par certains auteurs[1,2] qui pensent pouvoir assimiler l'action estérasique à l'effet neurotoxique du venin de cobra.

De même que l'ésérine, le D.F.P. n'a aucunement protégé les souris et les cobayes intoxiqués par le venin et les animaux sont morts dans les mêmes délais que les témoins et en présentant des troubles tout à fait analogues.

En résumé, l'application de la méthode manométrique de WARBURG nous a permis de poursuivre une étude plus poussée de l'action estérasique du venin de cobra. Nous avons rapidement constaté que, contrairement à l'opinion généralement admise, ce ferment n'est pas une cholinestérase, car son action s'étend de façon bien plus générale aux esters d'acides et d'alcools renfermant le radical acétyl et de poids moléculaire peu élevé. Ce ferment pourrait donc être plutôt appelé une acétylase.

L'action inhibitrice de certaines substances caractérise bien le caractère propre de cette diastase: la myristicylcholine, par exemple, qui inhibe l'action estérasique du venin de cobra, reste sans action sur la cholinestérase contenue dans le sérum de Chien (fig. 4 et 5).

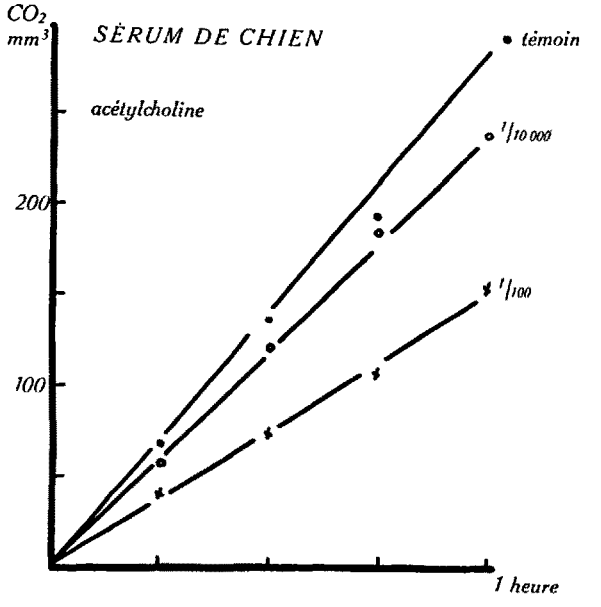

Fig. 5. Effet de la myristicylcholine sur la cholinestérase du sérum de Chien.

F. BOVET NITTI

Laboratoire de chimie thérapeutique, Institut Pasteur, Paris, le 12 mai 1947.

Zusammenfassung

Mit Hilfe der WARBURG-Methode wird die Esterasewirkung von Kobragift geprüft. Das Ferment wirkt nicht nur auf Acetylcholin, sondern auch auf verschiedene andere Ester mit kleinerem Molekulargewicht, die die Acetylgruppe enthalten. Es ist demnach nicht als Cholinesterase, sondern als Acetylase zu bezeichnen. Myristicylcholin beeinflußt die Cholinesterase im Blutserum des Hundes nicht, hemmt dagegen die Acetylase im Kobragift.

[1] N. K. JYNEGER, K. B. SEHRA, B. MUKERJI et R. N. CHOPRA, Current Science *7*, 51–53 (1938).

[2] R. N. CHOPRA et J. S. CHOWHAN, Ind. med. Gaz. *75*, 69–75 (1940).

Failure of Increase of Bisulphite-binding Substances after Fat and Protein Intake during Pregnancy

The level of bisulphite-binding substances (B.B.S.) after fat and protein intake or protein intake increases in the blood of healthy persons[1]. All substances containing the aldehyd- or keto-group bind bisulphites. The increase of these substances in our experiments are chiefly due to

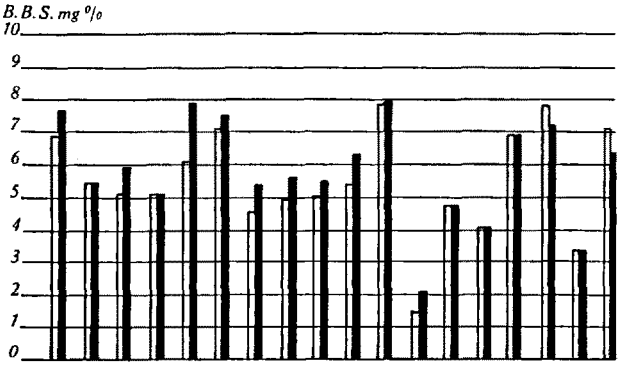

Fig. 1. Level of B.B.S. in blood before and after fat and protein intake in pregnancy after the III[d] month.

