

or from the femoral vein under light ether anesthesia, in the chick directly from a wing vein into a fine glass capillary tube and in the dog by cardiac or venous puncture. Coagulation time was determined by breaking the capillary tube and confirmed with a drop of blood on a glass plate. Determinations were made on individual animals before injection and at 6 and 24 hours afterward, then daily for several days.

Five to 7 days after bile duct ligation the average clotting time in 30 old male rats weighing 300 grams or more was elevated to 10 minutes. Young male rats weighing 100 to 200 gms did not develop this hemorrhagic deficiency to the same extent, the average clotting time in 30 animals being only 3 minutes in from 6 to 12 days after the operation. Average results after injection of 60 and 70 mgm of the crude sterol extract and 15 mgm of the fraction which was not precipitated by digitonin are shown in the table. Reduction of the clotting time to a normal level occurred within 6 hours and persisted for 24 to 48 hours. Pure cholesterol and cholesterol recrystallized after digitonin precipitation exerted little if any effect as compared to the sesame oil controls. In smaller amounts, 14 to 20 mgms, the crude extract was less effective. Female rats were found to develop the hemorrhagic tendency after bile duct ligation more slowly than the males, showing an average clotting time of 3½ minutes in 6 to 8 days post-operative and 9 minutes in 14 to 22 days. Their response to injection of the various extracts was essentially negative.

TABLE 1

EFFECT OF INJECTED LIVER EXTRACTS ON THE BLOOD CLOTTING TIME (IN MINUTES) OF JAUNDICED RATS AND VITAMIN K DEFICIENT CHICKS

Material injected	Mgm injected	Subject	No. averaged	Hours after injection		
				0	6	24
Pig liver extr. ....	60	Old rat	5	7	2	3
Non-dig. ppt. fract. .	15	" "	2	6	2.5	
Cholesterol .....	10-25	" "	3	13	8	12
Pig liver extr. ....	70	Young rat	4	4	2.3	3
Cholesterol .....	25	" "	3	2.7	2.6	3
Lamb liver extr. ....	20	Chick	8	20	8	3.5
Pig liver extr. ....	24-60	" "	6	14	5	4
Non-dig. ppt. fract. .	15	" "	5	15	8	5
Dig. ppt. fract. ....		" "	2	14	3	6
Cholesterol .....	25	" "	8	7	6	4

Subcutaneous injection also was effective in chicks on a vitamin K deficient diet. The average clotting time was 17 minutes for 36 chicks when 14 to 18 days old. After injection of 20 to 60 mgm of the active extract or 15 mgm of the non-digitonin precipitable fraction this was markedly reduced within 6 hours and was decreased further at 24 hours. The effect persisted for several days in some chicks, in others the clotting time increased again after the third day. The small amount of material precipitated by digitonin treatment was very active when tried in 2 chicks, whereas pure cholesterol in 25 mgm doses caused only

a slight diminution in the clotting time. We are indebted to Dr. Robert Moore, of the Department of Pathology, for determining that the average prothrombin time was lowered from 10 min. in the controls to 3 min. in the chicks injected with the liver extract.

Normal male rats in a few experiments showed about a 50 per cent. fall in clotting time after administering 15 mgm of the crude extract subcutaneously. In three female dogs, one of which was jaundiced from bile duct ligation, a single intravenous injection of 10 or 15 mgm in lecithin emulsion produced a similar reaction. The clotting time remained at this low level for 48 hours and then gradually increased again. The effect of the intravenous injection was not directly on the blood, since the addition of the extract to freshly drawn dog blood *in vitro* tended to prolong rather than to reduce the coagulation time.

These results indicate that the liver contains a sterol which is active in reducing the blood clotting time of normal and jaundiced dogs and rats. A single intravenous or subcutaneous injection maintains this effect for several days. The extract is similar in action to vitamin K in that it will correct the hemorrhagic tendency in vitamin K deficient chicks when injected subcutaneously. Its sterol nature and resistance to alkali differ from the properties described for vitamin K.<sup>7</sup>

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### THE BLOOD VESSELS IN THE CENTRAL NERVOUS SYSTEM OF THE KANGAROO

WISLOCKI and Campbell<sup>1</sup> have recently demonstrated that in the opossum the tissue of the central nervous system is not vascularized by a continuous spongy reticulum of capillaries such as exists in the brains of other mammals, so far as known. Instead, it is supplied by vessels which run in very closely associated pairs, arterial and venous, each member of the pair branching when the other does, and the branches ending as simple loops without any anastomosis. Such an arrangement had formerly been known only in certain lizards (Schöbl<sup>2</sup> and Sterzi<sup>3</sup>) and, in much simpler form, in tailed amphibians (Schöbl,<sup>4</sup> Sterzi<sup>3</sup> and Craigie).<sup>5</sup>

The phylogenetic relationship of the non-anastomosing capillary loops and the freely anastomosing capil-

<sup>7</sup> See references 4, 5 and 6.

