pioneers like Pearl Kendrick, Margaret Pittman, L B Holt, and members of the WHO group, and I gave relevant references. If Dr Preston objects, he should refute their work not mine. He might also take issue with Dr Griffith, who says (and I do not doubt it) that his company's vaccine contained all the main antigens from 1964 or earlier. Addition of antigen 3 to all British vaccines did not stop the major outbreaks of 1967-8, 1970-1, or 1974-5 during a period when vaccine acceptance was much higher than it is now; nor did it bring any change in the fact that 25-35% of proved cases, now as well as then, occur in fully vaccinated children not only in Britain but also in the United States,¹ Canada,² Australia,³ Sweden,⁴ and elsewhere. In parts of Scotland in 1977-9 the incidence of whooping cough in fully vaccinated children exceeded this range,⁵ and it could be argued that the loss of immunity two to three years after vaccination is the main determinant of the otherwise unexplained 44 month periodicity of outbreaks of whooping cough in Britain (personal report to Department of Health and Social Security).

I imagine that most of your readers are bored, confused, or exasperated by the continuing controversy about this one, relatively unimportant infection and its relatively ineffective vaccine, which is disproportionately important because so many children receive it. Might I therefore state yet again the central plea in my own argument for the need to repair "the national deficit in epidemiological data and intelligence,"⁶ because without some improvement, and not only about pertussis vaccine, we are abusing the trust of the public in medical judgment and in medications.

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¹ Pertussis surveillance, Georgia. *MMWR* 1977;26:307-8.

² Mathias RG. Whooping cough in spite of immunization. *Can J Public Health* 1978;69:130-2.

³ Bennet NM. Whooping cough in Melbourne. *Med J Aust* 1973;ii:481-7.

⁴ Eksmyr R. Kikhosta-en oppnevdsstudie. *Lakartidningen* 1979;76:4818-21.

⁵ Stewart GT. Vaccination against whooping cough: efficacy versus risk. *Lancet* 1977;i:234-7.

⁶ Ditchburn RK. Whooping cough after stopping pertussis immunisation. *Br Med J* 1979;ii:1601-3.

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

Effects of pirbuterol and sodium nitroprusside on pulmonary haemodynamics in hypoxic cor pulmonale

SIR,—I would like to take issue with the methodology used by Dr W MacNee and others (22 October, p 1169) for measurement of pulmonary vascular resistance and the effects on this variable of the two drugs pirbuterol and sodium nitroprusside.

The authors state: "Left atrial pressure is not always easy to assess from pulmonary artery wedge pressure in these patients." The formula for measuring pulmonary vascular resistance is therefore invalid, as it includes no estimate of the pressure difference across the pulmonary circuit. Whether one believes in the concept of "resistance" in the pulmonary circuit or "impedance," I am sure that most workers would argue that the formula used in this study was wrong.^{1 2}

Furthermore, it is not valid to assume that long term administration of pirbuterol had beneficial effects, when no estimate is made of cardiac output. Thus a reduction purely in systolic pressure does not seem clinically

important in the pulmonary circuit when there is no estimate of flow through it.

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¹ Foex P. *Pulmonary dynamics*. In: Prys-Roberts C, ed. *The circulation in anaesthesia*. Oxford: Blackwell Scientific Publications, 1980:258-9.

² Kaplan JA. *Immunodynamic monitoring*. In: Kaplan JA, ed. *Cardiac anaesthesia*. New York: Grune and Stratton, 1979:95.

*.*The authors reply below.—ED, *BMJ*.

SIR,—Dr D W Green is, of course, technically correct. In any segment of the circulation the resistance is defined as the drop in pressure across the segment divided by the rate of volume flow through it. Thus the pulmonary vascular resistance is expressed as the difference between the mean pulmonary arterial pressure and the mean left atrial pressure divided by the cardiac output.

