

Draft - Wellington

1984 draft

Revised at Meet. 15/2/83

W. L. Carter Centre

Present:

Wellington	Teedler
Centras	Compton
Northon	McClelland
Barber	

Agreed. Wellington put a paper before
 CDR Meet to study based on
 background + first test method
 cont. i.e. as under test
 and with clinical F.U. To
 include essay capacity to
 screen another center.

DONOR SCREENING USING NON SPECIFIC TESTS TO RECOGNISE HIGH RISK GROUPS

Unique Number
 10225

PREAMBLE

The Acquired Immuno Deficiency Syndrome (A.I.D.S.) is a serious disease new to the developed world and present in epidemic proportions in certain of its communities. Epidemiological studies based on criteria set out by the Centres for Disease Control, Atlanta (C.D.C. Surveillance Definition for AIDS) suggest strongly that an infectious agent is responsible for A.I.D.S. but this agent remains unidentified. Many of its likely characteristics are revealed by its epidemiology as observed in the U.S.A. Canada and certain of the countries of Europe. This predicts an agent, very probably a virus that is transmitted by sexual contact, blood and blood products. The disease remains predominantly a problem of homosexual men. Studies of cases where single blood transfusions appear responsible emphasise the conclusions of the epidemiological studies, they also suggest that a pre-symptomatic carrier state exists an observation of crucial importance to blood transfusion practice (1, 2.)

Ignorant of the identity of this putative infectious agent it is impossible to screen directly for this carrier state. However, A.I.D.S. patients show evidence of a disordered immune system and past or present infection with a variety of agents, particularly venereally transmitted pathogens. Various studies (3, 4) in at risk homosexual men define these abnormalities. These are non specific tests which might be used to identify blood donors at risk of transmitting the putative infectious agent of A.I.D.S.

We propose a study based on screening samples from blood donors for antibody to HBc. This antibody is present in most patients with A.I.D.S., A.I.D.S. related syndromes and members of 'at risk' groups particularly homosexuals and intravenous drug abusers. There is considerable experience of use of a one step radioimmune assay for its detection within two Regional Transfusion Centres which shows that this is practical as a screening test. Screening will be performed in four Regional Transfusion Centres. In order to investigate the value of this approach, positive bloods and suitable matched controls will then be subjected to tests for other abnormalities known to be present in 'at risk' groups. Both the donors and recipients of their blood will be followed for the appearance of A.I.D.S. or A.I.D.S. related conditions by seeking the collaboration of their General Practitioner.

This study is of vital importance to transfusion practice within the British Isles. In addition to establishing tests sufficiently discriminating to eliminate donors at high risk of transmitting A.I.D.S. it will also establish the effect of such testing on the supply of blood and blood products within a Transfusion Service totally dependant on volunteer donors. As a bonus samples will be provided that allow the pursuit of new discoveries reflecting directly on the etiology of A.I.D.S. Although based on four Transfusion Centres this study will seek the collaboration of Laboratories expert in each area of testing. In addition to ensuring efficiently conducted tests this approach will increase the opportunities for original research.

REFERENCES

- 1) J.W. Curran et al. (1984) 'Acquired Immunodeficiency Syndrome (AIDS) Associated with Transfusions'
N.E.J.M. 310 p. 69.
- 2) J.R. Bove (1984) Editorial 'Transfusion - Associated AIDS - A Cause for Concern'
N.E.J.M. 310 p. 115.
- 4) R. Detels et al. (1983) 'Relation between Sexual Practices and T cell subsets in homosexual active men'.
Lancet 1 p. 609.
- 4) A.J. Pinching et al. (1983) 'Studies of cellular immunity in male homosexuals in London'.
Lancet 2 p. 126.

OBJECTIVES

To determine in a prospective study of volunteer blood donors taking the presence of anti HBc as reference point:-

- the prevalence of non specific laboratory markers that suggest a high risk of A.I.D.S. transmission.
- the prevalence of clusters of markers that might increase the discriminating power of laboratory tests.
- the impact on donor availability if one or more markers were chosen as an exclusion criterion.
- on repeated sampling if markers are constantly present or fluctuating.
- through General Practitioner follow up of HBc Ab positive donors and recipients of their blood the clinical implications of the laboratory findings.
- in a cohort of donors undertake clinical assessment of donors with and without positive markers to assess relevance of markers to donors 'risk' status. This to be linked to a study of a group of homosexual men who could be considered sufficiently healthy, to be accepted as donors if they were to attend a session.

