applying this method to several important problems and in describing in this book the processes used by him. This method undoubtedly has a great future, and will make possible computations that are so laborious by ordinary processes as to make them impracticable. The cost of renting the machines, which at present is the only way they are made available, is necessarily high; but with their more extended use this cost will unquestionably be reduced. In the meantime astronomers have reason to be grateful to the Thomas J. Watson Astronomical Computing Bureau for its services, which cost nothing more than the salaries of the operators on any piece of work accepted by its Board of Managers. Yale Observatory has especial reason to express such thanks, several very large projects having been made possible in this way.

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JOHN ALFRED BRASHEAR

John Alfred Brashear, Scientist and Humanitarian. By HARRIET A. GAUL and RUBY EISEMAN. viii + 220 pp. Philadelphia: University of Pennsylvania Press. 1940. $2.25.

THIS biography of a man who was born a hundred years ago and died twenty years ago, is a sympathetic portrayal of the life of a man who was not great in his scientific achievements, but who had a great influence upon others, who in their turn gave money to encourage and support scientific and educational enterprises in Pittsburgh. It is written not for the scientist but for the layman and is one in a series of lives of prominent Pennsylvanians. The life of "Uncle John" is a success story of the nineteenth century. Here a young man of humble parentage and little book learning rises from millwright to helper of the eminent Langley and to friend of the millionaires, Frick, Schwab, Phipps, Thaw and Carnegie. He is recognized in science for the "Brashear" method for silvering mirrors and for the fine optical instruments, including spectroscopes, rock-salt prisms and telescopes, made in his shop. But this book does not dwell at length on these achievements as much as on the civic responsibilities he assumed and on the influence he had over educational Pittsburgh at the turn of the century as the director of the Allegheny Observatory, as the chancellor of the Western University of Pennsylvania—now the University of Pittsburgh—as a trustee of the Carnegie Technical Schools, and finally, as the administrator of the Frick Educational Commission. The biography is simply written in a conversational style; it is at times amusing when anecdotes relating to the "Mill Lords" are told.

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SPECIAL ARTICLES

PARTIAL PROTECTION OF RATS BY RIBOFLAVIN WITH CASEIN AGAINST LIVER CANCER CAUSED BY DIMETHYLAMINOAZOBENZENE*

THE regular production of hepatic cirrhosis and cancer by the oral administration of dimethylaminoazobenzene (butter yellow) to rats has been reported by Kinosita.[1] The animals were fed 20 cc of a 3 per cent. solution of the chemical in olive oil mixed with 1,000 grams of a diet composed of unpolished rice supplemented with carrot. Subsequently, Nakahara[2] and his co-workers showed that no cirrhosis or cancer developed when this régime was supplemented with liver, and Ando[3] found that yeast had a similar effect.

Kensler, Sugiura and Rhoads[4] measured, by a modification of the method of Hodson and Norris,[5] the riboflavin levels in the livers of rats fed upon the basal diet as used by Kinosita, but without added butter yellow. The levels were found to be significantly lower than those of rats fed a stock laboratory diet. Moreover, if butter yellow was mixed with the rice, even less riboflavin was present in the livers. Most striking was the fact that the tumors which resulted from the carcinogenic régime contained only about 20 per cent. of the amount of riboflavin found in normal rat livers. If a protective supplement of yeast (Fleischmann 20–40) was administered, however, normal riboflavin levels in the livers were maintained and no cirrhosis or cancer resulted.

Further studies provide evidence that the basal diet as fed in this laboratory is inadequate in its content of riboflavin, since it supplies only about 6 micrograms of the vitamin daily. It is usually stated that about 15 micrograms daily are required to maintain rats in health. Furthermore, experiment proved that the animals fed the basal diet alone excrete in the urine very little riboflavin (2 micrograms daily per rat), less than 20 per cent. of that excreted by animals which receive the usual laboratory ration. If butter yellow is administered with the basal diet, a

* A grant from Standard Brands, Inc., and the Jane Coffin Childs Memorial Fund for Medical Research, in support of this work is gratefully acknowledged.

1 R. Kinosita, *Trans. Soc. Path. Jap.*, 27: 665, 1937.

2 W. Nakahara, T. Fujiwara and K. Mori, *Gann*, 33: 57, 1939.

3 T. Ando, *Gann*, 32: 252, 1938.

4 C. J. Kensler, K. Sugiura and C. P. Rhoads, SCIENCE, 91: 623, 1940.

5 A. Z. Hodson and L. C. Norris, *Jour. Biol. Chem.*, 131: 621, 1939.

primary increased excretion of riboflavin is followed by a progressive decrease until markedly subnormal levels are found. The direct fluorometric method of Ferrebee[6] was employed in these studies.