the augmented quantity of keto-compounds, because we found acetonuria in cases with high B.B.S.-content of the blood following fat and protein intake. In one of our cases the B.B.S. failed to increase after administration of fat and protein. The person investigated was pregnant. Therefore we determined the B.B.S. after fat and protein intake in 21 cases of pregnancy.

Blood was taken from the pregnant women in the morning before breakfast, and 6 hours later they were given a meal consisting of 120 g of bacon and 100 g of cheese. (In two cases only 100 g of cheese was given.) In both specimens the quantity of B.B.S. was determined with the method of CLIFT and COOK[2]. Out of 18 pregnant women, whose pregnancy was beyond the third month, in 17 the level of B.B.S. in blood remained unchanged, while in 27 of 32 non-pregnant women an increase from 1·1 mg per cent to 5·1 mg per cent was found after intake of the same amount of fat and protein. The average increase was 0·31 mg per cent in pregnant cases, a value not exceeding the limit of error, as against 1·92 mg per cent in non-pregnant cases. In three cases of early pregnancy (II[nd]–III[d] month) the response was similar to that of non-pregnant cases.

Our results may be explained by the impaired hormone production of the anterior pituitary gland during pregnancy after the third month. PHILIPS observed that in pregnancy the gonadotrophic activity of the pituitary gland is reduced after the third month. YOUNG[3] observed that pituitary extracts have no diabetogenic effect during pregnancy. The essential difference between our experiments and those of YOUNG consists in the fact that in his cases an extract administered was ineffective, whereas in our investigations the diabetogenic hormone production of the experimental subjects themselves was wanting. This could be explained by the early investigation of BURLANDO[4], who found in the liver of pregnant animals

[1] GÓTH and BIKICH, Nature *159*, 170 (1947).

[2] CLIFT and COOK, Bioch. J. *26*, 1789 (1932).

[3] YOUNG, Schweiz. med. Wschr. *76*, 894 (1946).

[4] BURLANDO, see MÖLLERSTRÖM, Das Diabetesproblem. Stockholm. Pag. 42.

more glycogen than in the liver of non-pregnant ones. It is known that in a liver richer in glycogen the quantity of keton bodies produced is diminished.

The theory of impaired diabetogenic hormone production is supported by our findings in cases of pituitary hypofunction. We could show in seven cases of hypopituitarism (dwarfism, obesity with amenorrhœa, Laurence-Moon-Biedl-disease, hypogenitalism) the failure of increase of B.B.S. after fat and protein intake; after treatment with pituitary extract (praephyson) the response became normal.

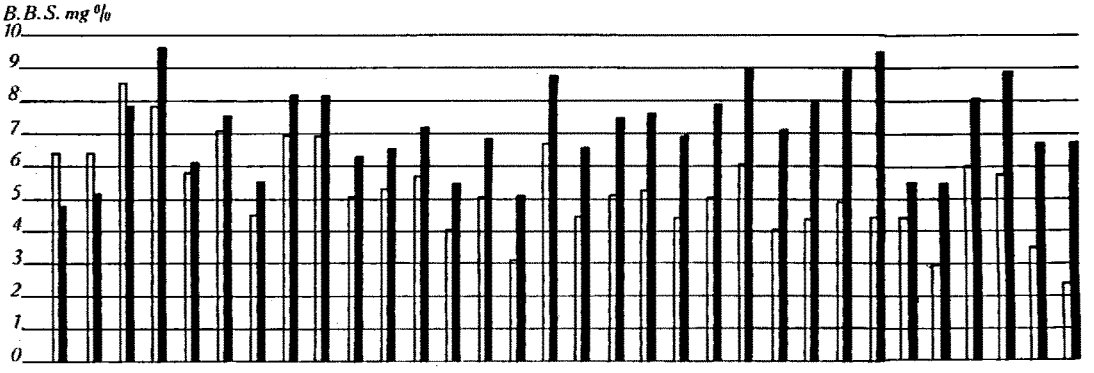

Fig. 2. Level of B.B.S. in blood before and after fat and protein intake in non-pregnant cases.

