

It was his opinion, long before editors discovered that this animal was good copy material, that the species was inconspicuous but relatively common.

I also discovered that several species of Hemiptera supposedly rare or absent in the Maryland fauna were quite common. Several presumably northern forms were found, not in the western part of the state where their presence would have been no surprise, but in a region that has a growing season of more than 200 days, at sea level. They were feeding on a host that is common only in the warmest parts of the state, and apparently no entomologist had ever taken the trouble to examine this plant during the autumn. It seems obvious that climate was not the factor that limited the distribution.

Without discounting the possibility of ecologic changes, increases in cold-hardiness, and similar factors, we ought to examine all reports of extensions into new territory with skepticism, unless they are supported by more than casual observation.

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## Mechanism of Suppression of Hemagglutinating Viruses

WE WISH to make confirmatory elaboration on the explanation of Groupe, Pugh, and Levine (1) for Newcastle disease virus inhibition by their achromobacter fermentation product (A.P.M.). They adduced evidence that A.P.M. probably acted by competition with a virus for receptors on the target cell rather than as a direct "virucidal" agent. On the other hand, McCrea and Duran-Reynals (2), in their report on vaccinia inhibition by hyaluronate-depolymer dialysate or glucuronolactone, imply virustatic or virucidal activity.

Preliminary clarification of the mode by which certain hemagglutinating-virus antagonists operate, pending appearance of a definitive report, may assist other investigators, because a hypothesis with seemingly broad implications has developed. Properties similar to those reported for A.P.M. had been encountered in the antibiotic-free and cobalamin-free carbohydrate fraction of the streptomycin fermentation residue made available as poultry feed (APF). Besides inhibiting vaccinia, Newcastle, and influenza virus hemagglutination, this fraction exhibited slight antihyaluronidase and antithrombic activity. The fraction was pigmented, so coprogen was tested and proved negative. However, lithium ferriprotoporphyrinate, a known antithrombic (3), as well as other vinyl porphyrins elicited decided inhibition of human erythrocyte hemagglutination (as evidenced in titrations with

type specific and "rhesus type" antibodies, the latter in both direct and "blocking antibody" phases), including that by influenza B, Newcastle, and vaccinia. Infectivity inhibition of the latter was also demonstrated, using NDV strain CVB-14 in the allantoic sac of eggs and lymph vaccinia (Lederle) in rabbit abdominal skin as described by McCrea and Duran-Reynals. As a matter of fact, ordinary "water-soluble chlorophyll" (which is a chemically defined genus of alkali cupri-monovinylidihydroporphyrinates) is a practically utilizable competitive inhibitor of the hemagglutinating viruses, duplicating the effect of A.P.M., or the depolymer dialysate of McCrea and Duran-Reynals, in 0.02-millimolar solution. Its inhibitory effect has been found to be competitive, as Groupe, Pugh, and Levine postulated for their "antivirals."

Further study with "chlorophyllin" allocated its competitive activity to the enhanced resonance conferred on the pyrroles by a chelated transition element metal. The carbocyclic ring of "dibasic chlorophyll" is noncontributory; "tribasic chlorophyllin" (in which this ring has been opened) is even more active (5). From consideration around isosterism of pyrrol and a potentially resonating furanoid structure for glucuronolactone, it had been postulated that low-molecular weight solutes having an "aromatic" heteropentacyclic ring might effect that resonance contribution which would be isosteric with the modality for virus (presumably the furanoid, ribose) attachment to the cell receptor and compete for the latter with the virus. The hypothesis became theory when Tamm, *et al.* (4) demonstrated influenza B inhibition by benzimidazoles, which have the postulated configuration. This inhibition, from their data, is evidently competitive.

It is fair to assume that, had thiazoles, pyrazolines, and thiophenes been tested under conditions which would have revealed competitive inhibition instead of having been tested for virucidal effect, the evanescent interest that they aroused as antivirals might have persisted. Their reexamination in this light seems warranted.

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## References

1. GROUPE, V., PUGH, L. H., and LEVINE, A. S. *Science* **118**, 187 (1953).
2. MCCREA, J. F., and DURAN-REYNALS, F. *Ibid.* **93**.
3. BARNARD, R. D. *J. Am. Pharm. Assoc.* **36**, 225 (1947).
4. TAMM, I., *et al.* *J. Exptl. Med.* **98**, 245 (1953).
5. BARNARD, R. D., KESSLER, L. N., GOLDMAN, B., and STANTON, H. T., JR. *J. Am. Pharm. Assoc.* In press.

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