after bilateral nephrectomy caused an intense diabetes in all of five dogs. The same result was observed in seven out of eleven dogs in which bilateral nephrectomy was performed 2–12 hr. after clamping and injecting alloxan.

Finally, after injecting the alloxan after clamping the vascular pedicle of the spleen and maintaining the vessels clamped for 15 min. after the injection, all of six dogs failed to develop diabetes.

These results confirm the observation that alloxan injection, immediately after clamping of both renal pedicles in the dog, fails to produce diabetes although microscopically lesions of variable degree in some β-cells of the islets have been found. The same protection has been produced: (*a*) by clamping either the renal vessels only or the nervous structures; (*b*) injecting the alloxan after denervation of both renal pedicles leaving intact the vessels; (*c*) injecting the alloxan after clamping the vascular pedicle of spleen.

Furthermore, the injection of alloxan after bilateral nephrectomy was followed by a full diabetic condition. Thus it seems that the presence of intact kidneys is not necessary in order to obtain diabetes after alloxan injection.

However, uræmia seems to increase the severity of alloxan diabetes, since when nephrectomy is performed 2–12 hr. after the alloxan injection in dogs with both renal pedicles clamped, diabetes developed in seven out of eleven dogs.

The results of these experiments suggest the possibility that some kind of vasomotor reflex in the pancreas can be elicited from the renal pedicles due to clamping, as was suggested by Gold[2]. In order to confirm this hypothesis, several experiments were carried out, injecting 3 c.c. of indian ink into the descending aorta, using a cardiac catheter introduced through the left carotid artery. The pancreas was removed 3 min. after the indian ink injection. The results were as follow: in four control dogs the pancreas showed a dark colour of variable intensity due to the indian ink injection; but in four dogs in which both renal pedicles were clamped immediately before the injection, the pancreas showed its normal colour or was just a little darker. Microscopical examination of the islets in the controls showed many capillary vessels with plenty of indian ink, while in the islet vessels of the clamped animals scarcely any indian ink was observed. These experiments seem to confirm the hypothesis suggested by Gold that a vaso-constrictor reflex in the pancreas can be elicited by the mechanical procedure of clamping, and thus prevents injected alloxan reaching the islets in sufficient concentration to produce destruction of β-cells and diabetes.

B. A. Houssay
C. Martínez

Instituto de Biología y Medicina Experimental,
Costa Rica 4185, Buenos Aires.
July 2.

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