and editorial assistance rendered by the Society of American Bacteriologists, the number of abstracts in Section C increased from 2,670 in 1938 to 3,657 in 1939. This represents an increase of almost 36 per cent.

All this was possible largely through two factors. In the first place, the ever-increasing efficiency of the editorial office played an important part. Here there was an increase of only one regular member and five temporary persons. In the next place success is due to the efforts of those able and generous collaborators, the section editors, who have contributed their valuable time and knowledge to the service. Eight new section editors were added to the staff during 1939.

One of the aims of *Biological Abstracts* has been to strive to maintain prompt publication of abstracts and indices. In October, 1936, only 24 per cent. of the abstracts of that number were from the current year's publications; in October, 1939, 82 per cent. of all abstracts were from papers published in 1939. The monthly issues are now on a regular schedule. The index to Volume 12 (1938) appeared within seven months and the last index in arrears (Vol. 11) appeared before the close of 1939. It is the hope and determination of all to better the Volume 12 record, if possible, with the Volume 13 Index.

It is interesting and significant that the number of paid subscriptions to *Biological Abstracts* increased from 1,660 for 1938 to 2,654 for 1939. This latter figure may be subdivided as follows:

Complete volume. U. S.	647
" " Foreign	632
Section A	338
" B	198
" C	387
" D	363
" E	89
Grand total	2,654

In this connection it should be pointed out that the income from subscriptions in 1939 was not alone sufficient to meet all the budgetary demands. If it were not for the support of various biological societies and income from advertising and the sale of back volumes, the financial statement would not appear to be so satisfactory. It should be clear to all that *more subscriptions are needed.* Development of the service giving further increases in coverage is dependent solely upon income. As more biologists come to recognize the value of this journal in economizing time and broadening their scientific range, and as more libraries subscribe, increased income will permit an expanded service.

BOARD OF TRUSTEES, BIOLOGICAL ABSTRACTS

SPECIAL ARTICLES

THE SYNTHESIS OF GLYCOCYAMINE IN RAT KIDNEY AND A MECHANISM OF CREATINE SYNTHESIS IN VIVO

GLYCOCYAMINE (guanidino-acetic acid) is converted into creatine (N-methyl guanidino-acetic acid) by surviving liver slices. The methylating agent may be methionine or a derivative of methionine.[1]

Liver slices of all animals investigated are capable of effecting this methylation[2] at a rate sufficiently fast to make good the total loss as urinary creatinine. It is highly improbable that this property of liver is a fortuitous coincidence of no physiological significance; the more probable inference is that methylation of glycocyamine is one of the important physiological mechanisms of creatine synthesis.

This conclusion was strengthened by the finding of Bloch and Schoenheimer, who, using N_{15} as a tracer, found that in the living animal (rat) glycocyamine is readily converted to creatine.[3]

The origin of glycocyamine has thus acquired an augmented physiological significance. We have found that rat kidney slices form glycocyamine from arginine and glycine with great rapidity. That the substance formed is glycocyamine was proven by the following tests: conversion to glycocyamidine by heating in acid solution; it was not digested by the NC bacteria of Dubos and Miller[4] under conditions in which creatine and creatinine are completely digested; a very strongly positive Sakaguchi test was obtained after all the arginine was removed by exhaustive adsorption on permutit; preparation of the characteristic glycocyamine acetate; isolation and its identity proven by elementary analysis.

With surviving rat kidney slices the rate of formation of glycocyamine from arginine and glycine is as rapid as urea formation by rat liver slices from ammonia and ornithine. This interaction of arginine and glycine is also catalyzed by thoroughly macerated kidney tissue suspended in a phosphate buffer at pH 7.4.

Surviving rat liver slices are incapable of carrying out this reaction.

Arginine and sarcosine also yield glycocyamine (not

[1] H. Borsook and J. W. Dubnoff, *Jour. Biol. Chem.*, 132: 559, 1940.

[2] *Ibid., Jour. Biol. Chem.*, in press.

[3] K. Bloch and R. Schoenheimer, *Jour. Biol. Chem.*, 133: 633, 1940.

[4] B. F. Miller and R. Dubos, *Proc. Soc. Exp. Biol. and Med.*, 35: 335, 1936; R. Dubos and B. F. Miller, *Jour. Biol. Chem.*, 121: 429, 1937.

creatine); this reaction is slower than the interaction of arginine and glycine. These two findings indicate that the sarcosine is demethylated first. This also is in accord with the findings of Bloch and Schoenheimer with N_{15}.