<sup>1</sup> G. B. Wislocki and A. C. P. Campbell, *Anat. Rec.*, 67: 177-191, 1937.

<sup>2</sup> J. Schöbl, *Arch. f. mikr. Anat.*, 15: 60-64, 1878.

<sup>3</sup> G. Sterzi, *Anat. Hefte*, I Abt., 24: 1-364, 1904.

<sup>4</sup> J. Schöbl, *Arch. f. mikr. Anat.*, 20: 87-92, 1882.

<sup>5</sup> E. Horne Craigie, *Proc. Amer. Phil. Soc.*, 78: 615-649, 1938.

lary network is a problem of much interest, and the discovery of Wislocki and Campbell at once raises the question whether or not the condition in the opossum is one characteristic of marsupials in general and of monotremes. It is to be hoped that the matter will soon be investigated where such animals are freely available.

Meanwhile it has been possible to examine sections of the cerebellar cortex and of the cervical region of the spinal cord of a specimen of *Macropus bennetti*. The specimen had been in formalin for some years, so that injection methods were not applicable, but a variety of stains were tried, of which that of Perdrau yielded

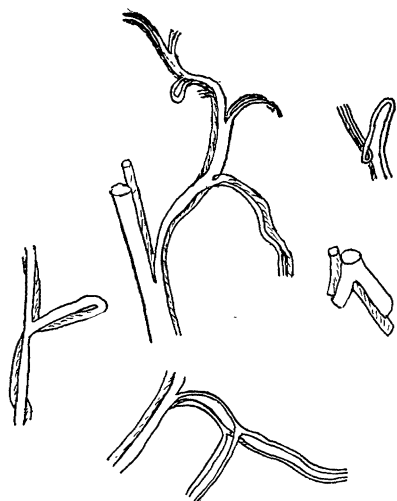


FIG. 1. Drawings of vessels in a section 150 micra thick of the spinal cord of *Macropus bennetti*, stained by the method of Perdrau.

the most useful, though not very good, preparations. These show clearly that the disposition of the vessels in the tissues examined is largely, and probably entirely, the same as that in the opossum. The vessels run in closely associated pairs, the one member usually noticeably larger than the other. Each member of a pair branches when the other does. The branches end in simple loops and there is no evidence of anastomosis. Thus it appears probable that the central nervous system of the kangaroo is like that of the opossum in being vascularized entirely by much branched, but strictly non-anastomosing, looped blood vessels. The fact that the two marsupials examined, representing different superfamilies and different geographical areas, both show this character suggests the likelihood that it is a feature of the Metatheria in general.

Scharrer<sup>6</sup> has emphasized the end-arterial character of the arteries entering the brain-substance of the opossum, but has pointed out that the branches of adjacent pairs of vessels interlace in such a fashion that any given mass of tissue is supplied by branches

<sup>6</sup> E. Scharrer, *Zeits. f. d. ges. Neurol. u. Psychiatrie*, 162: 401-410, 1938.

from several of them. The close association between the two members of a pair throughout their length does not appear to have been discussed, however. Mossman<sup>7</sup> has shown that in the placenta of the rabbit the maternal and foetal vessels run parallel to each other in opposite directions, so that as fetal blood runs through the placental capillaries it comes into association with maternal blood of increasing purity and may be in approximate equilibrium with the arterial blood of the mother when it reaches the umbilical vein. It seems possible that a somewhat analogous situation exists in the central nervous system which is vascularized by capillary loops. A spongy reticulum permits a more or less free distribution of blood in all directions through the tissues, but when the supply is entirely by closed, non-anastomosing loops, the venous limb of each loop would tend to carry less oxygen and nutriment and more waste products than the arterial limb. If the limbs were spread widely apart, the tissue immediately surrounding each venous limb would thus be supplied with blood poorer than that supplying the tissue surrounding each arterial limb. The two limbs being so closely associated as they are, however, the blood flowing along the venous limb and tending to decrease in purity is associated with blood of increasingly arterial character in the arterial limb. Thus a relatively uniform condition of the blood throughout the capillary loop may be maintained and every part of the tissue through which the loop passes is more likely to have an adequate supply. Such an arrangement would be of obvious value in the salamander brain, where the loops are simple and there is no extensive interlacing of branches, and would doubtless be equally important in the nervous system of the warm-blooded animal, with its greater metabolic requirements.

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<sup>7</sup> H. W. Mossman, *Am. Jour. Anat.*, 37: 433-497, 1926.

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