In stating this, however, Dr Green has ignored the controversy that has existed for the past 20 years or more as to whether measurement of pulmonary capillary wedge pressure accurately reflects mean left atrial pressure in patients with severe chronic bronchitis and emphysema, such as those studied in our paper. Fishman states: "Pulmonary capillary wedge pressure and pulmonary diastolic pressure are unreliable indexes of left atrial pressure" in such patients as "either venoconstriction or anatomic change in the intervening vessels may invalidate these measurements."¹ Recent authors support the view that the measurement of pulmonary capillary wedge pressure should be interpreted with caution in patients with disordered pulmonary mechanics,² and in such patients "a simple mean of the wedge pressure can be raised secondary to positive intrathoracic pressure during expiration."³ Although Lockhart has not ascribed the rises in pulmonary capillary wedge pressure in patients with obstructive lung disease to a generalised rise of intrathoracic pressure, close scrutiny of this paper (fig 4) shows a variability of 5 mm Hg between pulmonary capillary wedge pressure and left ventricular end diastolic pressure measured at rest.⁴

It is for these reasons that we chose to measure total pulmonary vascular resistance, so avoiding the effect of a possible error in the measurement of resistance. As pulmonary artery pressure in our patients was high and we have assumed that left atrial pressure was low (as all of our patients had well preserved left ventricular function) this is not dissimilar to the approach in calculating systemic vascular resistance, where the right atrial pressure is not usually considered. It was for similar reasons that total pulmonary vascular resistance was measured in the MRC long term domiciliary oxygen trial⁵ and that the largest single series of measurements of pulmonary haemodynamics in patients with obstructive lung disease does not mention measurements of pulmonary capillary wedge pressure.⁶ We cannot therefore agree with Dr Green that "most workers would argue that the formula we used in this study was wrong." We have defined total pulmonary vascular resistance (kPa s/cm⁵) as the mean pulmonary artery pressure divided by the cardiac output times 8—a definition used by many other workers.⁷

We would also point out that the beneficial effects of long term administration of pirbuterol were based on a reduction of systolic pulmon-

ary artery pressure and an increase in right ventricular ejection fraction. Cardiac output was not measured in order to reduce the number of invasive measurements made during the chronic study. As the increase in right ventricular ejection fraction paralleled the increase in cardiac output during the acute study and as a consistent increase in right ventricular ejection fraction occurred in the chronic study, we have assumed that cardiac output would also increase.

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² O'Quin R, Marini JJ. Pulmonary arterial occlusion pressure: clinical physiology measurement, and interpretation. *Am Rev Respir Dis* 1983;128:319-26.

³ Rice DL, Awe RJ, Gaasch WH, Alexander JK, Jenkins DE. Wedge pressure measurement in obstructive pulmonary disease. *Chest* 1974;66:628-32.

⁴ Lockhart A, Tzareva M, Nader P, Leblanc P, Schriren F, Sadoul P. Elevated pulmonary artery wedge pressure at rest and during exercise in chronic bronchitis: fact or fancy. *Clin Sci* 1969;37:503-17.

⁵ MRC Working Party. Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. *Lancet* 1981;i:681-6.

⁶ Bishop JM, Cross KW. Use of other physiological variables to predict pulmonary artery pressure in patients with chronic respiratory disease. *Eur Heart J* 1981;2:509-17.

⁷ Morrison D, Goldman S, Wright AL, et al. The effect of pulmonary hypertension on systolic function of the right ventricle. *Chest* 1983;84:250-7.

Recognising placental steroid sulphatase deficiency

SIR,—The determination of the steroid sulphatase activity in leucocyte homogenates (23 July, p 293)¹ certainly meets the demand for an "easy diagnostic method for X-linked ichthyosis suitable for routine clinical biochemistry laboratories" put forward in the leading article by Dr R A Harkness and others (2 July, p 2). Unfortunately, we observed a considerable variation of the steroid sulphatase activity among obligate carriers of the steroid sulphatase deficiency trait. This limits the ability of our simple method¹ to recognise heterozygotes, which can be needed urgently in cases of low urinary steroid excretion during pregnancy as this may be caused by steroid sulphatase deficiency.

The results of the steroid sulphatase activity determination proved the heterozygosity for this trait in only 14 out of 18 carriers (figure). The much greater variation in the carrier group than in the healthy normal group is not likely to be due to technical differences, as all assays were carried out in the same period by one person.

