

possible. Mrs. Gaskell's book can hardly be considered a contribution to the problem of abiogenesis and the nature of life, however interesting it may be as a speculative essay.

H. F. ISRAEL,
L. P. HERRINGTON

STANFORD UNIVERSITY

SPECIAL ARTICLES

A POSSIBLE METHOD OF ENHANCING THE THERAPEUTIC ACTION OF ANTIBACTERIAL SERUMS

THE therapeutic effect of antibacterial serums designed to act directly upon bacteria, as contrasted with antitoxic serums which act on their soluble toxins, has been notoriously disappointing. This seems surprising in view of the demonstration in such antisera of antagonistic substances which are known to combine with bacteria and lead directly or indirectly to their destruction in the test-tube and even in the animal body. It is our opinion that only one antibacterial serum, namely that directed against the meningococcus, can be regarded as having approached expectation. For many years efforts have been made to increase the effect of such antibacterial serums by intensifying their content in antibodies or by attempting to conserve original antigenic complexes in the bacteria used for immunization. We believe that we may now be in a position to explain the reason for the inadequacy of antibacterial serums in general and to hint at possibilities for its remedy.

In a series of articles for the past ten years, we have been interested in emphasizing the importance of fixed and mobile tissue cells of the mononuclear series (clasmatoocytes, polyblasts or histiocytes), particularly as they exist in granulation tissue, in enhancing the natural resistance of animals to localized infections. It has been found that non-specific mobilization of these clasmatoocytes causes an area in which they have been accumulated to be markedly resistant to an otherwise extremely pathogenic strain of streptococcus. Moreover, it has been shown¹ that these cells, once accumulated, are, within certain limits, mobile from one part of the body to another in response to a localized infection. For example, the transfer of an irritated omentum containing large numbers of these cells from one animal into the peritoneum of another will, to a moderate degree, lead to increased resistance in the recipient's pleura. It is possible, even, to use the omentum of another animal species, like the guinea-pig, in the rabbit.

¹ Gay, Clark and Linton, *Arch. Path.*, 1: 857, 1926; Linton, *Arch. Path.*, 6: 615, 1928.

Our own experience, as well as the results of others, have brought the realization that this simple accumulation of clasmatoocytes, although markedly successful against streptococcus and staphylococcus, does not protect against other micro-organisms such as the *Treponema pallidum*, the Pasteurella group² and particularly the pneumococcus. The hitherto unpublished studies of one of us (A.R.C.) with the pneumococcus have thrown an extremely interesting light on this apparent ineffectiveness of clasmatoocytes. The prepared pleural cavity of the rabbit, which protects the animal so well against the streptococcus, has not, alone, the slightest effect in protection against the pneumococcus, although the strain of this latter organism employed was apparently of the same grade of pathogenicity as the streptococcus against which marked protection was assured. Washing the pneumococcus led to no greater protection. When, however, the pneumococcus was treated with a small amount of antiserum, a very marked protection resulted. The same sensitized pneumococci in the doses used were rapidly fatal for unprepared rabbits and for rabbits whose pleural cavity exhibited an acute inflammatory exudate. (Polymorphonuclear.)

These results are one step beyond those obtained by Singer and Adler³ and Tudoranu,⁴ who have come to the conclusion that active immunity in animals against both pneumococcus Type I and pneumococcus Type III infections is due to a cooperation of mononuclear cells and the antiserum, the first factor being the more significant one. This explanation is paralleled by a similar explanation of active acquired immunity to the streptococcus suggested by Bass⁵ and Kanai.⁶ The brilliant experiments of Stuppy, Cannon and Falk⁷ still further emphasize the characteristics of active anti-pneumococcus immunity. These authors have recently found that when rabbits are locally immunized against pneumococcus through the respiratory tract a reinfection by this route is harmless, and is accompanied by a massing of mononuclear cells in the alveoli.

Our own experiments, then, have demonstrated that pneumococci differ from streptococci in regard to protective mechanisms in that the former require for disposal not only an adequate number of mononuclear cells, but tropinization by immune serum. The importance of the mononuclear cells, however, remains equally significant in both instances. We have further been able to show that, although two hundred lethal

² Halley, Chesney and Dresel, *Bull.*, Johns Hopkins Hospital, 41: 191, 1927.

³ *Zeit. für Immunitäts.*, 41: 418, 468, 1924.

⁴ *Annal. Pasteur*, 40: 606, 1926.

⁵ *Zeit. für Immunitäts.*, 42: 261, 1925.

