dose. The distributions of dicumarol between heptane and water at various pH values were compared with those of the apparent compound extracted from plasma. The results showed that within experimental error the apparent and authentic compound had the same solubility characteristics and were, therefore, presumably the same compound (Table I).

Basic organic drugs do not interfere in the procedure for dicumarol since they are not extracted at an acid pH. The following acidic or neutral drugs were tested for their interference in the procedure for dicumarol: acetanilide, phenacetin, antipyrine, phenobarbital, sulfanilamide, sulfadiazine, sulfathiazole, penicillin, vitamin K, nembutal, pentothal, and salicylic acid. Only pentothal and salicylates interfered in the procedure and consequently these substances should not be present when analyses for dicumarol are being made.

*Summary.* A simple and sensitive spectrophotometric method for the estimation of dicumarol in plasma and urine is described. Dicumarol is isolated from the biological material by extraction into heptane. The drug is returned to alkali and measured spectrophotometrically at 315 mμ. The method is specific in that it does not include metabolic products of the drug.

## 17037 P

## Seasonal Variations in the Choline Content of Human Serum.

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In the literature there are but few reports of studies on serum choline content (Guggenheim and Loffler,[1] Sieburg and Patzschke,[2] Luecke and Pearson,[3] and Schlegel[4]).

It appears from these studies that the concentration of choline in human serum ranges from about 0.2 to 2 mg %. As far as has been ascertained, no records are available of studies presenting evidence of seasonal variations in serum choline content.

The present study comprises 142 duplicate determinations of serums obtained from both men and women in the period from May 1, 1947 to May 1, 1948. Determinations of choline were made according to the method of Abdon and Ljungdahl-Ostberg[5] by converting choline into acetylcholine, which physiologically is about 100,000 times as active as choline. Its action was determined

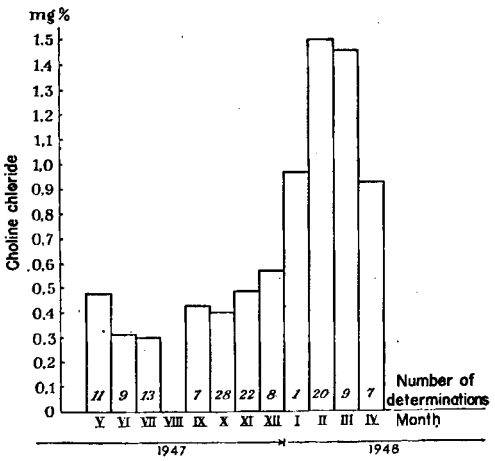


FIG. 1.

The average serum choline content during the different months of the year.

[1] Guggenheim, M., and Loffler, W., *Biochem. Z.*, 1916, **74**, 303.

[2] Sieburg and Patzschke, *Z. d. ges. exp. Med.*, 1923, **36**, 324.

[3] Luecke, R. W., and Pearson, P. B., *J. Biol. Chem.*, 1944, **153**, 259.

[4] Schlegel, J. U., Variationer i Serumcholinindholdet hos Mennesker, Copenhagen 1948 (Thesis).

[5] Abdon, N. O., and Ljungdahl-Ostberg, K., *Acta Physiol. Scandinav.*, 1944, **8**, 103.

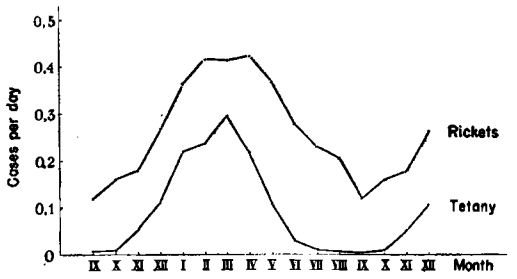


FIG. 2.

Monthly distribution of the incidence of rickets and tetany during the years 1924-35 incl. The material is from Borne-hospitalet, Fuglebakken, Copenhagen.[6]

biologically on intestines of guinea pigs. The accuracy of the method is 12% on single determinations, 9.4% on duplicate determinations.[4]

Fig. 1 shows the results of these determinations for choline over a 12-month period.

It will be seen that the average choline content is lowest in the month of July (0.3 mg %), the concentration being 5 times as high in the months of February and March.