Scientifically, these results are most interesting as they indicate that no complete escape from X-chromosomal inactivation of the steroid sulphatase locus seems to occur in leucocytes. This, however, differs from the results with cultured fibroblasts initially reported by Shapiro *et al* for four obligate carriers² and reported by Müller *et al* for five obligate carriers,³ which suggested complete escape of inactivation. The reported steroid sulphatase activity in leucocytes⁵ and in lymphocytes⁶ of normal persons and further work of Shapiro's group on cultured fibroblasts from carriers of the steroid sulphatase deficiency trait⁷ indicate, though, a differential expression of the steroid sulphatase locus.

Steroid sulphatase activity in 31 healthy controls (15 males aged 9 to 68 years and 16 females aged 4 to 62 years, one of whom was seven months pregnant), 18 healthy obligate carriers (aged 10 to 47 years), and 10 patients with X-linked ichthyosis (aged 0-80 years). Determination of activity was based on the hydrolysis of ^3H -dehydroepiandrosterone sulphate² expressed in pmol ^3H -dehydroepiandrosterone sulphate/h/ml homogenate of leucocytes.

Differential expression seems to be consistent with our results and those of others,⁸ which show a steroid sulphatase activity ratio of about 1.5 between normal female and male controls. In case of complete inactivation a ratio of 1.0 would be expected and in case of non-inactivation a ratio of 2.0 would have been observed.⁹

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² van der Loos CM, van Breda AJ, Meijer AEFH, Jöbbs AC. Biochemical investigation of the reliability of the histochemical demonstration of microsomal arylsulphatase activity in cryostat sections. *Histochemistry* 1981;71:161-4.

³ Shapiro LJ, Mohandas T, Weiss R, Romeo G. Non-inactivation of an X chromosome locus in man. *Science* 1979;204:1224-6.

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⁵ Epstein EH, Leventhal ME. Steroid sulfatase of human leukocytes and epidermis and the diagnosis of recessive X-linked ichthyosis. *J Clin Invest* 1981;67:1257-62.

⁶ Müller CR, Migl B, Traupe H, Ropers HH. X linked steroid sulfatase: evidence for different gene dosage in males and females. *Hum Genet* 1980;54:197-9.

⁷ Migeon BR, Shapiro LJ, Norum RA, Mohandas T, Axelmann J, Dabora RL. Differential expression of steroid sulphatase locus on active and inactive human X chromosome. *Nature* 1982;299:838-40.

⁸ Bedin M, Weil D, Fournier T, Cedard L, Frezal J. Biochemical evidence for the non-inactivation of the steroid sulfatase locus in human placenta and fibroblasts. *Hum Genet* 1981;59:256-8.

⁹ Lyon MF. X chromosome inactivation and developmental pattern in mammals. *Biol Rev* 1972;47:1-35.

*Dr Harkness's reply follows.—Ed, BMJ.

SIR,—There is agreement with the main point of the letter by Dr Jöbbs and colleagues. One of the reviews we cited presented further evidence for and considered the problem of apparent incomplete escape from X-chromosomal inactivation.¹ It is also relevant that this Dutch group take great care with their leucocyte preparations and enzyme assays, being performed "in the same period by one person."

It is unfortunate, however, that their letter should not consider the answer (3 September, p 692) to the cited letter of Dr Burton (23 July, p 293). The misunderstandings on this subject are shared by Dr Ervin E Epstein and others (17 September, p 841) and rest on what is practicable in a routine district general hospital laboratory. This may differ between countries, and our remarks are based on experience in the United Kingdom. It may therefore be significant that these points come from Holland and the United States.

There are a variety of diagnostic methods suitable for academic centres, reference laboratories, or both. Experience in the United Kingdom in placental steroid sulphatase deficiency and in many other inherited metabolic diseases has shown that such methods are rarely practicable in the routine laboratory of a district general hospital and must be confined to reference or academic centres. Such a network can be used even with common diseases when a stable specimen can be easily transferred from a peripheral centre to the reference laboratory. Leucocytes are, however, unstable and thus the patient rather than the sample has to go to the reference centre.

