and Bourgeois[3], but this was shown to be incorrect by Fischer and Skita[4]. Foreman[5] isolated a compound from casein which he believed to be this amino-acid; but its melting point was lower than that reported for the synthetic product of Fischer and Mouneyrat[6]. Recently, Dent[7] has found it in the urine, blood and dilute acetic acid extracts of yeast.

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Citric Acid in Semen

The discovery of citric acid in mammalian semen is due to Scherstén[1,2], who was also the first to point out that the acid originates in the accessory glands of reproduction, chiefly the seminal vesicles. In this respect citric acid resembles another more recently discovered component of semen, namely, fructose[3], which has similarly been shown to be secreted mainly in the seminal vesicles[4,5]. The present study was undertaken primarily with the view of investigating the possibility that there may exist a link between the two substances with regard to their formation, distribution or function in reproductive organs and semen. Citric acid was estimated colorimetrically[6,7]. The results were briefly as follows.

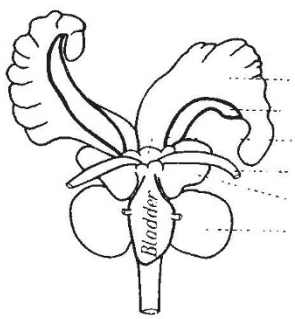
(1) Citric acid constitutes a major component of the seminal plasma. With the exception of the rabbit, it is usually absent from epididymal semen. It can be present, however, already in the ampullar semen (bull, ram), although in a much smaller concentration than in the whole ejaculated semen. A high concentration of citric acid in whole semen (mgm./100 ml.) is characteristic for bull (510–1,100), ram (110–260) and rabbit (110–550), all of which are distinguished at the same time by a high level of seminal fructose. It is, however, also present in boar (130) and stallion (55), which have a very low content of seminal fructose. On the whole, there is no correlation between the contents of citric acid and fructose, and the ratio between the two substances can undergo considerable fluctuations, even in the same individual. Occasionally, samples of semen are met with which contain only one but not the other component; for example, on two occasions we had the opportunity of examining samples of fish semen (*Scylliorhinus caniculus*) which contained fructose but not citric acid. On the other hand, dog semen seems to be devoid of both fructose and citric acid.

(2) The accessory organs of reproduction are the chief contributors of both seminal fructose and citric acid, yet the two substances can be shown to originate in different parts of the genital system. In rabbit, for example, citric acid is met with principally in the glans vesicularis and is associated frequently with the gel formation, whereas fructose is found in the highest concentration in the prostate organ[8]. An even clearer picture was obtained through the study of the reproductive organs in the rat. The distribution of citric acid and fructose in the various parts of the reproductive system of the male rat is shown in the accompanying sketch, where it can be seen that citric acid occurs chiefly in the ventral prostate and in the seminal vesicle, whereas fructose is found mainly in the dorsal prostate and in the 'coagulating gland', that is, the structure adjacent to the seminal vesicle proper.

(3) Following castration, there is a remarkable fall in the citric acid content of semen. In this respect, citric acid resembles fructose[9]. However, the post-castrate disappearance of citric acid is not so rapid as that of fructose. In rabbit, for example, the decrease may not become noticeable until three weeks after castration, whereas fructose has usually disappeared almost completely by the end of the second week. Similarly, the reappearance of citric acid in response to testosterone usually follows some time after seminal fructose.

(4) When fresh semen is incubated *in vitro*, citric acid disappears. The rate of disappearance, however, is much lower than that of fructose. In bull and ram semen, for example, the rate of fructolysis[10] at 37° C. is 1·5–2 mgm. fructose/10^9 sperm cells/1 hour, as compared with some 0·05 mgm. citric acid. Moreover, the rate at which spermatozoa metabolize fructose is not affected by the presence of citrate. On the other hand, the process of 'citricolysis', although very slow, may continue in semen for some time after the spermatozoa have exhausted the entire reserve of seminal fructose, that is, after the 'fructolysis' has come to an end.

(5) The observation has been confirmed that mammalian spermatozoa contain aconitase and that they are able to synthesize citric acid from oxaloacetic acid[11]. However, the bulk of the citric acid present in whole ejaculated semen is derived from the seminal plasma and not from the spermatozoa. It can be removed by centrifuging the semen and by washing the spermatozoa with Ringer solution. Citrate added to washed ram spermatozoa is incapable of maintaining the sperm respiration. In this respect it differs from fructose as well as from many organic acids such as lactic, pyruvic, oxaloacetic, acetic, propionic and butyric, all of which can maintain and prolong the respiration of washed spermatozoa.



