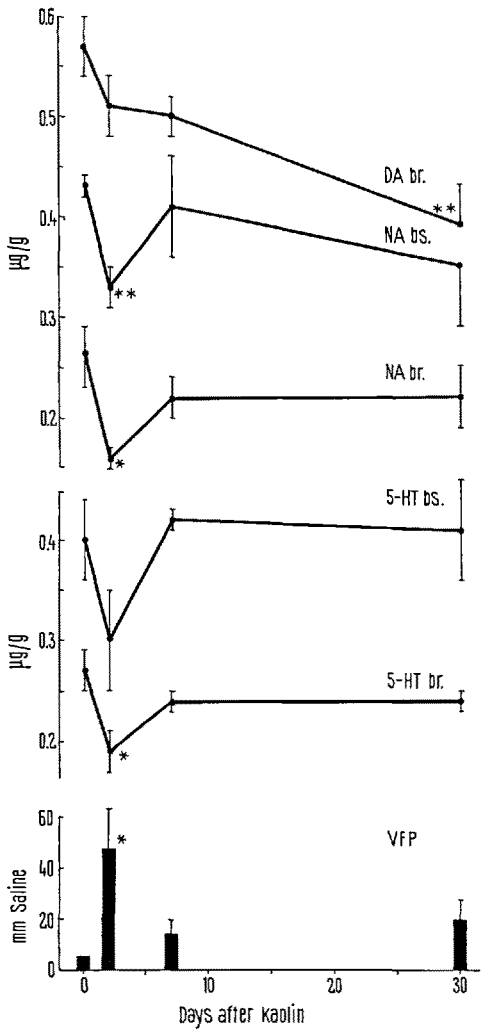

Relation between ventricular fluid pressure (VFP) and the concentrations of dopamine (DA), noradrenaline (NA), and 5-hydroxytryptamine (5-HT) in brain (br.) and brain stem (bs.) at various time-periods after intracisternal injection of kaolin. Mean ± S.E.M. Differences between injected animals and non-injected controls (time 0) according to Student's t-test: * $0.01 < p < 0.05$; ** $0.001 < p < 0.01$.

bolism known to occur in brain during intracranial hypertension[9,10]. The reduction in the amine concentrations may be the consequence of an impaired synthesis and/or an increased turnover and breakdown. The recent finding[11] that homovanillic acid is reduced in the brain during intracranial hypertension incidates that the observed reduction, at least in brain DA, is a consequence of an impaired synthesis. This supports the assumption that the increase in the level of acid amine metabolites found in the cerebrospinal fluid of kaolin-treated animals[12] and hydrocephalic patients[13] reflects a lowered absorption from the ventricular system.

The DA level in the brain showed a progressive fall after the kaolin injection, also when the VFP was normalizing, whereas the reduction in NA and 5-HT was only transient, accompanying the intracranial hypertension. The difference may be due to the different topography of the corresponding neuron systems: the majority of the DA terminals are present in the neostriatum bordering the lateral ventricles. This is consistent with the observations that the structural damage during hydrocephalic conditions affects the periventricular structures more than areas away from the ventricles[14–16].

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Electrolyte Transport in the Seminiferous Tubules of the Rat Studied by the Stopped-Flow Microperfusion Technique

Recently[1] micropuncture and catheterization techniques were used to collect fluid from the seminiferous tubules and rete testis of rats. Three fluids were collected and analyzed: 1. Rete testis fluid; 2. Free-flow fluid, i.e. the fluid which normally lies in the lumen of an undisturbed seminiferous tubule; and 3. Primary fluid, i.e. the fluid which is secreted by the seminiferous tubules after they have first been emptied of free-flow fluid by injection of oil. It was found that primary fluid was extremely rich in potassium (and probably bicarbonate), that rete testis fluid was rich in sodium and chloride and that free-flow fluid had an electrolyte composition intermediate between the other two secretions. To account for the difference between the composition of primary and free-flow fluids it was proposed that the seminiferous tubules secreted only a potassium-rich secretion (the primary fluid) which then mixed by an ebb and flow process with a sodium-rich rete testis secretion to produce an intratubular fluid of intermediate composition (the free-flow fluid).

To test this hypothesis, seminiferous tubules have now been studied by the stopped-flow microperfusion technique[2,3]. Oil was injected into the tubule over a length of 1–2 mm and perfusion fluid was injected into the column so as to split it into two. After a varying interval of time, the sample was re-aspirated for analysis. By this means, a sample of perfusion fluid can be held in contact with the tubule epithelium for any desired length of time without it becoming contaminated with free-flow fluid lying else-

