

furnishes to the growth of connective tissue—a stimulation also probably partly to be explained on mechanical grounds.

The question naturally arises, granting the abnormal coagulability of the blood, why thrombi should occur in cerebral venules rather than elsewhere. It is well recognized that venous blood coagulates more readily than arterial, perhaps because of its higher hydrogen-ion concentration, and the oxygen consumption of the brain exceeds that of other organs.¹⁰ Further, the cerebral venules are unusually small, variable in caliber and tortuous¹¹—structural factors which impede the flow of blood and so doubtless favor clotting. But perhaps it should be admitted that we have no data in regard to the presence of thrombi in venules in other parts of the body. It is quite possible that they do occur, disappear and, except in the nervous system, leave no trace behind.

The problems of the precise nature of the change in coagulability of the blood, of its cause, and whether it may be influenced by any therapeutic procedure, are still under investigation.

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THE MUCOID PHASE OF *STREPTOCOCCUS HEMOLYTICUS*

IN a recent communication¹ evidence was presented to show that *Streptococcus hemolyticus* possesses three chief variant phases: (1) M (mucoid); (2) S (smooth); and (3) R (rough). Further evidence was presented to show that these three chief variant phases of *Streptococcus hemolyticus* correspond closely with the three chief variant phases of a wide variety of other bacteria. Three similar variant forms have also been identified for pneumococcus.² In the case of the latter bacterial species, however, there exists an unfortunate inconsistency in the terms employed to describe those phases which correspond with the chief phases of other bacteria.

The nature and the significance of the mucoid phase of *Streptococcus hemolyticus* have recently been investigated in this laboratory. It has been shown that the use of Neopeptone rabbit's blood agar plates, to which 0.2 per cent. dextrose has been added, facilitates the development of mucoid colonies. Three hundred and sixty-three strains of *Streptococcus hemolyticus* have been examined on this medium. The strains have been obtained from a wide variety of sources and include 118 freshly isolated cultures. The

freshly isolated strains have been grown on Neopeptone media exclusively. The stock strains had been subcultured in a variety of media prior to the present study; they were then subcultured three times on Neopeptone blood-agar plates. The lack of uniformity in the cultural methods previously employed to grow the stock strains may therefore have appreciably affected the nature and appearance of the resulting growth. Under the conditions of the present study, however, the cultures exhibited a considerable degree of stability.

The source and nature of the cultures examined were as follows:

	Mucoid	Smooth
(1) Stock strains	108	137
(2) Freshly isolated strains	64	54
Total	172	191

Particular significance is attached to the origin of the mucoid and smooth variants, especially in the case of freshly isolated cultures. It can be definitely stated that there is a close parallelism between the type of infection and the variant form associated with that infection. Thus, with possibly one exception, all acute and fulminating infections have yielded mucoid organisms, while the smooth variant has almost invariably been associated with milder or more chronic forms of disease. Furthermore, there is suggestive evidence that, as the acuteness of the infectious process subsides, the organisms frequently change from the mucoid to the smooth phase. On the other hand, mucoid organisms have occasionally been encountered in the throats of individuals long after the acute stage of the infection has subsided.

Two main varieties of smooth organisms have also been identified; one of these produces convex, glossy colonies of moderate size; the other forms larger, flatter, faintly granular colonies with a "porridgy" consistency. The former variety is frequently associated with sub-acute or subsiding infections and the latter variety is commonly found in more chronic conditions and in apparently normal throats. The evidence suggests that these two forms constitute different phases of the same organism and that the larger colony represents the initial stage of a transformation to the true R form.

Virulence: Cultures exhibiting a high degree of virulence for white mice are usually, if not always, in the mucoid phase. On the other hand, all mucoid cultures are not necessarily virulent. Smooth cultures are definitely less virulent: in moderate dilutions they may cause the death of animals, but cultures from the peritoneum and heart's blood of such animals usually yield mucoid organisms. In these cases it seems reasonable to assume that there has been a change from the smooth to the mucoid phase within the animal body.

¹⁰ W. Lennox, *Arch. Neurol. and Psychiat.*, 6: 719-724, 1931.

¹¹ R. Pfeifer. Berlin: Julius Springer, 1930, pp. 220.

¹ M. H. Dawson, *Proc. Soc. Exper. Biol. and Med.*, 1934, 31, 590.

² M. H. Dawson, *Proc. Soc. Exper. Biol. and Med.*, 1933, 30, 806; *Jour. Path. and Bact.* (in press).

Capsule formation: Organisms in the mucoid phase form definite capsules. Such capsules can be readily demonstrated by Muir's stain in peritoneal exudates and with somewhat greater difficulty on organisms grown on solid media.