The cause of these seasonal variations is not known, but we wish to call attention to the remarkable correspondence of the serum choline curves in Fig. 2, showing seasonal variations in the incidence of rachitis and tetany (Horstmann and Petersen[6]).

With the view of ascertaining the relationship between the choline seasonal curve and the curves (Fig. 2) of minimum accumulation of light,* which is secondarily manifested by deficiency of vitamin D, a few experiments were carried out in which the response of the serum choline level to irradiation was studied. Table I shows the results obtained in these experiments.

It appears from the 5 irradiation experiments that the serum choline content dropped quite considerably subsequent to about three weeks of carbon-arc light irradiation . It should be pointed out, however, that the last 3 experiments were carried out in the latter part of April when the average choline content had already dropped.

From the present studies it seems justifiable to reckon with the possibility that the variations in serum choline content within the various months of the year may be related to the effect of light accumulation in the same way as is the case with vitamin D, except, however, for showing an opposite course, with minimum values in the winter months of February and March, instead of the summer months.

It is impossible, on the basis of the present

TABLE I.

Results Showing the Effect of Carbon Arc Light Irradiation on the Serum Choline in Five Different Persons.

| | Case | Course of light treatment | | | Final effect |
|---|---|---|---|---|---|
| Date of initiation of irradiation and subsequent choline determinations | a | 3/2/48 | 3/2/48 | 3/10/48 | 3/22/48 |
| | b | | 3/3 | 3/10 | 4/12 |
| | c | | 4/2 | 4/ 8 | 4/22 |
| | d | | 4/2 | 4/ 8 | 4/22 |
| | e | | 4/2 | 4/ 8 | 4/22 |
| Minutes of exposure to carbon arc light at two day intervals | a | 0 | 4 | 14 | 30 |
| | b | | 0 | 4 | 16 |
| | c | | 0 | 10 | 24 |
| | d | | 0 | 10 | 20 |
| | e | | 0 | 6 | 20 |
| Serum choline (mgm %) | a | 1.37 | 1.51 | 2.14 | .48 |
| | b | | — | 1.41 | .61 |
| | c | | — | 1.33 | .49 |
| | d | | — | 2.55 | .78 |
| | e | | — | 1.94 | .98 |

[6] Horstmann and Petersen, H., *Acta paed.*, 1947, **33**, 203.

* For full clarification of the term "light accumulation" the reader is referred to the work of Horstmann and Petersen.[6] In brief, it refers to a delayed, cumulative effect of light upon the organism.

studies, to evaluate the consequences of the observations made, in the same way as it seems difficult to understand the cause of the probable significance of light in relation to the concentration of choline in serum. It seems, however, that determinations for choline in serum might present a possibility of measuring—by a fairly simple method—the effect of light on the organism. Furthermore, the variations seem to be so large that a chemical method of determination might well be employed.

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## The Pathogenicity of Bagasse, II. Effect on Rabbits of Prolonged Exposure to Bagasse.*

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The clinical and industrial health problems of Bagasse Disease have attracted increasing attention.[1-12] In spite of careful observation and biopsies on patients suffering of this disease, its pathogenesis remains obscure.[2]

Various factors have been suggested as etiologic agents: the particular composition of the fiber itself, fungi and micro-organisms attached to the fiber, and the high silica content. Allergic phenomena also entertained as a possible etiologic mechanism[3] seem, on the basis of experimental evidence,[4] less likely to be involved.

The problem of establishing whether the fiber itself, or the micro-organisms growing in abundance on it,[4,5] is responsible for the disease was approached experimentally by comparing the lesions produced by either untreated, autoclaved, or formalized bagasse.[4] In short term experiments a striking difference was observed. Rabbits developed a rapidly progressing, even fatal, disease after intravenous or intratracheal administration of fresh bagasse, while the autoclaved or formalized material produced only a foreign body reaction limited to the lungs. In the present report these experiments were extended in order to study the character of the lesions at longer intervals, to resolve the complex histopathology of the lesions into components that could be correlated with the various ingredients of bagasse dust, and to compare the morphology of the experimental lesions with that of the human disease.

*Material and methods.* For intratracheal insufflation, a procedure described earlier was employed.[4] The attempt to expose animals

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