the pharmaceutical company concerned. Nevertheless, the Department of Health and Social Security insists that the reporting doctor should remain anonymous when details of adverse reactions are passed to pharmaceutical companies, and any representations to allow the name of the doctor to be conveyed to the company have failed.

I suggest, therefore, that the yellow report form should be produced in triplicate rather than singly. The reporting doctor would then retain a copy of what he had reported. The top copy would still go to the Committee on Safety of Medicines, and the second copy, without the name of the patient, would go to the Association of the British Pharmaceutical Industry, which would act as a clearing house for forwarding to the relevant company. Just as the top copy is Freepost to the committee so the second copy would be Freepost to the association. The major advantage of producing a form in triplicate would be that the decision to send a second copy to the pharmaceutical company would remain with the reporting doctor. Obviously, I would hope that most second copies would indeed be sent to manufacturing companies. The introduction of the triplicate form and the cohort identification system would enhance the notification of adverse drug reactions and would make a system that is already probably better than any other in Europe the best in the world.

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Primary pulmonary hypertension

SIR,—Drs Celia Oakley and A Rozkovec (10 January, p 122) regard long term prostacyclin infusion as an unnecessary, complicated, and dangerous treatment for primary pulmonary hypertension. We believe that we are the only group with experience of this form of treatment and that their conclusions are speculative.

The patients seen at Papworth have been referred for heart-lung transplantation. In those whose haemodynamic function deteriorates despite treatment with oral vasodilators, including nifedipine, and who fall into the poor prognosis group we use a prostacyclin infusion to buy time and improve the quality of life. Such patients have a pulmonary arterial blood oxygen saturation of less than 63% and only a 17% chance of surviving for three years.[1] Prostacyclin sustains these patients during the necessarily long time (up to two years) that they spend on the waiting list for the operation. For obvious reasons the number of patients so treated is very small, but our experience suggests that prostacyclin is no more complicated and dangerous to use than the previously ineffective oral vasodilators.[2]

The other point that needs clarification is Drs Oakley's and Rozkovec's belief that the gas transfer for carbon monoxide is always reduced in primary pulmonary hypertension, a belief not shared by others.[3-5] It is fairly straightforward to explain why patients with pulmonary vascular disease, including pulmonary hypertension, may have a normal carbon monoxide transfer factor.[4] If the capillaries are not directly affected by the obliterative or obstructive lesions they will contain red blood cells capable of taking up carbon monoxide. Filling of these capillaries depends on the various pressures acting on the pulmonary vascular bed and may be augmented by collateral blood flow from bronchial arteries.[4,6] In addition, such patients also seem to have a normal ventilation to perfusion ratio,[7,8] suggesting that many will indeed have a normal carbon monoxide transfer factor.

Finally, Drs Oakley's and Rozkovec's distinction between thromboembolic veno-occlusive disease and primary pulmonary hypertension according to the response to vasodilators is unfortunately spurious. It probably requires the detailed pathology of the patients' vascular disease to be correlated with premorbid or pretransplant physiological results. Such studies are only just beginning, and initial evidence suggests that all the pathological types of the syndrome show some degree of vasodilation with treatment.[9] Studies of thromboembolic disease certainly indicate that pulmonary hypertension may be partially reversible with vasodilators.[10]

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**This correspondence is now closed.—ED, *BMJ*.

HIV transmitted by kissing

SIR,—Dr J W G Smith has responded (14 February, p 446) to my letter published in the *Guardian*, in which I challenged the Chief Medical Officer or any of the medical and scientific experts advising the government on the acquired immune deficiency syndrome (AIDS) to cite "even one published paper which gives detailed laboratory evidence that there is any cell-free infectious virus (human immunodeficiency virus or HIV) in semen; or cite even one published paper specifying the number of cells in semen containing either viral RNA, or pro-viral DNA, or both."

