MEDITEL
Bedford Chambers, The Piazza, Covent Garden,
London WC2 8HA. 01-836 9216/9364

March 21st, 1990

Notes on meeting with Dr Ian Weller
Reader in Genito-Urinary Medicine at UCMS.
University College and Middlesex Hospital.

(Michael and Joan were present)

I shall begin with the most alarming part of our conversation with Dr Weller. He said the Concorde trial is designed to run for 3 years and will go on to the very end unless unacceptable levels of toxicity can be demonstrated. Both AZT and the very similar drug DDI are known to have serious side effects. When asked why it is that nobody has ever documented a death from AZT side effects, yet seven deaths have already been reported from DDI side effects. He said that the DDI side effects were specifically pancreatitis, which has no connection with the AIDS syndrome. However, AZT side effects are the same as some of the AIDS symptoms. (E.g. bone marrow reduction, anaemia, etc.)

So how, we asked, will it be possible to assess unacceptable levels of toxicity if the side effects are indistinguishable from the supposed progression of the disease?

He shrugged his shoulders and opened the palms of his hands as if to say "Ask me another".

(Burroughs Wellcome must feel very secure in the knowledge that no patient will sue for damages from side effects as they will not be discernable!)

If you give AZT you only see a window if efficacy, he said. I think we will find out that this is related to the emergence of resistant HIV strains. This puts another nail in the anti HIV lobby, said Dr Weller.

Dr Weller was keen to speak about the Concorde trial and said he had allocated us one hour of his time. He did not ask us what approach we were taking to the subject of AIDS in our film.

He said there was a fundamental difference in philosophy between his trial and the US 019 trial.

The US trial was set out simply to see if early use of AZT could prevent the progression of disease in people who were already considered to be ill. The trial was stopped in August 1989 after only a few months because the results were said to be so good. (Details of the press statement of 019 trial to follow).

The Concorde trial is looking primarily at the effect of AZT (or Zidovudine as he now calls it) on overall survival.
In fact the trial is looking at three things:

1. Progression of disease
2. Overall survival
3. Severe toxicity. (By that he means adverse reactions strong enough to affect a doctor's decision on whether to use the drug or not).

The Concorde trial was started in the UK at the end of 1988 and is designed to run 3 years. It involves 1415 people, all of whom are HIV positive and asymptomatic. 60% have lower than 500 CD4 count and 40% have higher than 500. The dose is 250 mgs of Zidovudine four times a day.

So far there have been 62 progressions and three deaths. It is not known whether the deaths involved people on the drug or not. However, the causes of death are:

1. Encephalitis.
2. Choking on vomit after excessive intake of alcohol.
3. Suicide following severe depression.

Dr Weller was aware of the fact that conducting a trial for as long as three years will be very expensive not only because of the drug itself but because of the monitoring, blood tests and transfusions involved.

When asked how AZT works he said, "I assume that the disease must be related to the amount of virus that is dividing. By inhibiting the virus (dividing) you are delaying progression of the disease."

He praised Burroughs Wellcome for wanting to go on with this trial. He said it was a duty to follow up long term effects of the drug. "If Concorde folds, society will never know whether the drug was of help. And people in future will never know. And there is a great danger in that".

Dr Weller seemed worried about the confusion surrounding CD4 counts. In fact he seemed worried about quite a lot of things. He says the count can vary by 50% between 11 am (when it is at its lowest) and 4.00 am (when it is at its highest). One test alone is not enough to determine a person's CD4 count. Yet many doctors prescribe AZT on the basis of this simple procedure. He feels that a person's CD4 trend has to be assessed and is very uncomfortable about basing treatment on one or two lab tests alone. He says that in the UK he believes the lower limit of normal for CD4 count is as low as 350.

In order to find those at high risk you have to treat so many. If only there were another marker for testing those at high risk, he says.

Dr Weller was worried about the signs of resistance to AZT that were appearing after prolonged periods of use.

He is a good friend of Dr Andrew Moss at San Francisco General and once said to Dr Moss that it might be better to follow up only those people who have now been HIV positive for 8 or 9 years. (I am not sure if he means simply to monitor them or give them AZT).

Anyway Dr Moss replied that the problem with that was that in a year or two's time Weller would be left with only 1 or 2 patients because all the others would have died.

We said we would be looking, in our programme, at the issue of whether HIV is the sole cause of AIDS. He gave a "yawn,-yawn" impression. I mentioned Peter Duesberg's point about low infectivity rate of HIV and he said that HIV should not be discussed only in the light of how few T cells it can infect but also in the light of how many nasty particles and latching onto cells floating about in the blood doing nothing in particular but eventually affecting lots of things badly! (e.g. Innocent viral products binding to cells causing indirect mechanism damage). He was happy to let the others "argue that out" and he would stick to the matter of the Concorde trialin our film.

Joan Shenton