Lack of type-specificity: Preliminary agglutination studies have failed to yield any evidence of type-specificity for organisms in the mucoid phase.

Soluble substance: Filtered saline suspensions of organisms in the mucoid phase give a definite precipitate with serum prepared against organisms in that phase. This precipitable substance appears to be different from any previously isolated constituent of *Streptococcus hemolyticus*. The indications are that this substance is common to the mucoid phase of the several strains examined. The chemical nature of this soluble substance is being further investigated.

SUMMARY

(1) The occurrence and distribution of the mucoid phase of *Streptococcus hemolyticus* is indicated.

(2) Severe and acute infections usually yield organisms in the mucoid phase: mild and chronic infections usually yield smooth organisms.

(3) Organisms which are highly virulent for mice produce mucoid colonies; but all mucoid cultures are not necessarily virulent.

(4) Organisms in the mucoid phase produce a soluble precipitable substance which is common to the several strains examined.

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AN EXPERIMENTAL ANALYSIS OF THE CAUSE OF POPULATION FLUCTUATIONS

It has previously been shown that populations of the confused flour beetle (*Tribolium confusum* Duval) which are confined in beakers of whole wheat flour come to a "steady state" or "quasi-equilibrium," especially with respect to the adult populations.^{1, 2, 3} Under such conditions the egg populations show certain interesting and periodic fluctuations. It has been the object of the experiments under consideration to determine the causes of these fluctuations.

¹ Royal N. Chapman, "Quantitative Analysis of Environmental Factors," *Ecology*, 9: 111-122, 1928.

² F. G. Holdaway, "An Experimental Study of the Growth of Populations of the Flour Beetle *Tribolium confusum* Duval, as Affected by Atmospheric Moisture," *Ecol. Monographs*, 2: 261-304, 1932.

³ John Stanley, "A Mathematical Theory of the Growth of Populations of the Flour Beetle, *Tribolium confusum* Duval," *Canadian Jour. Res.*, 6: 632-671 and 7: 426-550, 1932.

When an experiment is initiated with a number of adult beetles that is well below the "saturation point," the number of eggs present in the environment increases until it approaches the "potential number"⁴ and then drops off to rise again when the daughters of the original population begin to lay eggs. Theoretically, the number of eggs present in the environment should remain at the "potential number" unless the females cease to lay their daily quota of eggs or some factor within the environment causes the eggs to disappear. The basis for this statement is the fact that the daily quota of eggs will accumulate each day during the period between oviposition and hatching. On the day that the first daily quota of eggs hatches an equal number of eggs will be laid and the number of eggs present in the environment should remain constant. If there is a change in the number of eggs present it must mean either that the oviposition rate has not remained constant or that some factor in the environment has interfered with the eggs. Good⁵ and others have shown that under ordinary conditions the females continue to lay eggs for over a year; hence it seems that some factor in the environment may be involved.

It has been shown repeatedly that the number of eggs rises to the potential number and then falls to a low level as the number of larvae in the environment increases.⁶ Park⁷ and MacLagan⁸ have called attention to the fact that the net number of eggs present in such environments, expressed as eggs per female per day, decreases as the population increases. The attention of these authors has been devoted primarily to the matter of adult populations and they have concluded that the reduction in the number of eggs and larvae has been due to a decrease in the rate of oviposition. It is difficult to prove that oviposition is the variable factor, because the coefficient of variability of the rate of oviposition of individual females has been determined to be as high as 62 per cent.⁹

In the experiments now being reported upon, "oviposition" was maintained constant in order to mea-

⁴ The "potential number" is the product of the average number of eggs laid per female per day, the number of days required for the eggs to hatch and the number of females present.

⁵ Newell E. Good, "Biology of the Flour Beetles, *Tribolium confusum* Duv. and *T. ferrugineum* Fab.," *Jour. Agr. Res.*, 46: 327-334, 1933.

⁶ Royal N. Chapman, "Animal Ecology," McGraw-Hill Book Co., pp. 212-214, 1931.

⁷ Thomas Park, "Studies in Population Physiology: The Relation of Numbers to Initial Population Growth in the Flour Beetle, *Tribolium confusum* Duval," *Ecology*, 13: 172-181, 1932.

⁸ D. S. MacLagan, "The Effect of Population Density upon Rate of Reproduction with Special Reference to Insects," *Proc. Roy. Soc., B.* 111: 437-454, 1932.

⁹ Royal N. Chapman and Lillian Baird, "The Biotic Constants of *Tribolium confusum* Duv.," *Jour. Exp. Zool.* In press.