tumors the sponges were completely or partially embedded in the tumor. In 1 case the sponge lay completely outside, but on the periphery of, a large tumor weighing 209 g.

All tumors appeared to be fibrosarcomas (Figure 2). No metastases were found in any of the animals, but local invasion and infiltration of adjacent tissues were evident in all. Attempts to transmit tumors to normal rats were made by injecting tumor cell suspensions subcutaneously and intraperitoneally. Out of 34 subcutaneous and 10 intraperitoneal injections only 1 'take' occurred. An intra-abdominal tumor became noticeable about 5 months after 1 of the intraperitoneal injections. About 2 weeks later this rat died with a tumor weighing 341 g.

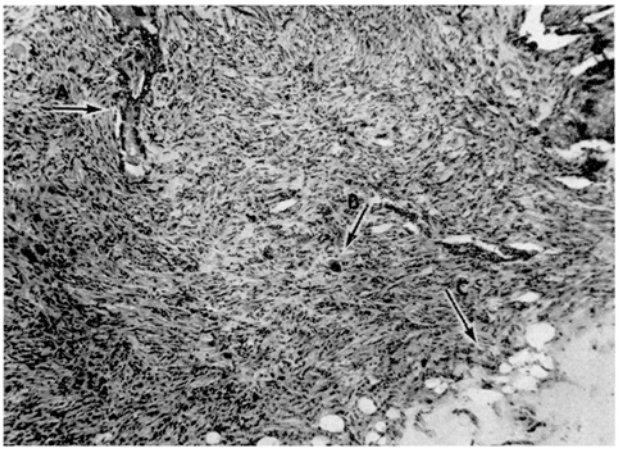

Fig. 2. Section through periphery of tumor showing sponge trabeculae (A), multinucleated giant cells (B), and invasion of adjacent adipose tissue (C). (× about 350 before reduction)

OPPENHEIMER et al.[3] reported a tumor incidence of 8.8% resulting from the subcutaneous implantation of polyvinyl alcohol (Ivalon) sponges in rats. In subsequent papers[4] they state that when plastics are embedded in forms 'such as textiles, sponges, or powders' (as contrasted to films), 'they induce tumors only rarely'. The high incidence of tumor induction in our animals may have been due in part to the strain of rat used, but may also have been influenced by our technique: (1) sponges were sterilized by autoclaving rather than by boiling, (2) sponges for implantation were wet with distilled water rather than with normal saline, (3) the screw caps of the glass vials in which the sponges were autoclaved had Vinylite liners. It is unlikely, however, that any of the details of technique would have more than a transitory effect on the tissues involved, whereas it takes almost 18 months for the first sponge-induced tumors to make their appearance.

Zusammenfassung. Polyvinylalkoholschwämme, in Tiergewebe eingepflanzt, sind weniger inaktiv als allgemein angenommen wird. Fibrosarkome entstanden in 75% der Ratten, welche die subkutane Schwammeinpflanzung mindestens 18 Monate überlebten.

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Androgenic and Anabolic Hormones: A new Group of Substances Stimulating Endogenous Ascorbic Acid Synthesis in the Rat

It is a well known fact that some animals are capable of synthetising ascorbic acid in their organism while others lack this quality. There are only few examples of the latter variety, viz. man, monkey, the Indian fruit bat and the guinea-pig, which cannot produce this vitamin[1].

Various drugs possessing completely unrelated chemical and pharmacological properties have been shown to enhance markedly the urinary excretion of L-ascorbic acid when administered to animals having the property of ascorbic acid synthesis. The following drugs belong to this group: Chloretone and barbital, aminopyrine and antipyrine, diphenhydramine and chlorcyclizine, 3-methylcholanthrene and 3,4-benzpyrene, orphenadrine and meprobamate, SKF 525 A and various substances having carcinogenic or toxic effect on the liver[2-4]. It is known that these substances have an effect on specific liver enzymes which are intimately connected in the synthesis of endogenous ascorbic acid. Chloretone, for instance, has been shown to accelerate the conversion of D-glucose to D-glucuronic acid *via* the oxidation of uridinediphosphate-D-glucose to uridinediphosphate-D-glucuronate by stabilizing UDPG dehydrogenase[5]. Growth hormone also stimulates endogenous ascorbic acid synthesis in rats[6]. This effect may be mediated through an increase in the biosynthesis of the specific liver enzymes.

Androgenic and anabolic hormones have a growth-promoting property like growth hormone. These hormones have also an increasing effect on amino acid activating enzymes[7]. The present investigation was undertaken to study the effect of these hormones on ascorbic acid synthesis.

The experiments were carried out by using female and male rats of Long–Evans strain. Both young, 2 months old, and adult, 4 months old rats were used with the average weight of 120 g and 200 g respectively at the beginning of the experiment. The animals were maintained on a standard diet chow and received water *ad libitum*. The young rats were divided into groups of 5 rats with equal group weight at the beginning. The adult rats were divided into groups of 3 rats with group weight averaging the young rat groups.