These facts prove that a riboflavin deficiency coincides with the susceptibility to the carcinogenic effect of butter yellow, and they suggested to us the possibility that riboflavin is the protective factor supplied by yeast. Nakahara,[7] however, was unable to show any protection from the use, as a supplement, of a liver eluate preparation which supplied 20 micrograms of riboflavin daily. Similarly, it was found in this laboratory that the oral administration of 5 mg daily of pure riboflavin[8] was almost without protective effect. It is clear that if riboflavin lack plays any part in the cause of the susceptibility to cancer production which results from the administration of the basal diet, some factor besides that vitamin is also wanting.

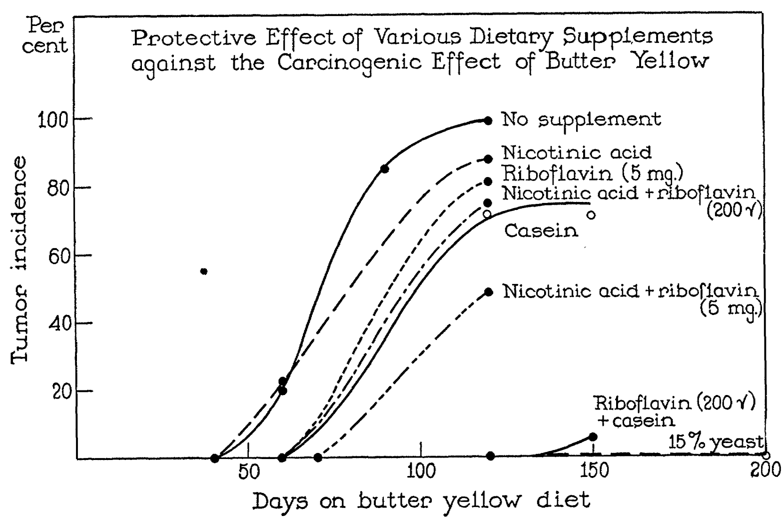

FIG. 1

Accordingly, various other supplements were tested with and without the addition of riboflavin. Among these supplements were nicotinic acid, corn oil and casein (Table I) of which none gave significant protection when administered alone. When nicotinic acid was combined with riboflavin (5 mg daily), however, a definite (50 per cent.) decrease in cancer incidence resulted. In a second experiment a smaller amount of riboflavin (200 micrograms daily) fed with the nicotinic acid resulted in a smaller decrease in incidence (10–20 per cent.).

When casein was administered as an additional supplement to the 200 micrograms daily of riboflavin, however, the protective effect was striking, though not absolute. From a cancer incidence of from 70 to 80 per cent., when either substance alone was employed, the figure decreased to an average of 3 per cent. (1 animal at 150 days) in 2 experiments which included 26 rats. The lack of gross morphological alterations in the livers of these protected animals was in accord with the measurements of the riboflavin contents of the same organs. Normal rat livers contain an average of 29.3 micrograms of riboflavin per gram, but those of rats taking the supplements of casein, corn oil or riboflavin alone contained an average of under 18 micrograms. When riboflavin was combined with casein the average content was 27.2 micrograms, a level close to the normal.

The relationship between the protection afforded by these various supplements and the length of time that the animals were fed butter yellow is shown in Fig. 1. Whereas none of the animals which received 15 per cent. of the diet as yeast (Fleischmann 20-40) showed any gross or microscopical evidence of liver damage at 200 days, one rat (Table I) which received the riboflavin-casein supplement had a hepatoma at 150 days. Furthermore, the livers of four of these animals showed microscopic evidence of damage without tumor formation, a picture comparable to that shown by rats given the unsupplemented basal diet with butter yellow for about 35 days.

From the evidence presented, it appears that at least two factors are lacking in the basal diet of brown rice and carrot which renders rats susceptible to the carcinogenic effect of butter yellow. One of these factors is riboflavin, and "vitamin-free" alcohol-extracted casein provides another. The means by which casein exerts its protective effect has not been identified, although work on this point is in progress.

[6] J. W. Ferrebee, *Jour. Clin. Investigation,* 19: 251, 1940.

