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COLLEGE "[ROC]
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Telephones-

OFFICE BENTLEY

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Dear Mr. Guthrie,

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I think I ought to bring you up-to-date with regard to the rasearch programme now being carried out here.

In the original suggested outline of research six specific questions were posed (see page three), about which, with the exception of question three, conclusions had been reached by the time I was appointed. With regard to question three, epidemilogical evidence here would appear to show that no beneficial advantage would be obtained from regular prophylactic injections, largely because of the short half-life of Factor VIII in the body.

The present research programme has been planned so that there should be no overlapping with that being carried out at Oxford. At present four separate projects are being undertaken.

Project I: Epidemilogical evidence collected here suggests that there is some seasonal variation in the tendency to bleed in both haemophilia and Christmas Disease. Recently Giordano and Radivoyevitch (1970) suggested that this may be mlated to a seasonal variation in the level of plasma-cortisol. It is thought that more evidence on these observations may be of fundamental importance and the plasma-cortisol levels of the boys suffering from these diseases is being routinely examined throughout the year. This investigation is being carried cut in co-operation with Dr. Stuart Shaw, Consultant Pathologist, and Mrs. Richardson, Principal Biochemist, at the Royal Hampshire County Hospital.

Project 2: The close resemblance of changes seen in the haemophilic joint and those of rheumatoid arthritis are sufficiently impressive to justify further investigation. Sera from these boys is being examined for the presence of Rheumatoid Arthritis antibody and to date a number of them have been found positive. This is a joint investigation, both clinical and pathological, and is being conducted by Mr. Stanley Evans and myself. It is a fairly long term project, and the relationship between Rheumatoid Arthritis Antibody and the possible development of Inhibitors for Factor VIII is being studied.

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Project 3: Recently Ali and Hobbs (1970) found that the Immunoglobulins in Haemophilia were sometimes abnormal, especially those in haemophiliacs with Inhibitors for Factor VIII. This was discussed with Professor Nicholas Martin and Dr. Rosemary Biggs and the serum of all our boys with haemophilia and Christmas Disease is being quantatively examined for the immunoglobulins likely to be involved. These investigations may indicate those boys likely to develop Inhibitors for Factor VIII and, if so, it is possible that this zerious complication of haemophilia might be prevented. This project is being uncertaken in co-operation with Professor Nicholas Martin and Dr. Jean Sharrard at St. George's Medical School, Hyde Park Corner.

Project 4: Investigations carried out in conjunction with The Virus Reference Laboratory (Public Health Laboratory Service) with Dr. Yvonne Cossart has shown that the incidence of Antibody to Australian Antigen is extremely high in our cases of Christians Disease and Haemophilia. Dr. Cossart has arranged to carry out regular examination of our cases for this Antibody and possibly to screen all the materials being administered for Australian Antigen. It is probable that much may be learned of the cause of serum hepatitis and its prevention could well be the outcome of these investigations. Furthermore, there is a serious shortage of sera for the detection of Australian Antigen in this country and the supply of sera from these boys will, therefore, greatly augment the present national bank of Australian Antibody sera, which will permit more widespread research into the relationship between the presence of Australian Antigen and hepatitis.

Dr. Biggs has approved this programme and all the projects are well under way.

GRO-C
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References: Nicholas D. Giordano and Milan Radivoyevitch, Lancet 31.1.70, page 249

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