NUMBERS

It is difficult to determine how many donors should be screened. Interim results from the study of a cohort of 6,800 homosexuals in San Francisco suggests that the yearly incidence of A.I.D.S. and A R C is approximately 5%. This is an area where A.I.D.S. is unusually prevalent. Therefore at very best if we expected to find a reasonable number of cases offering real risk (100) we would need 2,000 anti Hbc positive donors. Experience at Bristol and Edware suggests that we would need to screen 200,000 donors to achieve this.

PLAN

- 1) Screen donors for anti HBc using a standardised one step radio-immunoassay to be supplied by Central Public Health Laboratory, Colindale.

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- 2) Positive donations - freeze serum from pilot tube in 200 micolitre aliquots, should be possible to obtain 7 after initial Hepatitis screening.

- count lymphocytes
- count T lymphocytes and T lymphocyte subsets
- save plasma from donation - 30 centigrade
- ? fate of rbcs if available for transfusion

-
- 3) Obtain matching controls on a daily basis.

REMARKS

- 1) To be conducted in four Centres, Bristol, Edgware, Edinburgh, Manchester.
All donors to be screened.
200,000 anti HBc tests.
? availability of the test material.

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- 2) To be conducted in four Centres.
? each needs small liquid nitrogen refrigerator dedicated to task.
? freeze lymphocytes or post immediately to Centre with FACS.
? specimen for lymphocyte numbers, citrated pilot tube or extra specimen taken especially for study.

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- 3) To be conducted in four Centres.

COSTS

- 1) Reagents ? £12,000. Central purchase of Removawells
Use local Hepatitis screening lab staff.

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- 2) Liquid Nitrogen refrigerators approx 4 x £400 = £1,600
Extra EDTA sample, ? 1p each = £2,000
-

PLAN

- 4) Distribute samples for further testing.
 - a) anti Hbc. confirm, 1 aliquot serum
 - b) circulating immune complexes, 2 aliquots serum
 - c) Beta 2 microglobulin, 1 aliquot serum
 - d) Alpha interferon, 1 aliquot serum
 - e) Thymosin alpha 1, 1 aliquot serum
 - f) immunoglobulins, 1 aliquot serum
 - g) ? plasma for further viral studies
 - h) ? frozen lymphocytes for viral studies
 - i) lymphocyte markers

- 5) Write to donor asking for details of General Practitioner. Write to G.P. asking for report on any suspicious illness. Repeat 6 monthly to 3 years. Follow up donation in similar manner obtaining detail from hospital record. ? closer study of smaller cohort in one centre.

- 6) Repeat tests when donor next attends to give blood.

REMARKS

4) Batched samples despatched frozen (dry ice):

- a) Colindale
 - b) Bristol
 - c) " ?
 - d) " ?
 - e) " ?
 - f) " ?
 - g) ?
 - h) ?
 - i) Bristol ?
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5) Needs Research Assistant/Secretary.

Needs computer based data processing.

Perhaps a smaller cohort could be selected for more detailed medical study in one Centre where a group of homosexual men could also be studied, ? Edinburgh.

6) Frequency of repeat testing will greatly effect costs.

COSTS.

- 4) a) £100
 b) £24,000 (based on 4,000 tests performed each 6 months for 3 years ???)
 c) £24,000 (£1/test ?)
 d) £24,000
 e) £24,000 (? availability)
 f) £6,000
 g) ?
 h) ?
 i) F.A.C.S. £75,000 including installation.
 reagents £30,000

Laboratory staff

S.S.O. £24,000

S.O. £15,000

- 5) Research assistant/Secretary £12,000
 Computer peripherals £3,000.

6).

TOTAL COST OVER THREE YEARS? VERY APPROXIMATE £276,700 weighted in first year for the purchase of capital equipment.