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INCOMPLETE FORMS OF INFLUENZA VIRUS

being

a thesis submitted by

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for the

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The work presented in this thesis was carried out during my three years' tenure of a Research Assistantship in Microbiology at the Australian National University, Canberra.

The field of research was chosen by my supervisor, Dr. S. Fazekas de St.Groth, who is also mainly responsible for deciding upon the general lines of approach. The detailed planning of experiments was always the outcome of free discussions, shared about equally between supervisor and candidate. The experimental work described in Chapters 3 and 6 was done entirely by me, as well as three-quarters of that in Chapters 5 and 7, and half of that in Chapter 4. The evaluation of the results was done jointly with my supervisor, except for Chapters 4 and 7 which was done by me.

Collection of the material for Chapters 1, 2, 9, 10 and 11 is my work, as is the setting out and composition of the thesis. In some sections of Part II I have included, without acknowledgement, paragraphs from papers published under joint authorship with my supervisor.

*Doris M. Graham.*

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## INTRODUCTION.

Viruses occupy a unique position in the hierarchy of physical objects as they can be regarded as the most highly organized chemical structures which do not metabolize, or alternatively as the lowest forms of life that reproduce themselves at the expense of higher organisms. They "live a borrowed life" as Laidlaw put it, and for this precise reason their study is likely to give a better and more direct insight into the fundamental secrets of life than studies at the biochemical, or strictly speaking, microbiological level.

All viruses share these advantages as objects of research, but some are preferred to others for further, mainly technical, reasons. Among the animal viruses influenza is perhaps the most natural choice; it has some drawbacks such as its instability, both physical and biological, but possesses the compensating attraction of being the easiest to assay by several independent and accurate methods. In this respect the virus of epidemic influenza compares more than favourably with any known virus, be it plant, bacterial or animal, and for this reason has been the favoured subject of quantitative virological studies over the last decade.

dicted the reigning hypothesis and a new interpretation was put forward to replace it. The present work was undertaken originally with the intention of examining this new hypothesis by testing some of its more obvious implications. Very early in the course of our experiments such results were obtained which rendered even this second hypothesis untenable. Thus, instead of continuing the investigation of the von Magnus phenomenon along predetermined lines and by classical techniques, we were soon forced to embark on an extensive set of exploratory experiments, to construct step by step a working hypothesis consistent with newly gained information and to design new ways of testing and checking the new and often unexpected assumptions that had to be made. As a result, the study has gone beyond the theme originally set for this thesis, and while two fundamentally new findings, namely, the graded production of incomplete virus and the chemical induction of the phenomenon have been fully established, several interesting lines of research opened by these discoveries have been covered by exploratory experiments only, and their comprehensive investigation must be left for the future.