SOME INCIDENTAL OBSERVATIONS ON THE POSSIBILITY OF A VIRUS AS PART CAUSAL FACTOR IN RHEUMATISM

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THE following observations, though inconclusive, are recorded because they seem to have some relevance to the question of a virus as part causal factor in rheumatism.

I. A case of multiple arthritis of some duration, with deformities and X-ray rarefaction (sedimentation rate unknown), developed a very acute exacerbation in one knee-joint. Fluid from this joint was sent to the author for examination. Films showed a number of polymorphonuclear leucocytes and some lymphocytes, but no organisms. Culture on a large selection of media, aerobically and anaerobically, showed no infection even after prolonged incubation. A portion of the fluid was injected intraperitoneally into a guinea-pig. This pig remained apparently well for three months, when it died quite suddenly. Post-mortem showed an extremely distended pericardium. No other lesion was observed. The fluid from the pericardium was dealt with in three ways: (a) It was injected direct into the peritoneum of another pig; (b) it was planted into broth containing chopped-up portions of the dead pig's spleen; (c) it was planted on to a blood-plate, and the colony growing on the plate was subcultured into broth.

0.2 c.c. of tenfold serial dilutions of (b), the first spleen-broth culture, and 0.2 c.c. of similar dilutions of (c), the broth subculture from the blood-plate, were injected into pigs. The following results were observed:

1. Pig injected with (a), the direct pericardial fluid, remained apparently well for two months, and then died suddenly as from acute heart failure, with P.M. appearance similar to the original pig.

2. Pigs inoculated with the spleen-broth culture died as follows: with the strong dilutions, they died of septicaemia within three days with no gross sign of pericarditis; with the weak dilutions they remained perfectly well for two to three months, and then died suddenly in the manner of the first pig with similar P.M. appearances.

3. Pigs inoculated with (c), the broth subculture from the blood-plate, showed the following results: those with the strong dilutions died within three days of septicaemia; the others remained perfectly well even after twelve months.

The pericardial fluid from one of the pigs dying after two months was again dealt with in the manner described above, and with the same results.

Pericardial fluid from one of the second group of pigs was again dealt with in the same way. But on this, the third passage, the experiment failed: the pig receiving the direct pericardial fluid lived, and all the other pigs, except those receiving the strong culture dilutions and dying within three days, remained perfectly well. The phenomenon of death at two to three months with a very distended pericardium was lost.

The organism proved to be a pneumococcus Type 19 (curiously enough, the patient subsequently developed pneumonia, but unfortunately the pneumococcus was not typed). Pneumococcus Type 19 is particularly virulent to pigs, but I am not aware of its capacity to produce death at the above delayed interval with pronounced pericardial distension. There may be several explanations of the above phenomenon, but the hypothesis which appeals to me is that there was a virus in the synovial fluid which energised the pneumococcus in weak doses, and which died out on the third passage.

II. A case of arthritis had a relapse accompanied by a sore throat. Unfortunately skiagrams of the joints and sedimentation rates were not obtainable. A broth gargle was procured which was kept at cool room temperature overnight, and delivered to me next morning. This broth was etherised to kill the organisms present and culture thereafter proved it sterile for bacterial organisms. It was then placed in the incubator at 35° C. for six hours (this temperature being adopted on the assumption that any virus on the surface of the throat where inspired air was passing might prefer a lower temperature than 37° C.). At the end of this time the broth was divided into two portions: (a) was formalised with 0.5 per cent. formalin in the hope of procuring a vaccine; (b) was divided into two portions of which one was untreated and the second was heated at 65° C. for an hour. (These were deliberately not centrifuged, in case any small amount of virus present should have been adsorbed on to any organisms present.) The portion heated at 65° C.

was injected into the pad of a pig without any appreciable reaction resulting. The unheated portion injected into another pad produced a mild reaction. This pad was ground up in broth (2 c.c. of broth to the pad) and 0.2 c.c. of the resulting lightly centrifuged emulsion was injected into the pad of another pig. This produced a still milder reaction than the first unheated pad. This second passage pad was dealt with as above described, and 0.2 c.c. injected into a third pad. This produced no reaction: the reacting agent had either died out or been diluted out.

The formalised portion made for a vaccine was given (0.2 c.c. dose of $\frac{1}{1000}$ dilution) to three rheumatoid arthritis patients with unsatisfactory results: each patient had a very marked exacerbation of the joint condition.

III. An experiment, introduced to me by Dr. Mervyn Gordon, was undertaken on the energising power of M4 testicular passage vaccinia virus on hæmolytic streptococcus in producing arthritis in rabbits. The original David hæmolytic streptococcus was found on subculture to contain two varieties: (1) a medium-sized flat colony growing smoothly in serum broth; and (2) a small colony tending to show granularity in serum broth. Six rabbits were available for this experiment and were injected as follows:

1. 0.25 c.c. virus M4 alone.
2. „ David small streptococcus alone.
3. „ „ large „ „
4. „ virus plus 0.25 c.c. David large streptococcus.
5. „ „ „ „ „ „
6. „ „ „ „ small „

Injections were given every fourth day intravenously. Two days after the fourth injection rabbits 4, 5, and 6—*i.e.*, rabbits given streptococcus plus virus—had all developed limps. The rest showed no sign of limping.

Rabbit 6 unfortunately died of pericarditis a few days after developing a limp before gross changes in the joint had had time to develop, though the limp was well marked at the day of death. Rabbits 4 and 5 have developed gross lesions, and are being kept to observe the progress of the joint condition. This result confirms Dr. Mervyn Gordon's original experiment.

(I wish to thank Dr. Taylor for assistance with the rabbit experiment.)