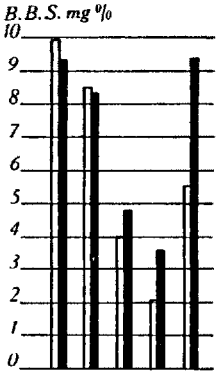

Fig. 3. Lactation.

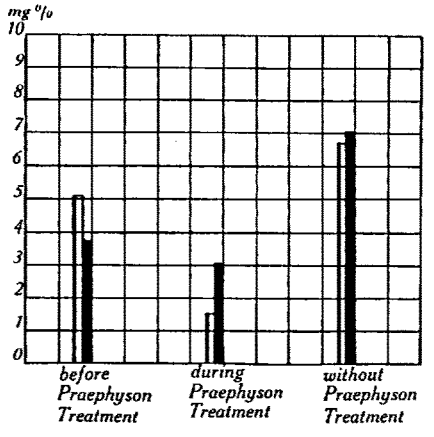

Fig. 4. B.B.S. before and after fat and protein intake in a case of pituitary hypofunction.

Our experiments throw a new light on the problem of diabetes and pregnancy. Though there are contradictory observations, most authors have reported on an amelioration of diabetes during pregnancy (FALTA[1], HETÉNYI[2], FORRÓ[3] etc.) Several authors emphasize the

Non-pregnant cases

Increase of B.B.S. in blood after fat and protein intake (5 hours) in mg per cent

1. Sound person	6·32	4·82	−1·50
2. Amenorrhœa	6·45	5·18	−1·27
3. Cirrhosis of liver	8·51	7·82	−0·69
4. Sound person	5·82	6·15	0,33
5. Sound person	7·06	7·50	0·54
6. Sound person	4·40	5·50	1·10
7. Sound person	6·95	8·20	1·25
8. Sound person	6·95	8·20	1·25
9. Sound person	5·06	6·31	1·25
10. Asthma bronchiale	5·32	6·57	1·25
11. Myodegeneratio cordis	5·70	7·21	1·51
12. Sound person	4·05	5·56	1·51
13. Sound person	7·84	9·50	1·66
14. Renal diabetes	5·06	6·76	1·70
15. Lues congenitalis	3·17	5·06	1·89
16. Myodegeneratio cordis	6·71	8·73	2·02
17. Sound person	5·99	8·03	2·04
18. Diabetes	4·45	6·57	2·12
19. Sound person	4·57	6·70	2·13
20. Diabetes	5·20	7·49	2·29
21. Osteomyelitis	5·30	7·64	2·34
22. Hyperthyreodism	4·42	6·90	2·48
23. Ischias	2·97	5·47	2·50
24. Sound person	5·06	7·84	2·78
25. Cancer of liver	6·08	9·00	2·92
26. Sound person	4·05	7·15	3·10
27. Sound person	5·75	8·91	3·18
28. Sound person	3·52	6·76	3·24
29. Cancer of stomach	4·41	7·98	3·57
30. Sound person	4·94	8·94	4·00
31. Myelitis	2·42	6·75	4·33
32. Cancer of stomach	4·41	9·48	5·07

Average: 1·92

[1] FALTA, Die Zuckerkrankheit, 1944, p. 161.
[2] HETÉNYI, Anyagcserebetegségek (Hungarian) (1933).
[3] FORRÓ, Wiener klin. Wschr. 2, 1337 (1933).

Pregnant cases

month	IInd–IIId month		
1. IInd	4·92	6·88	1·96
2. IInd	4·05	5·68	1·63
3. IIId	4·12	6·92	2·80
	IIId–IXth month		
4. IIId	6·90	7·77	0·87
5. IIId	5·45	5·45	0
6. IVth	5·12	5·95	0·77
7. Vth	3·44	3·44	0
8. Vth	5·06	5·06	0
9. VIth	6·20	7·87	1·67
10. VIth	7·06	7·51	0·45
11. VIth	7·21	6·45	−0·76
12. VIIth	4·69	5·45	0·76
13. VIIth	4·94	5·86	0·76
14. VIIth	5·06	5·57	0·51
15. VIIth	5·45	6·32	0·83
16. VIIth	7·84	7·97	0·13
17. VIIIth	1·40	2·16	0·76
18. VIIIth	4·78	4·78	0
19. IXth	4·10	4·10	0
20. IXth	6·95	6·95	0
21. IXth	7·72	7·20	−0·52
Average (IIId–IXth month): 0·31			

action of the fœtal pancreas contributing with its insulin production to the sugar metabolism of the mother. This explanation cannot be regarded as satisfactory. Our results speak in favour of the assumption that the secretion of diabetogenic hormone is greatly diminished in pregnancy after the third month, and that this is the cause of amelioration of diabetes in pregnancy.