A plea for further research to reduce overall costs before a method is handed over to routine laboratories has already been presented.² Stable, easily prepared samples and robust methods are needed for routine clinical biochemistry in district general hospitals in the United Kingdom.

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¹ Rose FA. The mammalian sulphatases and placental sulphatase deficiency in man. *J Inherited Metab Dis* 1982;5:145-52.

² Harkness RA. Current clinical problems in placental steroid or aryl-sulphatase C deficiency and the related 'cervical dystocia' and X-linked ichthyosis. *J Inherited Metab Dis* 1982;5:142-4.

Legislation and teenage sex

SIR,—Since the publication of the General Medical Council's *Fitness to Practise*¹ widespread concern has been expressed about the new guidelines on confidentiality in respect of minors and contraceptive practice. Prescribing the contraceptive pill to girls aged under 16 years has been linked with an increase in promiscuity, venereal disease, and legal abortion² (3 September, p 687).

We have found no evidence to support this claim. We have recently studied the case notes of all sexually active girls aged under 16 attending the Praed Street Clinic in the years 1972 and 1982. The clinic is a large department of genitourinary medicine situated in west London; the atmosphere is informal, and patients are seen without referral.

In 1972 24 girls aged under 16 were diagnosed as having a sexually transmitted disease; five were taking the contraceptive pill, and 13 had a regular boyfriend (defined as one sexual partner only in the preceding three months). Pregnancies had occurred in three girls, resulting in one legal abortion. In 1982

13 girls under 16 were seen, of whom five had a sexually transmitted disease; two were using oral contraception, and eight had a regular boyfriend. Three girls had a pregnancy, one of which was terminated.

These figures show that the prevalence of neither sexually transmitted disease nor promiscuity has increased in our clinic population of girls under 16 years, despite the availability of the oral contraceptive pill. The more disturbing finding is that most girls in this group are unprotected against unwanted pregnancy.

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¹ General Medical Council. *Professional conduct and discipline: fitness to practise*. London: GMC, 1983.

² Riches V. Myths that surround child contraception. *Daily Telegraph* 1983;Aug 30:8.

SIR,—Your leading article on "Legislation and teenage sex" (17 December, p 1826) manages to get even the title wrong. For the issue that you in fact discuss is not teenage sex but under age sex. What people think of teenage sexuality is, despite your assertion, nowhere near the heart of the matter. I for one regularly prescribe the pill to older teenage girls, allowing their choice precedence over my convictions. What is central is the law, which regards intercourse with a girl known to be under 16 as a criminal offence. That law in turn reflects society's wish to prevent sexual exploitation and abuse.

Your complacent assumption that the BMA's recent press conference on the subject can be taken, apparently ex cathedra, as a reflection of what doctors think and behave is totally erroneous—unless the considerable minority of us who think differently are to be regarded, Russian dissident style, as mentally aberrant and in need of corrective treatment.

Apart from such general strictures, several statements need to be called in question. Where is the evidence that sexual relationships at this age are "often stable?" What Aunt Sally are you setting up by suggesting that some people see pregnancy as punishment for illicit sex? Why talk only of the 14 and 15 year olds who have been prescribed the pill without mention of those even younger?

I find myself in broad sympathy with your final paragraph. Intending legislators do indeed need to be certain that they have found a better answer. Perhaps Mrs Gillick's view of the present law will be found on appeal to be correct. If so, it would only serve to underline my view that you, sir, are also in urgent need of better answers.

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SIR,—I had decided before I read your leading article (17 December 1983, p 1826) to resign from the British Medical Association on this issue. Your article merely reinforced my decision. In paraphrasing Jane Austen you say that parliament should not make new laws when "those most closely affected" advise that the proposed legislation is unwise and unworkable. By "those most closely affected" you obviously mean doctors, but I would put it to you that "those most closely affected" are not, however great our ego, doctors, but the unfortunate parents of the many children for whom you seek licence for