munity, has the effect of the gas on unhealthy lung tissue been investigated? (2) In view of the fact that CS gas is based on chlorobenzene, have animal experiments shown any evidence of possible liver and kidney damage? (3) Is there experimental work available to demonstrate the possible toxicological effects of the hundreds of empty gas canisters left lying on the streets of the Bogside, with particular reference to possible effects on children?

The question concerning empty gas canisters has already been clearly answered by Sir Harold during his recent visit. These canisters constitute a definite health hazard, and he recommended that they should be handed in to a central location for disposal. I anticipated this answer and have been trying to collect these canisters for the past two weeks. Unfortunately, many are being retained as souvenirs of the defence. Sir Harold made reference to the fact that he had not seen evidence of permanent damage caused by the gas to healthy persons. I would agree with this statement, but with some reservation pending further details of the Porton Down experiment, evaluation of the American experimental work, and details of the experience gained by medical workers in Paris subsequent to the use of CS gas in that city during their recent disturbances.

The most important question which may emerge is that relating to possible damage of already diseased lung tissue. The following is a clinical history of one patient whom I have followed fairly closely as a sample case.

A young man aged 22 years came from Liverpool to reside in Londonderry. I first examined this man in August 1968. At that time he complained of a slight chest cold and admitted to a couple of very minor attacks suggestive of an asthmatic complaint in childhood. On examination his chest was clinically clear, chest x-ray was normal.

Vitalograph lung function test showed: F.E.V.₁ = 3.6 litres. F.V.C. = 5.05 litres giving F.E.V.₁/F.V.C. = 72%. This was marginally below the expected 75% for the average healthy adult, but none the less a reading which I considered acceptable, and consistent with his history.

During October 1968 this man was absent from work for a period of about three weeks with a chest cold, described on his doctor's certificate as asthmatic bronchitis. On return to work his respiratory system was clinically clear, and he was symptom free. He lives in the Bogside area and was exposed to CS gas during the recent disturbances from 12 August until 14 August.

He came to see me on 28 August, stating that he had some tightness in his chest since the time of the disturbances, but over the past few days he was feeling much worse. His presenting complaints were dyspnoea, especially on exertion, productive cough, and sore throat. He stated that he had some diarrhoea subsequent to the disturbances, but this had long since cleared up.

On examination there was some erythema of the fauces. There were generalized signs of bronchospasm in both upper and midzones and some moist sounds present in both lower zones; temperature was normal. I recommended Ledermycin caps. (demethylchlortetracycline hydrochloride) 150 mg. 2 b.i.d. × five days and Franol tabs. 1 t.i.d. Vitalograph lung function test at this time showed: F.E.V.₁ = 1.85 litres; F.V.C. = 3.15 litres, giving F.E.V.₁/F.V.C. = 58%. After inhalation of isoprenaline the reading showed: F.E.V.₁ = 2.15 litres; F.V.C. = 3.65 litres, giving F.E.V.₁/F.V.C. = 58%. I would have expected the F.E.V.₁ level to have risen in greater proportion to the F.V.C. following isoprenaline, and this was a rather puzzling factor.

The next day the patient showed a marked clinical improvement and was advised to continue treatment. I saw him again on Monday, 1 September, when he complained of recurrence of some tightness in his chest, particularly on exertion. On examination there were again signs of bronchospasm in both upper and mid-zones, although not so marked as previously. The moist sounds in both bases had disappeared completely. I advised him to continue his present treatment. I saw him again on Wednesday, 3 September, when he stated that he was feeling fairly well. Respiratory examination showed some evidence of bronchospasm remaining in both upper and mid-zones. Vitalograph lung function tests at this time showed: F.E.V.₁ = 2.25 litres; F.V.C. = 3.55 litres, giving F.E.V.₁/F.V.C. = 63%.

I intend to continue reviewing this man at periodic intervals, and it will be most interesting to discover if his lung function returns to its original level. He works as a chemical operator, and his future employment on a chemical plant is an important factor in this case. There are several other cases in the area, most of which could have a constitutional theoretical cause for deterioration. Each one individually could be explained, but the large number of cases with unusual complaints must, I feel, pose questions for the visiting team.

Sir Harold is reported as making reference to those who had suffered the most intense exposure. I can assure Sir Harold that neither he nor his team saw any of those who suffered the most intense exposure, with the possible exception of two persons. Those who suffered the most intense exposure had no inclination of presenting themselves for an examination of this nature. This is entirely due to fear of recrimination and is an unfortunate fact which we must accept.

Finally, I should like to make some comment on your leading article. I am extremely interested in your statement concerning reports of extensive liver, kidney, and brain damage after exposure to high concentrations of CS gas. One would presume that the gas would be metabolized in the liver and excreted via the blood stream, through the kidneys and urine. It should be possible to pick up minute quantities of a metabolic end product in the urine by means of gas chromatography. I wonder if this has been done in experimental work?