A. GÓTH, G. BIKICH, H. HARMATH

St. János Hospital, Medical Department I, Budapest, February 28, 1947.

Résumé

6 heures après l'absorption de graisse et d'albumine, on constate dans le sang une augmentation de la concentration des substances qui fixent le bisulfite. Cette augmentation, due à des combinaisons cétoniques, ne se produit pas pendant la grossesse à partir du 3me ou du 4me mois. Elle fait aussi défaut, dans certains cas, pendant la lactation. Du moment que l'augmentation de la teneur du sang en bisulfites ne se produit pas non plus lors d'une déficience du lobe antérieur de l'hypophyse, il semble que l'on en peut conclure que durant la grossesse la sécrétion de l'hormone diabétogénique du lobe antérieur est fortement diminuée ou que l'action de celle-ci est enrayée.

The Mechanism of the Biochemical Activity of Acridines

In two preceding papers[1] we have shown: (1) that acridines (and basic dyes in general) inhibit the respiration and the growth of baker's yeast; (2) that the inhibition of respiration can be reversed not only by means of nucleic acid and of nucleotides, but also by means of salts. This paper offers an explanation of the above stated facts.

In first instance we have now proved that acridines are bound by the nucleoproteids of the yeast cell; indeed, we were able to show that dried and alcohol-fixed yeast cells are no longer colored by acridines after treatment with cristalline ribonuclease.

The binding of acridines (and other basic dyes) is based upon the formation of an electro-adsorption complex between the negatively charged nucleoproteids and the acridine ions. We can represent such complexes as follows:

$$(NP^{x-})\ (x\ acri^{+}).$$

That such complexes are really built can be shown readily by desorption experiments by means of different cations, such as H^+, Na^+, Ng^{++}, Al^{+++}. In our experiments we proceeded in three different ways:

(1) On a series of watch glasses we put 0,1 ml of a 1% suspension of baker's yeast; we dry it at a temperature below 70° C, fix it during 10 minutes by means of alcohol and stain with acridines (trypaflavine); then we wash with alcohol until the washing fluid is colorless. The preparations thus stained lose their color partially or completely when treated with different salt solutions, in which the cation is the active agent. We have found that the power of the cations to wash out the acridines depends on their valence. The position of the hydrogen ion is, however, an outstanding one.

We admit that when Mg-ions are employed to wash out the acridines, a new complex is built such as:

$$(NP^{x-})\ \left(\frac{x}{2}\ Mg^{++}\right).$$

This means that in the adsorption complexes we admit the possibility of a competition between cations, and that mixed complexes exist such as:

$$(NP^{x-})\ \left(\begin{matrix}H^+\\ Mg^{++}\\ Al^{+++}\\ A\end{matrix}\right)$$

x positive charges.

It is to be recalled that here MAC CALLA[1] proved the existence of a competition between different cations in complexes formed between negatively charged bacterial cells and cations.

(2) We have stained dried and alcohol-fixed yeast cells on the one side with acridines (or other basic dyes) and on the other with acridine solutions containing different concentrations of different cations (H^+, Na^+, Mg^{++}, Al^{+++}); we have then measured the amount of acridine fixed in the two cases. We have found that the same laws apply as in the first series of experiments; that is to say, in the presence of cations no or less acridine is bound, and the valence of the cation (except for H^+) is the determining factor.

(3) With living yeast cells the same facts were observed. We have treated living yeast cells with acridines in the presence and in the absence of different cations. After centrifuging the color of the supernatant fluid was determined.

[1] L. MASSART, G. PEETERS, J. DE LEY, and R. VERCAUTEREN, Exper. *3*, 119 (1947); *3*, 154 (1947).

[1] MAC CALLÁ: stated by G. B. WISLOCKI, Physiol. Prev. *26*, 3 (1946).