might be the natural factor which, in hemorrhage, induces the damage of both the cortical circulation and of the glomerular function. The mechanism assumed is a functional disturbance of the thick segment of the ascending limb in the loop of Henle.

We must emphasize that medullary circulation in rats is more active than in other species[6,16].

Zusammenfassung. Es wird eine durch Blutung und hämorrhagischen Schock hervorgerufene intrarenale Neuverteilung der Durchblutung beschrieben. Der wesentliche Effekt ist eine verminderte Blutversorgung der äussern Markzone.

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Nephrectomy and Anaphylactoid Edema

It is known that certain organs play an important role in the formation of anaphylactoid edema (AE). Removal of the adrenals increases[1] while both exclusion of the insular apparatus[2] and hypophysectomy[3,4] prevent the development of the AE. On the basis of our earlier experiments we assumed that the kidneys may participate in the genesis of the AE. Therefore, in the present experiments we wanted to examine whether the AE can be influenced by nephrectomy in rats.

The experiments were carried out on female albino rats of the same strain weighing 150–165 g. Local and generalized AE were induced: by subplantar injection of dextran (900 μg Intradex in 0.1 ml), by i.p. administration of dextran (120 mg/kg body weight) and of egg white (25% in physiological saline given in a dose of 1 ml/100 g body weight). The changes of the volumina of the hind paws were measured by a method using displacement of mercury 90 and 120 min following the application of the edema-producing agents. The degree of inhibition produced by the manipulations was expressed as % of the control value. Nephrectomy and the sham operation were carried out in hexobarbital-Na anaesthesia (50 mg/kg body weight i.v.) 24 h before the experiments.

Nephrectomy inhibits, 24 h after removal of the kidneys, the edema-inducing effect of dextran given s.c. into the hind paws by 67%, while the sham operation only produces an 11% inhibition. Nephrectomy also inhibits to about the same extent (65%) the effect of compound 48/80 injected into the hind paws (25 μg in 0.1 ml), however, it does not influence the edema formation evoked by subplantar injection of 5-HT (serotonin-creatinine sulphate, 5 μg in 0.1 ml). Table I.

The generalized AE induced by dextran is suppressed by nephrectomy to an extent of 71% and in the case of the administration of egg white the inhibition is 77% as compared with the control values. The sham operation causes only a moderate inhibition (14%) of the dextran induced generalized AE (Table II).

Insulin increases in normal animals[5] and restores in diabetic rats[2] the effect of agents inducing AE. In our experiments insulin (4 IU s.c.; 10 times crystallized, glucagon-free, Novo[6] administered simultaneously with dextran counteracts the inhibiting effect of nephrectomy. In the insulin-treated animals, bilateral nephrectomy results in a 38% inhibition of the generalized AE only (see Table II).

The fasting blood sugar levels and the blood pressures measured in nembutal anaesthesia do not differ in nephrectomized animals from the control values. The blood urea nitrogen (BUN) is 103 $\pm$ 19 mg in 100 ml blood. Beside the elevation of the BUN there are no considerable changes in blood constituents 24 h following nephrectomy[7].

In addition, according to our preliminary observations, nephrectomy inhibits, to an extent of 85%, the formalin induced inflammation, too, while the sham operation increases the effect of formalin considerably (by 20%).

The mechanism of the AE is not yet cleared. A mediator role was attributed to histamine and 5-HT[8]. As the edema-

Table I. The volume of hind paws in ml before (A) and 90 min after (B) the local administration of edema producing agents

Treatment (No. of experiments)	Vol. of the hind paws in ml	Inhibition in % of control value	P
Dextran, control (20)	A 0.398 $\pm$ 0.006 B 0.665 $\pm$ 0.027	–	–
Dextran, sham operation (10)	A 0.383 $\pm$ 0.014 B 0.620 $\pm$ 0.018	11	$\cong 0.2$
Dextran, nephrectomy (10)	A 0.393 $\pm$ 0.004 B 0.485 $\pm$ 0.010	67	< 0.001
Compound 48/80, control (15)	A 0.410 $\pm$ 0.006 B 0.593 $\pm$ 0.027	–	–
Compound 48/80, nephrectomy (10)	A 0.398 $\pm$ 0.025 B 0.463 $\pm$ 0.042	65	< 0.001
5-HT, control (15)	A 0.396 $\pm$ 0.005 B 0.538 $\pm$ 0.050	–	–
5-HT, nephrectomy (10)	A 0.374 $\pm$ 0.018 B 0.504 $\pm$ 0.020	9	$0.5 > P > 0.2$