	Weight of organ (mgm.)	Citric acid (mgm./100 gm. tissue)	Fructose (mgm./100 gm. tissue)
Seminal vesicles	780	39	9
Coagulating glands	130	0	172
Median prostate	20	60	90
Ampullæ vas. def.	70	0	10
Dorsal prostate	250	20	82
Ventral prostate	320	122	0

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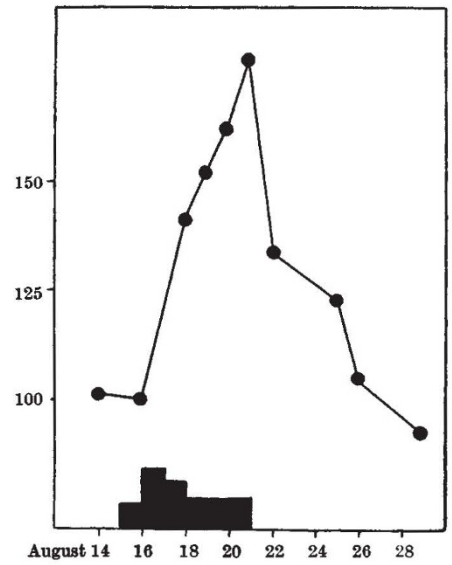
Effect of *p*-Aminobenzoic Acid on the Leucocyte Count in Leukæmia

A LEUCOPENIC effect of *p*-aminobenzoic acid has been noticed in several studies on the treatment of rickettsial infections in man with this drug[1].

In the Radiumstationen in Aarhus we have investigated this effect of *p*-aminobenzoic acid on the leucocyte count in leukæmia. The drug was given to a few patients with chronic leukæmic leukæmia (four patients with chronic lymphatic leukæmia and two patients with chronic myeloid leukæmia). The administration and dosage were at first as recommended in rickettsial infections (about 2 gm. every second hour); later the dosage was considerably decreased without any influence on the effect. In all six cases the administration of *p*-aminobenzoic acid caused an abrupt rise in the leucocyte count, which continued to increase so long as the drug was given. The daily increase was 10,000 to 100,000 or more cells per c.mm., demonstrated both in capillary blood from the ear lobule and in the venous blood from the cubital vein. When the leucocyte count had been increasing for four or five days, the patients often complained of pressure and soreness in the swollen lymph glands and in the enlarged spleen, and consequently the administration of *p*-aminobenzoic acid was stopped. Hitherto X-ray therapy has been instituted immediately after the withdrawal of *p*-aminobenzoic acid, and the decrease in leucocytes has followed as usual or perhaps a little more rapidly. The increase in the leucocyte count caused by *p*-aminobenzoic acid was accompanied in the myeloid leukæmias by a slight shift to the left, which could be demonstrated more clearly in the bone marrow. Corresponding changes could not be demonstrated in the lymphatic types. Hæmoglobin and erythrocyte count were unaffected.

The mechanism of the effect of *p*-aminobenzoic acid in leukæmia is not yet clear. Experiments concerning this point are in progress in this Laboratory. Experiments have shown that an acidosis produced by ammonium chloride does not affect the leucocyte counts in leukæmic patients, so we may exclude the possibility that the slight acidosis which often results from treatment with *p*-aminobenzoic acid is the cause of the rise in leucocyte counts.

p-Aminobenzoic acid has been given to eight patients with non-leukæmic diseases (normal blood picture) without causing any significant variations in the leucocyte counts. Consequently there seems to be a difference in the effect of *p*-aminobenzoic acid on the normal and leukæmic leucocytes.



EFFECT OF *p*-AMINOBENZOIC ACID IN A CASE OF CHRONIC MYELOID LEUKÆMIA. THE LEUCOCYTE COUNT (THOUSANDS PER C.MM.) PLOTTED AGAINST TIME. THE BLACK AREA INDICATES THE DISTRIBUTION OF *p*-AMINOBENZOIC ACID, WHICH WAS GIVEN FROM AUGUST 15 UNTIL AUGUST 20 INCLUSIVE, 1946, THE TOTAL DOSE BEING 52 GM. X-RAY THERAPY WAS INSTITUTED ON AUGUST 21

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Electron Microscope Observation of Renosine

RENOSINE is the structure-protein of the kidney discovered by I. Banga and A. Szent-Györgyi[1]. It constitutes up to a third of the total protein content of the kidney, is highly viscous, exhibits thyxotropy and an intense negative double refraction of flow. It contains inextractable phosphorus and seems thus to be a nucleoprotein.

To determine visible renosine micelles, the following electron microscopical investigations were carried out. Renosine extracts were prepared, according to a method similar to that described by Banga and Szent-Györgyi, from guinea pig kidneys by means of Edsall's solution containing 30 per cent urea. For further purification, the renosine was precipitated and dissolved once more. The solutions tested were centrifuged (10,000 revolutions) for one hour, and 1 ml. of the top layer was diluted with the solution used in the extraction in the ratio of 1 : 100 or more. A droplet of the diluted solution was placed upon the aluminium film of the specimen grid. After drying, it was rinsed for a short time with twice-distilled water and dried again.

The electron micrographs of such renosine preparations show filaments that tend to branch and split