

considering that 0.7 per cent of flavin phosphate found by Haas<sup>3</sup> in his flavo-protein from yeast is the highest flavin content so far obtained.

The new flavo-protein is readily soluble in distilled water, giving a greenish yellow solution. The prosthetic group can replace quantitatively the coenzyme of the *d*-amino-acid oxidase and is considered to be the same compound.

The details of the purification will be given elsewhere.

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<sup>1</sup> Straub, F. B., *NATURE*, **141**, 603 (1938).

<sup>2</sup> Keilin, D., and Hartree, E. F., *Proc. Roy. Soc., B*, **125**, 171 (1938).

<sup>3</sup> Haas, E., *Biochem. Z.*, **298**, 378 (1938).

### Sulphanilamides and Rabies

HITHERTO, chemotherapy has seldom been successful in virus diseases, but the use of sulphanilamides in lymphogranuloma inguinale<sup>1</sup>, choriomeningitis<sup>2</sup>, and trachoma<sup>3</sup> has opened new possibilities in this field during the past year. There is, so far, no record of experimental work giving favourable results in the chemotherapy of rabies, however, and from an observation in Khartoum, the sulphanilamides appear to have no effect in this condition.

Four rabbits, of approximately equal size and weight, were infected subdurally with an emulsion of fixed virus (Paris strain), and three of these were given 1 c.c. Prontosil Soluble daily by the intravenous route for the following six days. The fourth was kept as a control, although this virus has never failed in Khartoum to produce paralytic rabies in six to seven days during numerous passages through sheep and rabbits since 1935, when it was obtained from the Public Health Laboratories in Jerusalem. By the seventh day all four rabbits were moribund, with typical signs of paralytic rabies, and were killed. No difference could be observed between the treated animals and the control, either in the incubation period or in any other feature of the disease.

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<sup>1</sup> MacCallum, R. O., and Findlay, G. M., *Lancet*, 136 (1938).

<sup>2</sup> Neal, J. B., *J. Amer. Med. Assoc.*, **3**, 1353 (1938).

<sup>3</sup> Kirk, R., McKelvie, A. R., and Hussein, H. A., *Lancet*, 994 (1938).

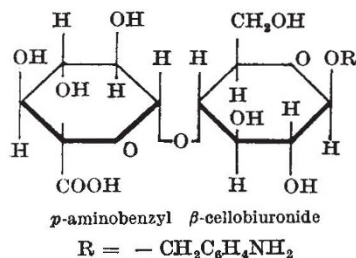
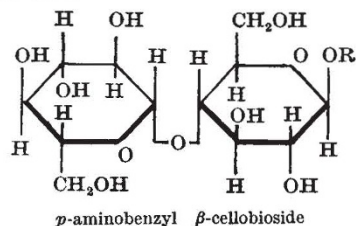
### Immunity to Experimental Pneumococcus Infection with an Artificial Antigen

FOR the past few years, we have been engaged in this laboratory in studying the factors which govern the immunological specificity of carbohydrates. This problem has been approached by an investigation of the chemical structure of the specific bacterial polysaccharides themselves and by a study of the immunological properties of artificial antigens prepared by combining the aminophenol or benzyl glycosides of saccharides of known structure with protein. The latter method has been of particular value in revealing certain of the fundamental factors which govern the specificity of carbohydrates. The stereochemical configuration of simple hexoses<sup>1</sup>, the

configuration of intramolecular linkages of disaccharides and the position of such linkages<sup>2</sup> are all-important determinants in orienting the specificities of these saccharides. More recently it has been found that the conversion of the primary alcohol group of a hexose to the carboxyl group likewise alters the immunological properties of artificial antigens containing the hexoses, as opposed to those containing the hexose uronic acids<sup>3</sup>.

Although antigens containing the hexose-uronic acids possess certain of the serological characteristics of the specific pneumococcus polysaccharides, for they precipitate in high dilutions in anti-pneumococcal horse sera of various types, it has as yet not been possible to produce anti-pneumococcal immunity by injecting animals with the glucuronic and galacturonic acid antigens. The reason probably is due to the fact that the hexose uronic acids do not approximate closely enough in structure to the more complex building stones of certain of the pneumococcus polysaccharides, the aldobionic acids. These observations have led to the belief that in order to evoke anti-pneumococcal immunity in experimental animals with an artificial antigen, it is not necessary to have as the immuno-specific group a long-chained type specific polysaccharide, but that a simpler saccharide, the pattern unit from which the polysaccharide is constituted, should suffice.

An artificial antigen has therefore been prepared by combining the diazonium derivative of the *p*-amino benzyl glycoside of cellobiuronic acid, the aldobionic acid from which the Type III pneumococcus polysaccharide is constituted<sup>4</sup>, with horse serum globulin<sup>5</sup>. For purposes of comparison, a similar antigen containing the corresponding glycoside of cellobiose has also been prepared. The chemical structure of the cellobioside and cellobiuronide is identical save for the grouping occupying the 12th position, as can be seen from the accompanying graphic formulæ.



This difference in chemical structure suffices, however, to confer on each antigen containing the glycosides vastly different immunological properties. The sera of rabbits injected with the cellobiuronic antigen precipitate the Type III pneumococcus specific polysaccharide, agglutinate Type III pneumococci, and produce a typical swelling of the capsule when living Type III organisms are mixed with the anti-serum.