Although Dr Smith gave 16 references, he failed to cite a single relevant paper in response to the challenge, for the simple reason that no such paper exists. He cited two studies in support of his claim that HIV "can be detected fairly easily in semen from infected people."[1,2] Only two people were described in the first study and one person in the second. In no case was any cell free virus detected in the semen, nor did spermatozoa contain any cell associated virus, nor could HIV antigen be detected in any lymphocytes found in the seminal fluid. Only after lymphocytes from semen had been cocultured for six to 11 days in the presence of other lymphoid cells and of T cell growth factor interleukin-2 were HIV antigens detected in any of them. These two studies, published in October 1984, proved no more than that at least one lymphocyte in a single specimen of semen from each of three men contained HIV proviral DNA. No viral RNA, or antigen, or any virion, could be detected until the semen had been subjected to prolonged, highly artificial laboratory conditions.

In the two and a half years since these two papers were published no further detailed laboratory study of the presence of HIV in semen has been published. Professor Jay Levy (personal communication) has detected HIV in the semen of only 10% of more than 50 men who had HIV in their blood. He has already published the finding that HIV can be detected in semen only if the lymphocytes in it "are cultured under optimal laboratory conditions"[3]; usually none can be found.

Understanding of the pathogenesis and transmission of a viral disease requires knowledge of the quantity of virus shed into bodily fluids, the duration and variability of shedding, the balance between cell free infectious virions and cell associated virus, the stability of the virus in the environment, and the route of entry into the host. This well established principle has been neglected by many experimental and medical scientists who, like Dr Smith and other members of the government's expert advisory group on AIDS, have accepted uncritically the hypothesis that "HIV is transmitted primarily by sexual intercourse." Many have been so certain of the validity of this flawed hypothesis that they have assumed that experimental studies support it, even though they do not.

Nineteen experimental scientists said in *Nature*: "High titres of cell free infectious virions can be obtained from AIDS patients' semen."[4] The papers in *Science* cited in support of this fact showed that no cell free infectious virion had been found in semen.[1,2] Eight medical and experimental scientists wrote in the *Lancet* that HIV "circulates as cell free virus in... seminal fluid."[5] They adduced as evidence the paper in *Science*, in which the authors reported that "because of the toxic effects of semen on target cells used for these isolations, it is unclear whether there is also cell free (HIV) in seminal plasma."[2]

Dr Robert Gallo, in a paper delivered to a plenary session of the second international conference on AIDS in Paris in June 1986, said: "We think that semen is a particularly rich source of virus," although he gave no scientific evidence to substantiate these thoughts. The BBC's Radio 1 programme *Play Safe—AIDS and You* (13 December 1986) asserted that "virus is present in semen in very high concentrations." Sir Donald Acheson, Chief Medical Officer; Dr Anthony Pinching, a member of the government's advisory group on AIDS; and Dr John Dawson, head of the scientific division of the BMA, were the medical experts speaking on the programme.

As to the infectivity of saliva, Dr Smith wrote: "The difficulty in determining the relevance of such *in vitro* studies is evident in the reference[6] quoted by Dr Seale on virus in saliva. The method of culture employed in that study could not have differentiated between cell free and cell associated virus." The relevant words in the text of the Groopman study are: "Saliva samples were diluted to a final volume of 2 ml in complete growth medium, incubated for 2 hours at 37°C, and centrifuged at 1000 *g* for 10 minutes at 4°C. Pelleted materials were fixed for electron microscopy, and supernatant fluids were filtered (0·45 μm) and used for transmitting virus to fresh peripheral blood lymphocytes."[6] Similar words were used in the caption to table I in the paper. Groopman and his colleagues make it crystal clear that cell free infectious virions were obtained directly from the saliva of eight of 18 men who had antibodies to HIV in their blood. Furthermore, figures 1c and 1d are electron micrographs of "mature virus particles... obtained from the saliva of patient No 8."

There are three essential properties that a parasitic microbe must have in its interaction with the human host if the disease it causes is to be transmitted characteristically by sexual intercourse. Firstly, the microbe must be shed in large quantities in genital secretions and not in other body fluids. Secondly, it must be able to enter a person only through the genitalia. Thirdly, it must perish within a few minutes outside the body. If any of these properties is missing the microbe may be transmitted by various means in addition to sexual intercourse. A major flaw in the hypothesis that HIV is transmitted primarily by sexual intercourse is that none of the pathogenic properties essential to make it so is present.

When HIV is indeed transmitted during sexual intercourse nobody knows if it is usually passed on in saliva, or in the serum from minor abrasions, or in genital secretions, or in some other way. Consequently, there are good reasons to doubt the claim made by experts advising the government