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Absence of 'Incomplete' Virus Production in certain Influenza Strains

CONCENTRATED allantoic inocula of PR8 (influenza A) virus give rise to particles having the antigenic make-up, haemagglutinating power and enzymic activity of the seed, but lacking infectivity. Since it bears some resemblance to interference by an unrelated virus, the phenomenon was named 'auto-interference'¹. The use of this term was rather unfortunate: partly because Ziegler *et al.*² had previously proposed it to describe the behaviour of old virus preparations containing a large proportion of non-viable particles, as first observed by Henle and Henle³; and partly as it led to the belief that incomplete virus was produced by cells infected by more than one virus particle. Indeed, extensive theoretical predictions have been based on this assumption⁴. Experiments, however, soon revealed that, whatever its mechanism, multiplicity of infection cannot be implicated to account for the facts, as incomplete virus was produced when only 1 per cent of the cells had been infected⁵. This piece of negative evidence brought forward by Cairns and Edney is in itself sufficient to invalidate the hypothesis; here positive proof is furnished that certain strains of influenza virus do *not* produce incomplete particles even under conditions of multiple infection.

Fresh preparations of influenza viruses were inoculated into groups of six 11-day-old eggs, 0.6 ml. volumes of undiluted seed ($10^{9.18}ID_{50}$) or a 10^{-4} dilution being given allantoically. Samples of allantoic fluid were removed at the height of infectivity (after 24 and 48 hr. respectively), and each fluid was titrated for haemagglutinin against 0.25 ml. 1 per cent fowl red cells, and for infectivity in log 0.5-fold steps employing five eggs per dilution. The results obtained with the two classical strains, PR8 (A) and LEE (B), are sufficient to establish our thesis; the detailed findings with these and several other strains will be published elsewhere.

Inoculum		Yield*			Evaluation†	
Strain	Dilution	ID_{50} /ml.	HA/ml.	ID/HA	F	P
PR8	10^0	7.44	3.34	4.10 ± 0.138	88.56	<0.001
	10^{-4}	9.97	3.47	6.50 ± 0.214		
LEE	10^0	9.56	3.20	6.36 ± 0.136	1.61	~0.3
	10^{-4}	9.46	3.22	6.24 ± 0.135		

* Geometric mean and standard error of six parallel experiments (expressed in $\log_{10}$ units).

† Results of an analysis of variance; F = variance ratio, P = probability of the difference being due to chance.

It is evident that whereas the PR8 strain shows the typical behaviour described by von Magnus¹, no non-infective virus is produced by the LEE strain, although multiple infection has been ensured by the fact that the initial inoculum contained approximately

eight times as many ID_{50} as there are infectible cells. Thus the simultaneous infection of a cell by several homologous influenza virus particles does not necessarily result in depression of infective virus production. Consequently, the term 'auto-interference' prejudices our understanding of the underlying mechanism, and should not be used in connexion with incomplete virus production; it is best reserved for the phenomenon to which it has been appropriately applied by Ziegler and his associates².

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Possible P-Q Type Variation in Infectious Laryngotracheitis Virus

FROM an outbreak of acute infectious laryngotracheitis in South Australia¹ a strain of virus was isolated which proved to be highly resistant to neutralization by antisera in the pock neutralization test. On intratracheal inoculation into susceptible birds, it gave rise to typical acute infectious laryngotracheitis in about four days, produced a typical vaccination reaction when given by the cloacal route and gave rise to antibodies fully active against a type infectious laryngotracheitis virus. On primary isolation it showed some degree of resistance to neutralization by its homologous and other infectious laryngotracheitis antisera, but after storage for eight months in the 'dry ice' refrigerator it was almost completely resistant to neutralization by all available antisera (see table). Prior to this outbreak, infectious laryngotracheitis was not known to be present in South Australia despite a careful watch being kept, and no spread of the typical explosive epidemic form of the disease in other flocks has followed this outbreak. A survey of hens throughout South Australia showed that, at the time of isolation of this strain, about 50 per cent of the flocks had birds with demonstrable infectious laryngotracheitis antibodies in their sera.

A similar phenomenon was reported by Burnet² in 1936 in strains of infectious laryngotracheitis isolated in Victoria and New South Wales. Burnet stated that "no qualitative antigenic differences can be detected amongst these strains but the epizootic (N.S.W. and BAI) strains are more readily neutralised by immune serum than the enzootic Victorian strains".

POCK NEUTRALIZATION TESTS

Exp. No.	Virus	Antisera	
		Local strain (A)	Reference strain (S)
1 Fresh virus	A	1.0	1.5
	S	1.8	1.9
2 Stored virus	A	0.3	0.0
	S	1.7	2.1

The figures are the logarithms of the ratio of foci developing on the experimental to those on the control membranes.