"The Psychological Aspects of Morale." The meeting was well attended and evoked considerable interest and discussion.

The Poteat Award was conferred on J. P. Decker, of Duke University, for his paper on "The Effect of Temperature on Photosynthesis in Red and Loblolly Pines." The High School award of $20 went to Ernest Hardwick and Arthur Budlong, of the Winston-Salem High School. They demonstrated a home-made stroboscope.

After a complimentary dinner given by the Woman's College, Dean Jackson in his address of welcome lauded two former academy members, also former teachers at Greensboro, for their achievement in the scientific world. They were Gilbert T. Pierson and E. W. Gudger. Dr. R. E. Coker then delivered the presidential address, taking as his subject, "What Are the Fittest?" The address was a zoologist's view of the present world conditions. After the address an informal open house gave opportunity for renewing old friendships and establishing new ones. During this time the group experienced its first blackout.

Committee reports were made in mimeographed form, and these along with the treasurer's preliminary report were adopted. The secretary reported the election of about 50 new members. This makes a total of more than 225 new members elected in the last three-year period.

The following officers were elected: *President,* H. F. Prytherch, of the Bureau of Fisheries; *Vice-president,* Eva G. Campbell, of Guilford College; *Secretary-Treasurer,* Bert Cunningham (re-elected for a three-year term), of Duke University; *New Member of the Executive Committee,* O. J. Thies, of Davidson College; *New Member of the Research Grants Committee,* J. P. Givler, of the Woman's College.

A more detailed report of the meeting will appear in the *Journal* of the Elisha Mitchell Scientific Society.

BERT CUNNINGHAM,
Secretary

SPECIAL ARTICLES

THE RELATION OF URINARY CITRIC ACID EXCRETION TO THE MENSTRUAL CYCLE AND THE STEROIDAL REPRODUCTIVE HORMONES

THE role of citric acid in mammalian metabolism still remains obscure. Some of the prevailing theories and factual observations relating to this metabolite may be reviewed briefly. It is present in small amounts in the tissues and body fluids, and is a constant urinary constituent, (0.2–1.2 gms/24 hrs. in man.) It is evidently a product of endogenous metabolism, since it continues to appear in the urine during starvation, and the amounts excreted under normal conditions are greatly in excess of those present in the food or stored in the tissues.[1] Krebs, as a result of studies on minced tissues,[2] has assigned to it an important role in carbohydrate oxidation, but his theory still awaits support from work on intact tissue. In the living organism, citric acid has been shown to enter the carbohydrate cycle, but in a manner not implicit in the citric acid cycle postulated by Krebs. It exerts an anti-ketogenic effect and overcomes insulin hypoglycemia.[3] It is converted almost quantitatively to glucose in the phlorhizinized dog, and deposited as liver glycogen when fed to normal rats.[4,5] It has also been found to be related to acid-base regulation. Alkalosis, however induced, leads to an increase in urinary citric acid, excretion generally varying directly with urinary pH.[6] Finally, the unusually high citrate content of bone[7] is suggestive of some connection with calcium metabolism. The present paper links citric acid to still another physiological process, the menstrual cycle.

We wish to report experiments with human subjects which have revealed a relation between citric acid excretion and the steroidal reproductive hormones. These experiments were carried out on five young women with regular menstrual cycles, two young women with amenorrhea, and one hypogonadal male. Except in the case of two female subjects, both laboratory workers, the studies were carried out in the Metabolism Ward of the Department of Medicine in order to insure accurate urinary collections and proper dietary control. Citric acid was determined by a modification of the pentabromacetone method.

Analysis of the daily urinary excretion of citric acid during six complete menstrual cycles of the five subjects studied, showed, in all cases, a characteristic cyclic alteration in the level of the citric-acid content during the different phases of the menstrual cycle. The lowest levels always occurred during menstruation, the highest, at about the middle of the cycle. The shape of the curve varied with the different subjects, both with respect to the rapidity and height of the midmenstrual rise, and the duration of the increased excretion. In one patient studied over two

[1] C. C. Sherman, L. B. Mendel and A. H. Smith, *J. B. C.,* 113: 247, 1936.
[2] H. A. Krebs and W. A. Johnson, *Enzymologia,* 4: 148, 1937.
[3] E. M. MacKay, H. O. Carne and A. N. Wick, *J. B. C.,* 133: 59, 1940.
[4] I. Greenwald, *J. B. C.,* 18: 115, 1914.
[5] C. A. Kuether and A. H. Smith, *J. B. C.,* 137: 647, 1941.
[6] O. Östberg, *Skand. Arch. Physiol.,* 62: 81, 1931.
[7] F. Dickens, *Biochem. Jour.,* 35: 1011, 1941.

consecutive cycles, the shapes of the excretion curves were similar in both cycles. In four cycles, a brief, but significant, fall in excretion occurred midmenstrually and lasted for one or two days. In four cycles, the higher level of citric acid excretion persisted during most of the second half of the cycle, to fall abruptly two or three days before the next flow. The maximal midmenstrual increases in citric acid excretion over the menstrual levels were 225, 240, 275, 350, 450 and 500 mgs for the six cycles studied.