Our findings account for the other observations of Bloch and Schoenheimer that when ammonia containing N_{15} is fed the isotope is found later in the amidine $\left(-\overset{\diagup NH_2}{\underset{\diagdown NH}{C}}\right)$ nitrogen of creatine. When glycine containing N_{15} is administered the isotope is found in creatine in the sarcosine nitrogen.

The formation of glycocyamine from arginine and glycine is a new biochemical reaction which may be called "transamidination." The discovery of this reaction in the kidney (the possibility of its occurring in other tissues is now being investigated) provides direct proof that arginine and glycine are precursors of creatine.

We have found previously that glycocyamine is not methylated in the kidney; this occurs in the liver.[2] Glycocyamine is formed in the kidney. Both kidney and liver therefore participate in the formation of creatine.

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NUTRITION AS A FACTOR IN THE DEVELOPMENT OF CONSTITUTIONAL BARRIERS TO INVOLVEMENT OF THE NERVOUS SYSTEM BY CERTAIN VIRUSES

RECENT investigations[1,2] have demonstrated that as animals grow older they may develop resistance to involvement of the nervous system by certain viruses not because of immunity acquired as a result of exposure to infection, nor because of a maturation affecting the whole animal or its entire nervous system, but rather as a result of changes in certain tissues or structures which those viruses must pass before they can give rise to paralysis or encephalitis. The purpose of the present communication is to report some preliminary experiments which indicate that the nutrition of the growing animal or even that of the mother during the nursing period can exert an influence on the development of those tissue changes which serve as barriers to the invasion of the nervous system by certain viruses.

The effect of intramuscular injection of vesicular stomatitis virus in mice was selected as the indicator of at least one type of such constitutional resistance because (1) under standard conditions mice of different ages react with great regularity, and (2) the pathogenesis of the disease and spread of the virus in both young and old has already been investigated in considerable detail. Preliminary tests on the albino mice used in the present experiments were in agreement with previous observations on another stock of albino mice in that it was found that at 2 weeks of age almost 100 per cent. develop a fatal ascending paralysis, at 3 weeks 80 to 90 per cent., and at 4 weeks only 10 to 20 per cent.; at 5 weeks of age the incidence of paralysis is 5 per cent. or less, and beyond the 6th week, resistance is close to 100 per cent. Previous studies have indicated that some change in the muscle cells or nerve endings or both of the maturing animals is responsible for the resistance, since the older mice remain susceptible to intracerebral or intraneural injection of the virus.

Because the change from 100 per cent. susceptibility to approximately 100 per cent. resistance occurs between the 14th and 35th days of life, and because mice continue to suckle for about 28 days, although during the last 7 or 8 days they also eat the maternal diet, two different types of feeding experiments were designed to test the role of nutrition. In one set of experiments the mothers were maintained on standard "adequate" diets throughout pregnancy and for 2 days after delivery, when they were given the various diets indicated in Table I; the offspring remained with their mothers for at least 28 days and then continued on the respective diets until the termination of the tests. In the second set of experiments, mice, suckling mothers which were receiving standard adequate diets, were weaned at 14 days; different groups made up of approximately equal numbers of siblings were given the various diets indicated in Table II. Different groups of mice were tested for resistance at 4, 5 and 6 weeks of age by an inoculation into the calf muscles of 0.2 cc of a 10 per cent. suspension of the brains of mice succumbing after intracerebral injection of the N. J. strain of vesicular stomatitis virus; this dose contains 1 to 10 million minimal cerebral lethal doses of virus. The potency of the virus was checked in each test by intracerebral titration.

The results presented in Tables I and II can be regarded only as indicating a certain trend, since the actual percentages of resistant animals in the various groups will probably change when the work is extended on larger numbers of mice. The following indications, however, are apparent:

I. When the maternal diet during the nursing period consisted of:

(a) *An artificial, purified stock diet adequately supplemented by the various vitamins*—the offspring appeared to develop their resistance normally, *i.e.*, at the same rate as when the diet consisted of a mixture of many natural foods.

[1] A. B. Sabin and P. K. Olitsky, *Jour. Exp. Med.*, 66: 15, 1937; *ibid.*, 66: 35, 1937; *ibid.*, 67: 201, 1938; *ibid.*, 67: 229, 1938; *Proc. Soc. Exp. Biol. and Med.*, 38: 595, 1938; *ibid.*, 38: 597, 1938.

[2] A. B. Sabin, SCIENCE, 91: 84, 1940.