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Description

Dr. Peter Jones, Director of the Newcastle Hemophilia Center of the Royal Victoria Infirmary in Newcastle, England organized England's first conference for health care of individuals relating to the problem of AIDS. The conference was supported through the Department of Health and Social Security and the Hemophilia Society. Commercial support was elicited from all suppliers of factor concentrates in the UK and commercial suppliers of diagnostic test kits. Approximately five hundred people attended from all parts of the UK including Scotland and Ireland. The vast majority of the attendees were nurses or allied health personnel. There were few physicians in attendance and only two hemophilia center directors (Jones and Aronstam). The conference was covered extensively by all UK television and NBC television crew and a large number of newspaper reporters. The coverage was focused mostly on the statements of Peter Jones. Copies of several articles are attached to this report.

Participation

A copy of the program and a list of the speakers is attached. Only two speakers outside of the UK were included. Both of these were from San Francisco. As indicated earlier, commercial support came from suppliers of factor concentrates and diagnostic test kits. A trade exhibition was conducted with a fair amount of traffic during the breaks in the program. Miles UK supported the conference through the purchase of a portfolio for all registrants and an exhibit stand. Attached is a copy of the trade exhibit floor plan showing the individual participants and their location.

Review of Papers

What follows are my notes taken during presentation of the papers. A complete book of the papers is being compiled and will be available in approximately two months.

Dr. Donald Acheson, Chief Medical Officer, Department of Health and Social Security. Dr. Acheson indicated that approximately one in 45,000 donations at the national transfusion service is positive for antibody to HTLV-III. He indicated that this was true for whole blood only. This figure was later confirmed in a second paper presented by Dr. Harold Gunson.

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Dr.Paul Volberding, Director of the AIDS Clinic, SF General Hospital reviewed the AIDS definition from the CDC as "An opportunistic infection or an unusual malignancy in an otherwise healthy individual". He indicated that the rate of disease increase last year was doubling approximately every nine months but now has slowed to a doubling rate of approximately twelve to fourteen months. He suggested the rate therefore is not increasing as rapidly. The overall mortality of people infected with AIDS approaches 100%.

Of major concern, Dr. Volberding indicated that he was seeing a growing incidence of AIDS in the IV drug abuser. This theme was repeated several times throughout the conference by other speakers.

Dr. Volberding indicates that the incubation period varies according to the individual and the risk group to which that individual belongs. For example, homosexual men develop antibody in approximately one to six months, and have an incubation period (from the time of infection to the clinical signs of the disease) that is approximately twelve to eighteen months. Heterosexual individuals and those who are infected by transfusion of contaminated blood or blood products may have an incubation period that is as short as two months or as long as fifty-seven months. Generally, the younger the individual the shorter the incubation period.

Dr. Volberding discussed the scale of the AIDS problem. He indicated that it did not exist prior to 1978. This was demonstrated by the absence of antibody in sera which has been tested retrospectively. He suggested that high risk groups such as the homosexual population show an antibody incidence of approximately 50% of the population, and suggested that over a million individuals were infected with the AIDS virus by the end of 1985. Ward 86 in SF General Hospital is the AIDS ward. The case load in this ward has risen from 300 cases in 1983 to over 12,000 cases in 1985. Kaposi Sarcoma was first seen in AIDS in 1981. It is a relatively rare disease and has, until recently, been restricted to the elderly.

Dr Volberding indicates that there have been several drugs which have been used to treat AIDS patients. These include Vinblastine, VP 16-213, Alpha Interferon (not very effective), Interleukin-II (didn't work - AIDS cells live in cells stimulated by IL-II), Suramin, HPA 23, Ribavirin.

Dr. Richard Tedder, Consultant Viroligist to the School of Pathology, Middlesex Hospital Medical School in London. Dr. Tedder began his paper with a definition of virus and retrovirus. Virus a very small germ which can transmit disease. It is a

true parasite and lives only within a cell. Retrovirus - until recently retroviruses were only considered a problem in animals.

HTLV is a retrovirus and is unique in that it lives in humans. It is the first human retrovirus to be described. It is quite evident in the Caribbean and the Japanese areas and is primarily known as the HTLV-I type. The HTLV-II is another leukemic virus and HTLV-III is somewhat different and causes the AIDS.

All three of the above viruses or types of viruses operate differently in the T cell. Types I and II cause a transformation, while type III causes a lysis of the T cell. A retrovirus is unique in that it incorporates the use of reverse transcriptease to insert the RNA into a cell DNA to change the cell expression. Hence the name retrovirus. Insertion of the virus into the host chromosome is just opposite to the normal development of things. A normal host cell must have a recognition site for the HTLV III. Once the virus has entered the cell it may then lie dormant or actively insert the RNA segment and then leave the cell through what is referred to as a "budding site".