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Table II. The volume of hind paws in ml before (A) and 120 min after (B) i.p. administration of edema producing agents

Treatment (No. of experiments)	Vol. of the hind paws in ml	Inhibition in % of control value	P
Dextran, control (40)	A 0.408 ± 0.016 B 0.609 ± 0.046	–	–
Dextran, sham operation (20)	A 0.401 ± 0.016 B 0.574 ± 0.015	14	$\cong 0.05$
Dextran, nephrectomy (20)	A 0.402 ± 0.018 B 0.461 ± 0.051	71	< 0.001
Dextran, nephrectomy, insulin (20)	A 0.381 ± 0.018 B 0.506 ± 0.044	38	< 0.001[a]
Egg white, control (20)	A 0.394 ± 0.010 B 0.544 ± 0.060	–	–
Egg white nephrectomy (10)	A 0.382 ± 0.014 B 0.416 ± 0.023	77	< 0.001

[a] Compared with the nephrectomized group.

evoking effect of 5-HT remains nearly unaltered after nephrectomy, it may be supposed that the susceptibility of peripheral receptors to the mediator substances does not change. We suppose that the inhibition develops in an earlier phase of the edema-producing processes.

The elevation of the BUN probably does not play a role in the prevention of the AE, as shown in our experiments in which urea administered i.p. in a dose of 200 mg/kg body weight was not able to prevent the formation of AE.

Zusammenfassung. Nephrektomie hemmt bei Ratten die Ausbildung des lokalen sowie des generalisierten Anaphylaktoid-Ödems erheblich. Die Wirkung der lokal injizierten Substanz 48/80 wird ebenfalls gehemmt, während der Effekt des in die Pfote verabreichten Serotonins unverändert bleibt. Insulin antagonisiert den Hemmungseffekt der Nephrektomie.

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Inhibition of the Morphogenesis of the Otoliths in the Chick Embryo in the Presence of Carbonic Anhydrase Inhibitors

The otoliths in the chick are composed of calcium carbonate in the form of calcite[1] and of an organic matrix which is formed in large part of acid mucopolysaccharides[2,3] and of protein which does not have the classical collagen structure[4].

The otoliths begin to differentiate in the chick at about the fifth day of incubation. The mode in which their morphogenesis is actuated is still obscure. Autoradiographic observations[5] have revealed a precocius localization and an active turnover of ^{45}Ca at the level of the endolymphatic sac and of the pars inferior of the labyrinth which gives rise to the sacculus and the lagena.

This paper reports the results of experiments[6–9] conducted with sulphonamides which are specific inhibitors of carbonic anhydrase.

Material and methods. The following sulphonamides were used: acetazolamide (2-acetylamino-1, 3, 4-thiadiazole-5-sulphonamide), dichlorphenamide (1-3-disulphamyl-4-5 dichlorobenzene), ethoxyzolamide (6-ethoxybenzothiazole-2-sulphonamide) and neptazane (5-acetylimino-4-methyl-Δ^2-1, 3, 4-thiadiazoline-2-sulphonamide).

The sodium salt of acetazolamide and dichlorphenamide (lyophilized) were dissolved in double distilled water and physiological solution respectively, ethoxyzolamide and neptazane were dissolved in dimethylsulphoxide (Fluka). The controls were injected with double distilled water, physiological solution and dimethylsulphoxide. The experimental and control solutions were injected into the egg albumen on the fourth day of incubation (Lillie stage 23[10]), a stage at which the morphogenesis of the otoliths has not initiated, but which immediately preceeds the initiation of active turnover of ^{45}Ca at level of the membranous labyrinth.

According to CONTI and MILIO[11], 0.01 ml of the solutions were injected. The embryos were fixed at different stages during development in neutral formalin, the heads were embedded in paraffin and sections were treated with the PAS reaction or were stained with alcian-PAS[12].

Results. The results of the various experiments are reported in the Table. The doses indicated in the Table are those which did not have a high toxic action; the mortality was only a little higher than that reported for the controls by CONTI and MILIO[11].

An examination of the Table shows that the substances used cause an alteration in the otoliths only, in which morphogenesis is inhibited in most cases.

The macular ephithelium is normal as are the other structures of the membranous labyrinth (cristae, maculae,

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