where in the tubule lumen. 5 perfusion fluids were used in the present experiments: 1. Isotonic sodium chloride; 2. Isotonic potassium chloride; 3. Isotonic mannitol; 4. and 5. Fluids with electrolyte composition resembling those of free-flow and primary fluid, respectively. Perfusions were carried out with contact times of 5–120 min. By incorporating inulin-^{14}C into the perfusion fluids it was possible to calculate the net trans-tubular water and electrolyte fluxes at each contact time. When this was done it was found that net water and electrolyte secretion declined progressively as perfusate/duct contact time increased so that net water and electrolyte fluxes approached zero at contact times of 30–60 min. A similar cessation of tubule secretion has previously been noted during collection of primary fluid samples[1]. The explanation for this is almost certainly the resistance to flow along the tubules offered by the train of intratubular oil droplets. We find that during injection of oil into the tubules the resistance to flow of oil along the tubule lumen is initially slight but, after a short time, it increases so that pressures of more than 300 mm Hg may be required to drive the oil along the tubules. This resistance could be due in part to physical forces associated with moving oil droplets at low velocity along water-filled capillary tubes[4–6] and in part to a gathering up and impacting of spermatozoa at the leading face of the advancing oil column. Whatever its origin, this resistance could be expected to prevent net water influx into the tubule lumen and, as electrolyte concentrations approached equilibrium values, it could result in cessation of net electrolyte secretion.

Table I shows the changes in the electrolyte composition of each perfusion fluid after it had been in contact with the tubule cells for 90–120 min. In all perfusion fluids it was found that the electrolyte concentrations in the collected perfusate stabilized at values not resembling those of free-flow fluid nor yet those of secretion (as we had expected) but rather intermediate between those of primary.

We had proposed that the tubules secrete a potassium-rich primary secretion which mixed with a sodium-rich rete secretion to give rise to free-flow fluid. If our hypothesis had been correct we would have expected that, following prolonged contact with the tubule epithelium, the electrolyte composition of all 5 perfusion fluids would have changed to one resembling that of what we termed 'primary fluid'. On the other hand, if the potassium-rich 'primary secretion' which we collected had been an artifact and the true tubule secretion were free-flow fluid, then the various perfusion fluids which we injected should have been transformed into a fluid resembling free-flow fluid. In fact, however, the perfusion fluids were transformed into a solution with electrolyte concentrations intermediate in composition between those of 'primary' and 'free-flow' fluids. This can be seen clearly in Table II which shows the mean concentrations of sodium, potassium and chloride for all 5 perfusion fluids, taken together, following 90–120 min in contact with the tubule epithelium.

Since both the magnitude and the direction of net electrolyte fluxes differed greatly from one perfusion fluid to another, the relative constancy of the composition of the collected perfusate, whatever the composition of the initial perfusion fluid, speaks strongly against the changes being artifactual. Hence it is necessary to explain why microperfusion fluid did not come to resemble primary fluid following prolonged contact with the tubule epithelium.

The measurement of electrolyte flux rates at various contact times showed that equilibrium conditions prevailed by 30–60 min so it cannot be that the contact time of 90–120 min was insufficient for the transformation of the perfusion fluids to be complete. One possible explanation could be that the tubules are not homogeneous with respect to their electrolyte transport and permeability properties. This would not be surprizing since tubule cells are known to undergo striking morphological changes during the various phases of the spermatogenic cycle, and all phases of the cycle are present simultaneously in successive regions of the tubules, running in a spiral wave-pattern[7–9]. Thus, it could be, that, at one particular phase of the cycle (e.g. the phase of sperm release), the tubules elaborate a potassium-rich primary secretion and at intermediate phases they do not secrete. This would mean that the primary secretion would tend to re-equilibrate with plasma as it

Table I. Electrolyte composition of perfusion fluids before and after stopped-flow microperfusion for 90–120 min[a]

	Isotonic NaCl	Isotonic KCl	Isotonic mannitol	Free-flow fluid	Primary fluid
Sodium					
before	165 ± 1	7 ± 2	2 ± 2	105 ± 1	57 ± 2
after	72 ± 6	76 ± 9	61 ± 16	80 ± 11	66 ± 18
Potassium					
before	2 ± 1	163 ± 3	1 ± 1	50 ± 2	113 ± 3
after	80 ± 14	83 ± 11	95 ± 15	77 ± 14	89 ± 17
Chloride					
before	164 ± 2	163 ± 3	2 ± 1	123 ± 2	77 ± 2
after	84 ± 7	108 ± 13	82 ± 13	85 ± 8	76 ± 5

[a] Values are means in mEq/l ± the standard error of the mean. There were 5 samples in each group.

Table II. Mean electrolyte concentrations in collected perfusate from all 5 perfusion fluids taken together following 90–120 min in contact with the tubule epithelium

	Primary fluid	Collected perfusate	Free-flow fluid
Sodium	46 ± 5	71 ± 6	107 ± 5
Potassium	120 ± 6	85 ± 6	47 ± 7
Chloride	72 ± 2	87 ± 5	121 ± 6
No. of samples	14	26	17

[a] Values are means in mEq/l ± the standard error of the mean.

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flowed from its site of secretion to neighbouring non-secretory areas. Thus, when the tubule was filled with oil, the flow resistance of the oil columns would prevent the primary secretion from growing and spreading over onto neighbouring non-secretory areas so that a sample of pure primary secretion could be obtained. During microperfusion, however, where the length of the injected column of perfusion fluid was many times greater than the largest column of primary secretion which we have ever observed, the perfusion fluid could be expected to come into contact not only with areas where primary secretion was being formed but also with areas where re-equilibration with plasma could take place. The composition of collected perfusate would thus come to be intermediate between that of primary fluid and serum.

