Isolation of the virus from the target organ is very strong evidence that pathological changes in the heart are the direct result of viral invasion of the cardiac tissue.—I am, etc.,

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SIR,—This subject was discussed at the third Scottish-Scandinavian Conference on Infectious Diseases in Finland, June 1968, when Dr. K. Lapinleimu described investigations of the Coxsackie B5 epidemic recently reported by Dr. M. Helin and others (13 July, p. 97). One of us (N. R. G.) presented 22 cases of myocarditis and/or pericarditis from the period 1959–68 with infections by the following Coxsackie viruses: A1 (one case), A4 (three), A9 (one), B2 (two), B3 (three), B4 (five), B5 (seven). Of these, eight were in the first decade of life, five in the second and third, and nine in the fourth to seventh decades.

We agree with Dr. G. S. Sainani (10 August, p. 375) and with Dr. W. G. Smith,[1] that adult heart disease due to Coxsackie viruses is probably commoner than generally recognized. Even when the diagnosis is suspected, there may be practical difficulties in achieving virological confirmation.[2] Nevertheless some impression can be formed from reported data. The 18 cardiac illnesses described by Dr. Helin and colleagues comprised 33% of the epidemic types of disease admitted to the Kuopio Hospital; Coxsackie B5 isolations were made from 12 (22%) and 4 others had serological evidence of infection. In her description of the wider virological study of which these cases formed part, Dr. Lapinleimu reported to the June conference isolations of 244 virus strains from 225 patients. In this larger group, which included less severe cases, cardiac illnesses numbered 27—that is, 12%. During the same year in Britain cardiac diseases contributed 5% of the 900 Coxsackie B5 infections reported to the Public Health Laboratory Service.[3] In the same outbreak cardiac syndromes comprised 2 (5%) of 37 Coxsackie B5 infections diagnosed in this laboratory by virus isolation, *and five* additional cases showed serological evidence of infection.[2] In their study of the Toronto epidemic of 1958, Dr. J. S. Walker and colleagues[4] isolated Coxsackie B5 virus from 59 children, of whom five (8%) had pericarditis.

Though mainly group B Coxsackie viruses have been implicated as causing cardiac diseases, reports of group A infections are accumulating. In addition to our own findings mentioned above there have been reports of Coxsackie A1 infection in an adult with pericarditis in the U.S.A., Coxsackie A4 infections in children with myocarditis in Brazil and the U.S.A., Coxsackie A9 infections in two infants with myocarditis and an adult with myopericarditis in the U.S.A., Greece, and Finland, Coxsackie A16 in two infants with myocarditis in the U.S.A., and Coxsackie A23 (Echo 9) infections in an infant and an adult with myocarditis in the U.S.A. In this last connexion it is interesting that von Oldershausen reported electrocardiographic changes in Echo 9 infections in 1957.[5] Coxsackie A8 virus was isolated from a 19-day-old infant who suddenly died and was found to have atrial and septal heart defects[6] and has recently been found by us in a 2-year-old girl with paroxysmal tachycardia. Our unpublished findings will be reported more fully elsewhere together with a full bibliography.

We thank Dr. D. R. Gamble, Epsom, for typing one of our isolates.

—We are, etc.,

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Headache on the Pill

SIR,—In your leading article on this subject (17 August, p. 388) you discuss the possible association between oral contraceptives and changes in the cerebral vasculature. You state that "other investigations into a possible association between oral contraceptives and cerebral vascular disease have so far proved negative," and quote our recent communication (27 April, p. 193) as the source of these negative findings.

We feel sure that you would wish your readers to know that we in fact found a significant association between the use of oral contraceptives and cerebral thrombosis. Although the numbers were small, five of ten women who died in 1966 from cerebral thrombosis without any recognized predisposing conditions had been using oral contraceptives. The corresponding number expected from the experience of a control group was only 1.5, and this difference was statistically significant ($P<0.01$). We also pointed out that five of the six women aged less than 40 when they died had been using oral contraceptives, while none of four over 40 had been doing so. In a second study (27 April, p. 199) five of nine women surviving after admission to hospital with a presumptive diagnosis of cerebral thrombosis had been using oral contraceptives. This number also represented a significant excess when compared with control patients.—We are, etc.,

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*** We regret our misleading reference.—ED., *B.M.J.*

SIR,—I read with interest Dr. Ellen C. G. Grant's paper (17 August, p. 402) and your leading article (17 August, p. 388) drawing attention to vascular changes in the endometrium in pill users, and pointing out a possible connexion with the incidence of headache at the end of the tablet cycle. In my recent multidose survey of over 1,000 endometrial biopsies from women taking ethynodiol diacetate/mestranol,[1] the incidence of highly developed spiral arterioles was not confirmed. At the 2, 1, and 0.5 mg. dose levels there was spiral arteriolar suppression, which is in agreement with other observers, with a slight increase at the lowest dose levels. As in Dr. Grant's study there were few biopsies in the 0.25 mg. range after day 20, but the peak of arteriolar development described was not found. The marked arteriolar development of the normal cycle, which is progesterone-dependent, was not seen in pill users except in an occasional biopsy in the 0.1 mg. series.

The connexion between vascular development and headache is an interesting one, as the normal cycle vasculature is not reflected by the presence of this symptom, possibly owing to the progesterone–oestrogen balance. The hypothesis of arteriolar proliferation and vascular disturbances is highly significant if correct, but the incidence of these changes is not supported by my survey. A special trial is being instituted to follow up this work.—I am, etc.,

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REFERENCE

1 Morley, F., *Clin. Trials J.*, 1968, Special Issue, January, **5**, 183.

Viruria as a Source of Infection

SIR,—Your leading article "Renal Damage in Chicken-pox" (3 August, p. 264) stated that "With better laboratory techniques viruria has been detected in such diverse infections as mumps, enterovirus, rubella, measles, cytomegalovirus, adenovirus, and vaccinia, to name but a few." The article then goes on to give examples of evidence of active infection of kidney cells in various virus infections, and in particular acute glomerulonephritis in chicken-pox.

These new findings have possible implications concerning the potential role of urine in the transmission of infectious disease. Present epidemiological practice has largely been formulated on the basis of experience with bacterial infections, where, apart from typhoid fever, the risk of spread of infection from urinary excretion has generally been regarded as slight. The important risk of the transmission of rubella from the urine of babies born with the congenital form of this disease has recently been established, and the spread of cytomegalovirus infection via urine is also well recognized. It now appears possible that other virus infections may be spread by means of infected urine.

Preventive measures against the spread of infectious disease have so far concentrated on faeces rather than urine. As urination takes place much more frequently than defaecation the opportunity for contamination of fingers is certainly greater, and there is also far less washing of hands after passing urine. The time would seem to be ripe for a reappraisal of the potential risk of urine in the spread of infectious disease. If the risk is in fact greater than at present realized, then account must be taken of this in the preventive measures advocated.—I am, etc.,

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Oxford. Medical Officer of Health.