The accompanying graph (Fig. 1) illustrates the

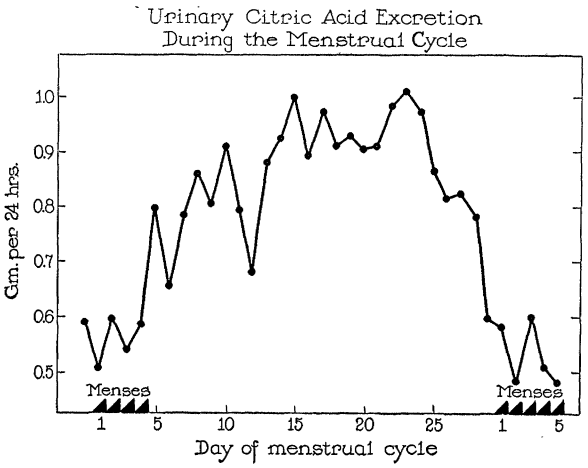

FIG. 1.

characteristics of the curve of citric acid excretion during the menstrual cycle of one of the subjects. The post-menstrual rise, the sharp midmenstrual dip, the persistence of the high level of excretion during most of the premenstrum, and the abrupt fall to the previous menstrual levels, were particularly striking in this subject.

Results, of a preliminary character, can be reported of experiments designed to analyze the relation of the individual steroidal reproductive hormones to the cyclic alterations in citric acid excretion during the menstrual cycle. An estrogenic hormone, (estradiol benzoate), was administered to two amenorrheic girls in amounts that did not exceed their estrous requirements, as judged by vaginal smears. Both subjects showed significant increases in citric acid excretion (230 and 500 mgs, respectively), during its administration, and a sharp return to lower levels on cessation of treatment. We are now investigating the possible influence of progesterone on citric acid excretion, in view of the fact that the high level of excretion is generally maintained throughout most of the second half of the cycle. The reverse effect on citric acid excretion was observed when an androgen, testosterone, was administered to a male with pituitary hypogonadism. During two courses of treatment, urinary citric acid fell significantly, (300 mgs/24 hrs.), below the control values and rose sharply to previous levels when treatment was terminated. In one amenorrheic girl, testosterone propionate likewise reduced the daily output of citric acid by 175 mgs. Additional studies on human subjects and animals are under way to ascertain the constancy and prevalence of these phenomena.

The studies on the female subjects were correlated with vaginal smears. The results of the correlation of this index of ovarian function with the excretion of citric acid will be reserved for a subsequent report.

These observations would appear to establish the existence of a cycle of citric acid excretion which bears a definite relation to the menstrual cycle and is probably hormonally conditioned. This cycle may result from a direct effect of the hormones involved on citric acid metabolism, or from their influence on some other mechanism, such as acid-base regulation, renal function or carbohydrate metabolism, which in turn influences citric acid formation and excretion. Since citric acid is but one of the organic acids eliminated in the urine, it will be necessary to determine whether or not excretion of other organic acids is also altered under these conditions, before the changes in citric acid excretion can be regarded as specific. The bearing of these results on all previous experiments dealing with citric acid excretion in women is obvious.

Although these experiments throw no new light on the basic problem of the endogenous metabolism of citric acid, they do point out a new functional relationship, and should provide a valuable tool to aid in its study.

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PHYSIOLOGIC STUDIES ON THE CORNEA

THE cornea is a composite membrane forming the anterior portion of the outer coat of the eye-ball. In all vertebrates it has on its anterior surface a thin, stratified epithelial layer and on its posterior surface a single layer of endothelial cells. Just anterior to the endothelium is a homogeneous elastic lamina (Descemet's membrane), and just beneath the epithelium there is, in some species, a homogeneous glass-like lamina (Bowman's membrane). The remainder of the cornea, the substantia propria, comprising about 90 per cent. of its total thickness, is made up of collagenous fibers and supporting cells arranged parallel to the surfaces of the cornea. These fibers