nerve fibres; but this is probably the result of a numerical preponderance of fibres normally going to fast muscles. Thus the end result after simple transection of the sciatic is that the slow muscle acquires many of the characteristics of fast muscles; almost as much as after the relatively more complicated procedure of cross-innervation. Similar conclusions have been reached previously by Yellin¹⁴ studying the histochemical pattern of rat muscles.

Another interesting point arises from our experiments on caffeine contractures. It is currently thought that this drug acts chiefly on the sarcoplasmic reticulum¹⁵⁻¹⁷. It therefore seems that these internal membranes of a muscle are under the control of a neural influence, similar to that which regulates ACh-receptors residing on the surface of the muscle fibre.

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Renal Hypertension in Rabbits Immunized with Angiotensin

RENOVASCULAR hypertension in man and in experimental animals has been attributed to increased production of angiotensin. The exact role of the renin-angiotensin system has remained obscure, however, and whether angiotensin is of prime importance in the pathogenesis of renal hypertension has been doubted¹. We have attempted to produce hypertension in rabbits immunized with angiotensin.

Immunization was carried out by intramuscular injections of synthetic Asp (NH₂)-Val⁶-Angiotensin II (Ciba) (pure substance) coupled to human serum albumin every third week for 6 months, and subsequently throughout the experimental period. Carbodiimide condensation² was used for coupling. Hypertension was produced with a modification³ of Page's technique as previously outlined⁴. The left kidney was wrapped in silk soaked in turpentine, and the right kidney was removed 4 weeks later. Daily measurements of blood pressure in the central ear artery were made with a Grant-Rothschild capsule⁵. The rabbits were fed a standard laboratory diet.

Three immunized and three control rabbits had similar blood pressures, all values below 106 mm Hg, in the last 10 days before nephrectomy, as shown in Fig. 1. One of the immunized rabbits died 5 days after nephrectomy when the blood pressure had risen 29 mm Hg above the mean pressure of the 10 days before nephrectomy; the standard error of the pressure rise was 1.7 mm Hg. In

Fig. 1. Arterial blood pressure in three normal rabbits (---) and three rabbits immunized with angiotensin (—), before and after nephrectomy. Measurements were performed on the central ear artery. +, Rabbit died on the fifth day after nephrectomy.

the remaining rabbits, the blood pressure had risen to 140–160 mm Hg 10 days after nephrectomy.

The efficiency of immunization was evaluated by determining the ability of rabbit serum to neutralize the pressor response of rats to angiotensin injected intravenously, by its ability to bind ¹²⁵I-labelled angiotensin, and by intravenously injecting the rabbits with angiotensin, renin and noradrenaline. In the neutralization test, 1 ml. of serum from any immunized rabbit bound at least 3,000 ng of angiotensin, and in the radio-immuno test 1 ml. of a dilution 1 : 8,000 of antiserum bound 90 per cent of 100 pg labelled angiotensin. Sera from non-immunized rabbits were inactive in control experiments.

Intravenous injections of 1 µg angiotensin II (Hypertensin Ciba) per kg body weight caused pressor responses of 55–65 mm Hg in the non-immunized rabbits, whereas the blood pressure remained unchanged in the immunized animals. To test the antibody specificity against the rabbits' own angiotensin, 2.5 Goldblatt units of hog renin (Nutritional Biochemicals Corporation) was injected. Renin gave 30–40 mm Hg blood pressure rises in control rabbits, but had no effect in the immunized animals. By comparison, noradrenaline (2 µg/kg intravenous) produced about equal pressor responses in both groups. The *in vitro* and *in vivo* tests were carried out both before and after the rabbits had developed renal hypertension.

From these experiments, it is evident that immunization with synthetic angiotensin II led to production of anti-angiotensin antibodies which also reacted with the homologous angiotensin. The pressure recordings indicate that arterial hypertension as a result of renal compression may develop in immunized rabbits in which angiotensin has no effect on blood pressure.

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