placed on the deficient diet after mating. These animals were then sacrificed on the 9th, 11th, 13th and 14th days after insemination, and the uteri examined. It was found that embryos of normal size and appearance were present on the 9th day, whereas by the 14th day almost complete resorption had occurred, the embryonic masses being then scarcely discernible. A similarly treated control animal sacrificed on the 14th day of gestation showed twelve normal sized embryos.

It would appear from the above experiments that tryptophane is a most important dietary essential for normal gestation and that the available stores of the adult female rat are depleted in the course of ten days of a tryptophane deficient regimen.

We have found no reports in the literature dealing with the effect of tryptophane deficiency on the female reproductive function. However, numerous studies are to be found[9] on the deleterious effects of low protein diets on the reproduction of farm animals, and Guilbert and Goss[10] have shown that feeding a low protein diet to female rats results in reproductive failure. In the light of our findings it is pertinent to raise the question whether these effects of a low protein diet may be attributed to a low tryptophane intake.

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INFLUENCE OF FEVER UPON THE ACTION OF 3,3′-METHYLENE-BIS-(4-HYDROXY-COUMARIN) (DICUMAROL)

FOLLOWING the isolation and synthesis of the anticoagulant Dicumarol (3,3′-methylene-bis-(4-hydroxycoumarin) by K. P. Link and collaborators,[1,2] this drug has rapidly gained the attention of scientists and clinicians alike. Since this drug will frequently be used in conditions accompanied by fever, it appeared desirable to investigate the influence of higher body temperatures upon its action. It is well known that biochemical reactions are accelerated by increase in temperature, but the degree of this acceleration varies greatly from instance to instance, depending on the type, and may show unexplained abnormalities.[3]

Fever was induced in rats by the injection of a yeast suspension or typhoid vaccine which resulted in a marked rise of temperature 5 to 15 hours later. If necessary, a second injection was made. Twelve hours after the administration of the pyrogenic agent, the rats were fed 2.5 mg Dicumarol orally. Prothrombin time was determined in 12.5 per cent. plasma 24 hours after Dicumarol administration, using the method described by Link and associates.[4] In normal rats this dose of Dicumarol raises the prothrombin time from about 45 seconds to 1 minute, 47 seconds. Fever alone causes no or only a very slight increase in prothrombin time. However, animals having received Dicumarol during fever showed a tremendous increase of the prothrombin time as compared with the rats having a normal temperature.

TABLE 1

EFFECT OF 2.5 MG DICUMAROL IN RATS (PROTHROMBIN TIME OF 12.5 PER CENT. PLASMA 24 HOURS AFTER ADMINISTRATION)

	Group				
	A	B	C	D	E
Maximal rectal temperature (°F)	99.2 ± .3	100.3 101.0	101.2 102.0	102.2 103.0	103.2 104.0
Number of animals..	9	7	10	7	11
Prothrombin time ...	1′47″	4′06″	5′55″	6′10″	8′55″
Standard error	0′10″	0′25″	0′50″	1′04″	0′56″
Group A : Normal rats		Group B–E : Rats in fever			

The degree of this increase of the prothrombin time varied considerably but tended to become more pronounced with higher temperatures. A response to Dicumarol falling within the limits of normal variation occurred only three times among the rats in the stage of fever. To facilitate tabulation the value of 12 minutes was deliberately attributed to experiments in which clotting was delayed for an indefinite period in excess of 12 minutes. This occurred once in Group C and D and five times in Group E. For classification we used the maximal temperature attained during the experiment. Due to the variation of the response and the necessary deliberate form of classification, the standard error of the single groups is considerable, but statistical evaluation has shown that the differences between normal and pyretic rats are significant.

Details and further work in which changes in the metabolic rate were produced by increasing the environmental temperature or by other methods will be reported later. As far as we know, no definite observations of this type have been published so far. Our observations suggest that the administration of this drug should be particularly watched in patients having an increased body temperature, to avoid a dangerous depression of the prothrombin level.

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