The AIDS virus causes severe immune depression and cell defects. Dr. Tedder feels that the AIDS virus is a sexually transmitted disease. He suggested that hemophiliacs may seroconvert at least a year after using heat-treated factor VIII concentrates because of the nature of the AIDS virus to either be latent or virulent. Of interest,

Dr. Tedder indicated he had just returned from Central Africa and he feels that that part of the world is at risk just the same as is Europe and the USA; that the disease there is sexually transmitted somewhat differently than that in the US; and that the disease did not originate in Africa.

Dr. Phillip Mortimer, Consultant Virologist, Public Health Laboratories Service, Virus Reference Laboratory, London. Dr. Mortimer reviewed the types of anti-HTLV III diagnostic tests which were employed in the UK and the relative accuracy of each test. He suggested that there are nine screening assays available in the UK. These are, in the order of accuracy in the hands of Public Health Laboratory: Abbott, Ortho, Behring, Welcome, DuPont, Pasteur, ENI, Organon, Lab Systems. The last three screening assay kits are considered less favorable than the others. Dr. Mortimer indicated that the conformitory practice for a positive donor for a positive donor is somewhat different in the UK than that in the U.S. The US pattern is to screen, repeat the test, use a western blot and patient assessment. The UK is to screen, repeat the test, and if still positive refer to a conformitory lab with another specimen. Dr. Mortimer gave the estimates for HTLV-III infected individuals in the UK for 1985:

Risk Group	Size	HTLV-III +	Percent	Trend
Hemophiliacs	4,000	1,000	25%	Declining
Blood Recipients	1,000,000	60	.006%	"
IV Drug Abusers	20,000	1,000	5%	Increasing
Homosexuals	500,000	15,000	3%	"

Dr. Marion McEvoy, Senior Medical Epidemiologist CDSC AIDS Surveillance Program UK in London. The number of AIDS cases in the UK as of January 1986 were 287, with 144 deaths. Three more cases were reported this month for a total of 290 cases as of the conference. Of these AIDS cases eleven are hemophiliacs, nine are blood recipients, 255 are homosexuals, two are IV drug abusers and ten are included in the "all other". Dr. McEvoy indicated that the number of hemophiliacs with AIDS as of September 1985 in Europe was 52 and indicated a major concern that eleven of those 52 cases were in the UK.

Dr. Harold Gunson, Director of Regional Transfusion Center in Manchester. Dr. Gunson suggested that there were three million blood transfusions in the US as compared with one million transfusions in the UK. He reviewed several basics of the anti-HTLV III testing and suggested that there were three factors for consideration: (1) Specificity, sensitivity, reproducibility of the test (2) false negatives of the tests (3) information about donors. Dr. Gunson suggested that the first tests that were used in the UK had an extremely high number of false positives. He didn't suggest any different numbers later in his program.

As of October 14, 1985 all regional (21) transfusion centers in the UK began routine screening for anti-HTLV III. Of the nine commercially available tests 16 centers are using the Burroughs Welcome test, five centers are using the Organon test. A test is considered positive if it is within 20% of the cutoff to be considered positive. Those centers using the Organon test have found that there are lot-to-lot variations which vary from 0.05% to 0.57% positive. The average is approximately 0.26% of the initial positives and upon repeat testing 0.11% are found positive. Dr. Gunson suggested that there is variation in lot-to- lot results in manufacturers tests. He gave the combined test results from October through December 1985:

Test	October	December
Welcome No. Positive	1.3%	.24%
Repeat Test	.014%	.01%
Organon No. Positive	.44%	.44%
Repeat Test	.1%	.06%

Dr. Gunson suggested that the Organon test picks up some lymphocytes that the Welcome test doesn't. Dr. Gunson also confirmed that the percentage of positives among blood donations is 0.002% or one in 45,731 blood donations.

Dr. Peter Jones, Director Newcastle Hemophilia Center, Newcastle Upon Tyne. The paper presented by Dr. Jones was by far the most controversial and ellicited the greatest media coverage. He suggested there are 5,000 hemophilia patients in the UK, 2,000 of which are severe hemophilia A patients, 1200 are positive for anti- HTLV III. To date there have been eleven AIDS cases among hemophiliacs with eight deaths.

Dr. Jones presented the history ot therapy of hemophilia as that progressed from whole blood and fresh frozen plasma prior to 1964 through cryoprecipitate into concentrates, heat-treated concentrates, the porcine factor VIII and through the recombinant DNA in the future. He suggested that concentrates require up to 30,000 donations per batch and that the chance of viremia from denatured protein is quite high. He reported that approximately 60% of the factor concentrate used in the UK is imported from the US.