[7] W. Nakahara, K. Mori and T. Fujiwara, *Gann,* 33: 406, 1939.

[8] Supplied through the courtesy of Merck and Company.

TABLE I

Length of time B.Y. diet (days)	Supplement		No. rats assayed	No. rats with liver cancer	Per cent. rats with liver cancer	Riboflavin liver levels micrograms/gram fresh liver (most normal tissue)
	Material	Am't/rat/day				
110–130	0	0	35	34	97	10.5
117–126	Riboflavin	5 mg	16	13	81	18.2
118–126	Nicotinic acid	3 "	15	13	87	20.0
115–145	Riboflavin	5 "	17	8	47	26.6
	Nicotinic acid	3 "				
124	Riboflavin	200 micrograms	8	6	75	21.2
	Nicotinic acid	3 mg				
120	Corn oil	400 mg	5	5	100	11.5
120	Riboflavin	200 micrograms	10	8	80	18.2
	Corn oil	400 mg				
120	Casein	2 gm	10	8	80	13.8
	Corn oil	400 mg				
120	Riboflavin	200 micrograms	10	0	0	28.4
	Casein	2 gm				
	Corn oil	400 mg				
149	Casein	2 gm	17	12	71	17.1
150	Riboflavin	200 micrograms	16	1	6	26.0
	Casein	2 gm				
160–210	Yeast (20–40)	1.5 gm	22	0	0	28.2
Rats fed normal diet, average						29.3
Rats fed basal diet of brown rice and carrot, average						17.2
Liver cancer which results from the feeding of butter yellow with basal diet, average						5.0

NOTE. The use of casein in these experiments was suggested by a joint study in progress with Professors Vincent du Vigneaud and Dean Burk, of Cornell University Medical College. With them various factors that might be involved in addition to riboflavin are under investigation, particularly the sulfur-containing amino acids.

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INHIBITION OF LIPASE ACTIVITY IN RAW MILK

ONE of the most objectionable flavors which occurs occasionally in milk is the so-called rancid flavor. This flavor is due to a partial hydrolysis of milk fat by lipase. The presence of free fatty acids of lower molecular weight in milk, and especially that of butyric, is responsible for this flavor.

Ordinarily, when cows have an access to green feed the problem of lipolysis in milk is not of great concern. However, in the winter time, when cows are on dry feed, the milk industry is confronted with a serious problem of spontaneous lipolysis in milk from cows that are usually late in lactation. The milk will become rancid without any apparent activation measures, such as homogenization, usually on standing four hours or longer after milking, unless the milk is pasteurized in time to inactivate the lipase.

In the course of a study of the factors responsible for the wide variation in the concentration of naturally active lipase in milk we were impressed with the phenomenon of the absence of lipolysis while the milk is in the udder, no matter how high the concentration of lipase in milk might be potentially. The speculation upon this feature, together with some other irregularities in the activity of lipase, led us to the discovery which, we hope, will give a sounder basis for further study of lipase activity in milk, and, in some measure, will be of immediate value to men in industry and of interest to biochemists.

We employed the measurements of surface tension of milk (as well as of pH and titratable acidity when it was feasible) to determine the rate of lipase action. Briefly, our data on milk containing a naturally active lipase, obtained from several cows at various times, show:

1. After milk is drawn from the udder the lipase is activated by cooling of milk. As long as the milk is kept at a temperature of the body or near to it the enzyme remains relatively inactive almost for the duration of the life of milk. In fact, the rate of lipase action is so negligible even at temperatures between 30°–20° C., that milk relatively high in lipase will still not become significantly rancid unless the milk is cooled during aging to a lower temperature. The critical cooling temperature appears to be between 20°–15° C. and the rate of lipase action is increased with progressive cooling to lower temperatures. The most important feature of the activation of milk lipase by cooling is that once the milk has been cooled, the activity of lipase is not materially affected whether the milk is aged in the cold or rewarmed immediately to 20°, 30°, or 37° C. after cooling and aged at those temperatures. Actually, the velocity of lipase action on milk fat is even slightly greater when cooled milk is rewarmed to 25° C. and aged at 20°–25° C., provided the milk is of low bacteria count. The rapid growth of certain bacteria and the development of acid, we know,[1] will hinder the speed of lipolysis. It is also clear that the

[1] N. P. Tarassuk and F. R. Smith, *Jour. Dairy Sci.*, 23: 1163–1170, 1940.