Under free-flow conditions, when no unphysiological hinderance to flow of fluid along the tubules would occur, there would be a continuous influx of water and electrolytes into the tubules and equilibrium conditions would not develop. Whether this fluid mixes with a sodium-rich rete secretion by ebb and flow, to give rise to free-flow fluid as we have previously postulated[1] remains an open question. What the present experiments make clear is that the seminiferous tubules do indeed secrete a 'primary' fluid which is richer in potassium and poorer in sodium than free-flow fluid, the secretion which normally lies in the undisturbed tubule. We are at present attempting to study formation of primary fluid further by continuous microperfusion in vitro of tubule segments.

Zusammenfassung. Mit Hilfe der «stopped-flow»-Mikroperfusionstechnik wurden am Samenkanälchen Elektrolyttransportprozesse untersucht. Es wurde gefunden, dass die Kanälchen ein kaliumreiches Primärsekret bilden. Dieses unterscheidet sich in seiner Zusammensetzung von dem Sekret, das man gewöhnlich unter ungestörten Fliessbedingungen findet.

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'Compensatory' Muscle Hypertrophy in the Rat Induced by Tenotomy of Synergistic Muscles

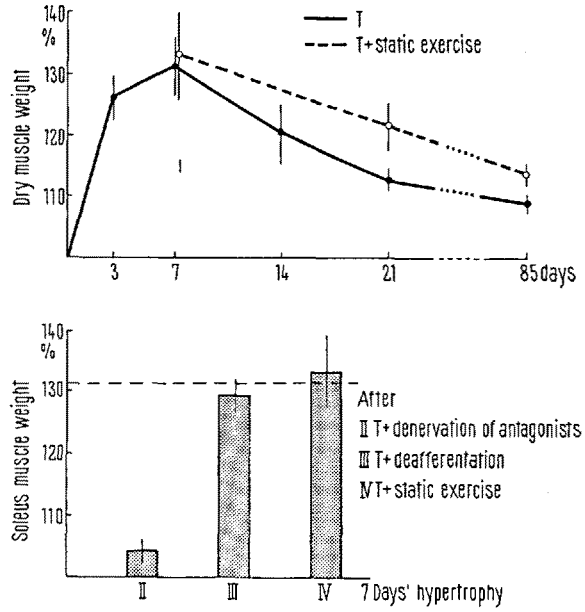
Several authors have described rapid hypertrophy of muscle following tenotomy[1] or denervation[2] of their synergists. Since the muscles undergoing hypertrophy could be expected to be under an increased functional load, compensatory hypertrophy seemed a reasonable term. However, it has recently been pointed out[3] that this particular type of hypertrophy is not apparently due to increased muscle activity, but rather to passive movements and mechanical tension of the hypertrophying muscles due to the action of their antagonists. The present report was intended to elucidate further the factors which are responsible for this type of hypertrophy.

In the 1st series of experiments (I) the tendon of the gastrocnemius muscle in 120–150 g male Wistar albino rats was sectioned under ether anaesthesia; a sham operation was performed on the contralateral side. Soleus muscles were excised 3, 7, 14, 21 or 85 days after the operation, respectively, weighed and then dessicated. The mean dry weight of the muscles on the operated side was expressed as percentage of the contralateral control.

In the 2nd series of experiments (II) tenotomy of the gastrocnemius was combined with section of the peroneal nerve which supplies the antagonistic muscle group. Tenotomy of the gastrocnemius was combined in the 3rd series of experiments with whole limb deafferentation (III) by ipsilateral section of L_1 – S_1 dorsal roots[4].

In the 4th series of experiments an attempt was made to increase muscle hypertrophy by an additional work load, either static or a combination of static and dynamic excercise (IV). Static training was achieved by making the experimental animal stand on a suspended wire ladder for 5 h a day starting on the day after tenotomy, while animals subjected to the combined training programme performed 85.5 h of static and 46 h of dynamic excercise by running on a tread-mill.

The maximum gain in weight in the soleus muscles was attained 7 days after tenotomy of the gastrocnemius (Figure 1, I). Thereafter, there was a relative loss of weight of the hypertrophied muscles, although their weight was still significantly higher than that of control muscles even after 85 days ($p < 0.001$). The initial rapid gain in weight is thus transient in character.



The time course and some factors affecting 'compensatory' muscle hypertrophy in the rat soleus after tenotomy of the gastrocnemius muscle. Above: I. dry muscle weight expressed as percentage of contralateral control (solid line), broken line indicates an analogous situation under additional static work load. Below: soleus muscle weight 7 days after tenotomy of the gastrocnemius and peroneal nerve section (II), limb deafferentation (III) and additional static work load (IV). Horizontal broken line represents soleus hypertrophy after 7 days (not combined with other procedures). Vertical bars denote standard error of the mean.