He suggested that all of the hemophiliacs that have been tested in the UK 59% of the severe A are positive for anti-HTLV III, 6% of the B hemophiliacs, and 5% of the vonWillebrands Disease, with an overall 44% positive for all hemophiliacs tested. Likewise he indicated there were age differences in that ten years and older up to 68% are positive. He also reported that exclusive use of cryoprecipitate has resulted in a 1% seroconversion. If NHS concentrate has been used approximately 10% seroconversion of the hemophiliacs are seen, whereas commercial concentrates are resulting in approximately 45% seroconversion.

Dr. Jones gave a review of the AIDS cases as they exist in the UK and compared those with the statistics from the US. He suggested that four percent of the hemophiliacs (11 cases) in the UK are known to have AIDS. In the US approximately 3% (135 cases) are known to have AIDS. (Note: These are percentages given. They do not tabulate with known data.)

He shocked the audience with an announcement that two additional cases of AIDS within the last two months have been seen, both with Kaposi's Sarcoma malignancy. He reported that Dr. Shelby Dietrich in L.A. has had three cases with Kaposi's. These are the first known cases of this malignancy in the US.

Dr. Jones suggested that the incubation period of the HTLV III in the hemophiliac may be as long as four years (see the review of

Tedder's paper). We are in a peak prevalence period now for AIDS cases among hemophiliacs. Dr. Jones suggests there will be additional cases in the next one to two years.

Dr. Jones stunned the audience by suggesting that complete AIDS inactivation cannot be guaranteed in heat-treated factor VIII and factor IX concentrates from commercial companies. He reported that seroconversion in hemophiliacs had been reported by Dr. Peter Levine in the US and by Dr. Breederveldt in the Netherlands. He suggested that these patients were give HT concentrate for one year and seroconverted after that time. Reportedly there were no other cofactors or other risk factors present in these patients. As a result, Dr. Jones recommended the use of alternative therapies including Cryo, tested for anti-HTLV III, taken from children and the extensive use of DDAVP.

It was reported that no seroconversion has been seen through casual contact with AIDS patients among 79 tested hospital staff at Newcastle. None are reportedly positive for anti-HTLV III. He suggested however that AIDS is transmitted sexually and that he has seen three females who were positive - all three of whom have had sexual partners who were positive males. Thirty-three positive males however have had thirty-three negative females. He reported that one positive female has delivered a positive child and that there is one positive female with PCP. There is a 10% transmission rate from positive male to female sexual partner. All these reports were picked up and reported on the front page of the newspapers and in the TV news programs.

During the question period, Dr. Tedder and Dr. Michael Adler stood and challenged Dr. Jones' suggestion that seroconversion after one year of treatment with HT concentrates indicted the heat-treatment processes. Dr. Tedder suggested that these individuals were likely infected prior to the introduction of the HT concentrate and that a cofactor stimulated the development of the antibody after a long latent period.

A spokesman from the National Transfusion Service offered a statement in the press which was read by Dr. Jones the following day to the effect that the NTS was confident that heat-treatment used in the UK is sufficient to eliminate the AIDS virus in known concentrates. Dr. Jones stated that he agreed and knows of no known breakthrough using BPL or Scottish Lab product. He then made several comments about the irresponsible reporting of journalist regarding this conference.

Observations/Action Required or Suggested

For the most part, the information presented by the speakers at the conference was interesting, useful and responsible. The comments regarding the seroconversion and breakthrough of

hemophilia patients following the use of heat-treated concentrates elicits what one might call the Scottish Rains Syndrome for the hemophiliacs. The aspect of AIDS has negatively affected the self image of hemophiliacs and the comments made by Dr. Jones tend to remove the confidence that they may have begun to enjoy as a result of the introduction of heat-treated concentrates.

Suggested action - As a follow-up contact Dr, Peter Levine regarding the three reported cases in the US and provide information obtained to Jack Wood and Linda Frith. Request Jack Wood obtain more information from Dr. Breederveldt in the Netherlands regarding the conversion reported by Dr. Jones.

Personal discussion with Drs. Tedder and Gunson regarding the ARV isolet of the AIDS virus. They indicated they have had no experience with it but did agree that more than 24 hours of heat-treatment is required to inactivate the AIDS virus. Dr. Tedder is very adamant that he feels the lability of the virus has been grossly overstated and agreed that process differences may be important. Dr. Gunson suggested that the moisture content of the lypholized concentrate prior to heat-treatment may play a role in the degree of viral inactivation seen during processing.

Possible action - continued use of data provided the UK office regarding ARV, LAV, HTLV III inactivation and the Cutter process as that compares with other manufacturers.

One can only surmise at the rationale and reasoning for the conducting of the AIDS conference in the UK. Whatever the reason, or the expected outcome, the publicity generated by statements made by Dr. Jones continues to undermine the confidence of the hemophiliac in the concentrates he must take. The course of action taken by Cutter in preparing such support materials as "The Matter of Factors" and the booklet on "Inactivation of the AIDS virus through heat treatment" may be of use in the UK in answering the questions raised by this conference.

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