| Personal memo from JOSHUA LEDERBERG | Par Mal Res Inst MAY 18 1988 |
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| Richetts | |
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| Hes any | enough detail to |
| settle that | once and for all? |
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| End. Reply to H. V | P. Wyett" Xatur UL 239, 1972 ERSITY NEW YORK 1 |

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To return to Griffith: his was the successful, but it was not an isolated exemplar of transmissible heredity in the lst quarter of the century. Literature is rife with "paragglutination" The principal marker available for bacteriological diagnosis was agglutination by immune sera. These were imputed with a specificity that went far beyond the reality, and great notice was given to a) natural occurrences of serolological crossreactions, and b) to modifications arising in mixed infections or in mixed culture in the laboratory. Few reports offered a consistent, reproducible protocol. They are difficult, therefore, to interpret even in hindsight. The majority were probably rough, non-specifically agglutinating variants selected either by the metabolic milieu of the mixed cultures, or, in some cases by smooth-specific, lysogenic bacterophages. In view of what we now know of lysogenic conversion of somatic antigens in Salmonella, some of these mouldy papyri might have been an authentic starting point of genetic enquiry, but with the exception of Griffith's transformation, none was systematically followed up. We have no indication whether "paragglutination" was on Griffith's mind when he did his experiment. He surely was aware of that literature, and especially of the Weil-Felix reaction. This is a cross-reaction of the somatic polysaccharide antigens of Proteus X strains with rickettsia. Originally, these Proteus strains were isolated from the urine of typhus fever patients and were thought to have some etiological significance. This was discounted, but agglutination of Proteus X by patient sera was used for diagnosis. Some bacteriologists thought the cross-reaction was evidence of an "exchange of receptors", we would now say a genetic homology between Proteus X and rickettsia. This seems implausible, but I am not sure decisive tests of DNA homology have been conducted to this day.