The following substances were injected subcutaneously in the rats: (1) testosterone propionate (Neo-Hombreol®) 10 mg/kg and 20 mg/kg; (2) 17β-hydroxy-19-norandrost-4-en-3-one-17 phenylpropionate (Durabolin®, abbreviated nor-TPP) 1.25 mg/kg, 2.5 mg/kg and 5.0 mg/kg; (3) 17β-hydroxy-19-norandrost-4-en-3-one-17 decanoate

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(Deca-Durabolin®, abbreviated nor-TD) 2.5 mg/kg and 5.0 mg/kg; (4) Ol. arach. 0.1 ml/kg.

The animals were kept in cages over funnels through which the daily urines were collected into bottles. Before the animals were injected with the hormones, the daily urines were collected separately for two days, which provided the control samples for each group. The urine samples were gathered 30 days after each single hormone administration. In each bottle, 5 ml of 5% oxalic acid was added and the bottles were stored in a −15°C refrigerator for serial determination of ascorbic acid (AA). The AA assay was carried out according to the method of SCHAFFERT and KINGSLEY[8].

The daily urinary total AA was 210 μg/100 g body weight in young male rats and 246 μg/100 g in young male rats. The corresponding AA excretion in adult female and male rats was 242 μg/100 g and 453 μg/100 g respectively.

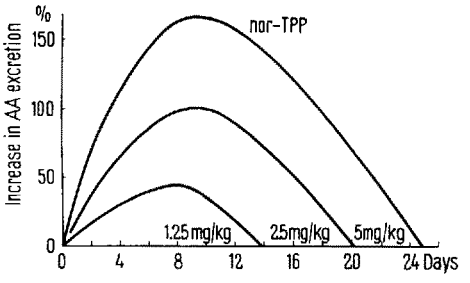
When injected in male adult rats only slight or no response was found after androgenic and anabolic hormones in the daily AA excretion. In young male rats a significant increase was observed. The most significant increase was found in the excretion of AA in female rats. Of these groups also the young female rats were more sensitive in this reaction. After testosterone propionate, the highest values were found on the 3rd and 4th day after its administration. With the doses used, the increase in the excretion of AA was, at its highest, 60–100% above the control values. The basal AA excretion values were restored on the 10th to 12th day.

When the anabolic hormones were injected, a highly significant increase in AA excretion was observed. The highest AA excretion values were found with both substances 8–10 days after their administration. After the top values the AA excretion decreased and the basal excretion was obtained. With nor-TD the basal level was obtained somewhat later than with nor-TPP with same doses.

The results obtained with nor-TPP with three various doses are graphically presented in the Figure. In each group the highest values were reached on the 8th to 10th day. With increasing dosage the AA excretion values are respectively higher and the basal values are obtained later.

The increase in the AA excretion depends on the increase in enzyme action in the liver. Repeated administration of drugs which increases the activity of drug-metabolizing enzymes also stimulates liver growth[9]. This suggests the possibility that the drugs may in some way cause an anabolic effect on protein metabolism in liver. It might be pertinent that testosterone and anabolic hormones which have an enhancing effect on protein metabolism increase also the activity of the microsomal enzymes intimately linked in the AA synthesis in the rat. On the contrary, estrogens which exert a catabolic effect on protein metabolism may have a decreasing effect on AA synthesis.

The effect of androgenic and anabolic hormones on the urinary AA excretion is probably identical with that of pituitary growth hormone[6]. Thus androgenic and anabolic hormones stimulate the synthesis of AA from glucose through the main glucuronic acid pathway as follows: D-glucose → D-glucuronic acid → L-gulonic acid → L-ascorbic acid[10]. In guinea-pigs, which cannot form ascorbic acid, these hormones may cause an increased excretion of glucuronic acid.



The percentage increase in the daily urinary ascorbic acid excretion after nor-TPP administration in three different doses to 2-months-old female rats.

Zusammenfassung. Die Wirkung einiger androgener und anaboler Hormone auf die tägliche urinäre Ascorbinsäureausscheidung junger und erwachsener, sowohl männlicher wie weiblicher Ratten wurde untersucht. Erwachsene männliche Ratten haben von Anfang an eine unabhängig von diesen Hormonen hohe Ascorbinsäureausscheidung. In den andern Gruppen steigern die verwendeten Substanzen die untersuchte Ascorbinsäureausscheidung deutlich.

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Influence of Drugs and Neocortical Spreading Depression on Hippocampal 'Arousal Reaction'

In unanaesthetized, curarized or freely moving rats with implanted electrodes the reversible functional elimination of neocortices by spreading depression (SD) does not influence the regular (4–8/sec) ϑ-activity in the hippocampus evoked by external or reticular stimulation (WEISS and FIFKOVÁ[1]; RÜDIGER, WEISS, and FIFKOVÁ[2]) and Physostigmine administration (BOHDANECKÝ, WEISS, and FIFKOVÁ[3]). This type of activity is highly sensitive to anesthetics (GREEN and ARDUINI[4]; GANGLOFF and MONNIER[5]; BRÜCKE, SAILER, and STUMPF[6]; BRADLEY and NICHOLSON[7] etc.). The question solved in this paper is whether the hippocampal activity after barbiturate and

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