⁶ *Verhand. der Japan. Path. Gesell.*, 9: 126, 1919.

⁷ *Proc. Soc. Exp. Biol. and Med.*, 36: 314, 1928.

doses of streptococci are ineffective in the presence of sufficient numbers of mononuclear cells alone, this resistance is still further enhanced to protection against some ten thousand doses if the streptococci are previously treated with immune serum. Such sensitization of the bacteria, however, does not suffice to afford protection in any degree to the normal animal or even when much larger amounts of immune serum are used.

Our suggestion, then, is that antibacterial serums fail to cure not through the absence of suitable or adequate amounts of antagonistic substances (tropins) but through the absence in the recipient of sufficient numbers of mononuclear cells necessary to accomplish the destruction of the tropinized bacteria. There is further evidence, which can not be recapitulated at this time, that the actively immunized animal varies from the normal animal in the rapidity with which mononuclear cells are mobilized at the point of inoculation, as is indicated by the work of Stuppy, Cannon and Falk, by certain types of local immune reactions and by the study of the conditions of local immunity. Furthermore, in spite of the fact that in the extensive studies of phagocytosis by polymorphonuclears it has been generally accepted that these cells do not differ in the immune animal from their originals in the normal animal, we believe that a study of the qualitative reactivity of the macrophages in the immune animal is indicated. It may well be that not only are mononuclear cells in sufficient number necessary, but that mononuclear cells of an actively immune animal are required to insure passive immunity. Either variety of cells could certainly be supplied from homologous or possibly heterologous animals, and the hypothesis here stated is at least capable of experimental study, whatever the practical outcome in serum therapy may be. Experiments along this line are actively in course.

FREDERICK P. GAY
ADA R. CLARK

COLLEGE OF PHYSICIANS AND SURGEONS,
COLUMBIA UNIVERSITY

THE COMPOSITION OF PECULIAR CLINKERS FOUND IN SNAGS AFTER FOREST FIRES

CONSIDERABLE interest is being shown by the personnel of the U. S. Forest Service over the occasional finding of peculiar rock-like clinkers in hollow snags which are sometimes left after a forest has been burned over. These clinkers usually have a greenish tint and by some people are thought to be of meteoric origin and responsible for the starting of certain forest fires. While this theory of their origin seemed improbable there was still a general feeling that the

presence of the clinker material might be associated with hold-over fires, and a definite knowledge of their composition was desired. The matter was referred to us by Dr. Raymond Kienholz, of the department of botany at the University of Illinois, and all samples analyzed by us were collected by him while he was engaged in forest research work in the northwest. A fuller account of the finding of these clinkers with respect to geographic distribution, forest species and fungal action will be reported later by Dr. Kienholz in the *Journal of Forestry*.

Samples I and II were found on the Kaniksu National Forest near Priest Lake in northern Idaho. Sample III was from the Wind River country of southern Washington, as was also the sample of sound wood. All were taken from the western hemlock (*Tsuga heterophylla*).

The results of the analyses are given in the following table.

CHEMICAL COMPOSITION OF THE CLINKERS AND ASH OF SOUND WOOD

Constituent	Percentage of constituent			
	Clinker I	Clinker II	Clinker III	Sound wood
Crude SiO ₂32	.38	.41
P ₂ O ₅	6.96	6.58	5.47	.0227
(Fe ₂ O ₃)				
R ₂ O ₃ (Al ₂ O ₃)	1.68	.99	.34	.0096
SO ₃	Trace	Trace	.67
Cl	Trace	Trace	Trace
CaO	22.02	21.90	21.79	.0424
MgO	6.28	4.48	4.06	.0226
Mn ₂ O ₄	1.21	1.32	7.17	.0252
K ₂ O	25.01	24.54	30.42	.0750
Na ₂ O	5.31	2.06	4.20	.0173
CO ₂	19.76	25.47
Total	88.35	87.72	74.47	.2148
Difference (including H ₂ O, carbon, etc.)	11.65	12.28	25.53 (incl. CO ₂)	

An examination of the table shows that the clinkers are all of quite similar composition. This is especially true of the two from the same locality. Very little data on the complete analysis of ash of American woods is available for the comparison of composition, but rather wide variation would be expected. The species, section of the tree from which the wood was taken, locality in which the tree was grown, and other factors would have a marked influence. If the ratio of each other constituent to K₂O be calculated for clinker III and the ash of the sound wood from the same locality a very close analogy of composition will be observed.