As your article suggests, the human "clinical trials" in the Bogside would support the theory of a high reluctance to be subjected to second dosage. However, I can assure you, it did not deter young men and boys who believed, rightly or wrongly, that they were fighting to preserve their homes and families. These young men and boys were subjected to several acute exposures, even to such an extent that many of them claimed that they were "becoming used to the gas." You mention experimental work on animals with induced bronchitis and pneumonia, without evidence of resultant serious pathology. I do not think that this type of experimental work will represent the effect of CS gas on previously diseased lung tissue, as presented by the established bronchitic and more particularly by the established asthmatic.

In conclusion, I sincerely hope that the "clinical trials" of the Bogside will eventually show that in fact no permanent change has resulted.—I am, etc.,

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Antidepressants and Serum Pseudocholinesterase

SIR,—The interrelationship of this enzyme, the monoamine oxidase inhibitors, and the tricyclic antidepressants is perhaps even more complex than is suggested by Dr. P. O. Bodley and others (30 August, p. 510).

In the spectrophotometric assay,¹ amitriptyline—whose chemical structure bears some resemblance to that of dibucaine²—appears to be an effective inhibitor of serum pseudocholinesterase. It would be interesting to know whether there is any clinical counterpart to this finding, and if phenelzine also inhibits the enzyme *in vitro*.—I am, etc.,

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Active Labour

SIR,—The paper by Mr. Kieran O'Driscoll and others (24 May, p. 477) interested me greatly for several reasons. In the first place, my colleagues and I affirmed in 1956 "that intact membranes during labour are a liability rather than an asset," and that "every woman, be she primigravida or multigravida, should be nearing delivery after she has been in labour for 12 hours."¹ We therefore examined patients early in labour, and if advance was not apparent low amniotomy was done, and when necessary an oxytocin drip was started. With improved ante- and intra-natal care oxytocin became less necessary in such circumstances. In these days prolonged labour is uncommon in good obstetric centres, and it is often claimed in clinics in the U.S.A. that the average duration of labour in primigravidae is about 12 hours, and in Mexico City I was told that the average was nearer six hours.

What is so pleasing about this paper is that it reports a prospective study, that such care was taken to ensure that the women were in true labour and were not dehydrated, and that they were visited by competent medical staff several times in the day and also late at night. It is not stated how many of these deliveries were premature, how many at term, and how many were postmature, whether many of them had hypertension or any other abnormal condition, whether the presenting part was invariably engaged, and what was the state of the cervix. In the group of 915 women definitely in labour amniotomy was done in 119 (13%), oxytocin was given to 35 (3.8%), whereas 796 (87%) required no such interference. It would be interesting to know the average amount of oxytocin given to these patients and the percentage that required operative delivery. The second group of 85 "additional cases" presumably belonged to an entirely different category. In them the membranes had either ruptured spontaneously or had been ruptured artificially, and their myometrial sensitivity to oxytocin may have been low. They therefore presented a twofold problem—to get them into labour, and to keep it short. It is most desirable to know the average amount of oxytocin used and the operative delivery rate in this group.

With regard to the "popular fallacies," it is probable that cephalopelvic disproportion is less common in Dublin than in some centres in Great Britain. During 1910¹ 4,449 deliveries occurred in the combined extern and intern departments of the Rotunda Hospital.² There were five caesarean sections, the forceps rate was 3.6%, the stillbirth rate 3.2%, and the hospital perinatal mortality rate was 4.8%. Such figures would not have been possible in Glasgow in 1911. Further, women of certain African tribes can expel infants through markedly contracted pelves, and large amounts of an oxytocic drug could mask slight degrees of cephalopelvic disproportion. Even if rupture of the primigravid uterus is uncommon it is reasonable to conclude that damage done during the first delivery might conduce to rupture in subsequent pregnancies.

It is difficult to grasp how a standard concentration of 10 units of oxytocin in a litre of glucose solution "increases the margin of safety" unless Mr. O'Driscoll has discovered some special means of controlling the drip rate which has eluded others. A variation in it of from 5 to 10 drops a minute would alter the amount of oxytocin delivered by from 3 to 6 mU./min. The authors give no indication as to what percentage of women were given 50 mU. oxytocin/min. and for how long, whether the infusion rate was lowered when uterine activity increased, how frequently foetal distress necessitated slowing of the drip and/or operative interference, and how uterine activity was monitored, whether electronically or by the hands of students or nurses.

Seeing that amniotomy *per se* increases the sensitivity of the human myometrium to oxytocin,³ it is clearly more dangerous to give massive amounts of oxytocin after the membranes have been ruptured than before amniotomy. Amniotomy followed by an oxytocin drop (or infusion), either to induce or to enhance labour, was started at Bradford and remains the Bradford technique whether 50 mU. instead of 5 mU. oxytocin/min. are infused (there are 450 million mU. in one gram of oxytocin), the only difference being in safety. Apart from trauma to mother or infant it is beyond doubt that such amounts of oxytocin are antidiuretic,⁴ and the delivery of 80 drops a minute of the recommended solution, or one litre in just over 3½ hours, might cause marked water retention which could not benefit the mother.

The vast majority of deliveries in Britain are done in non-teaching hospitals, and it is idle to expect that a special care unit comparable with that at the National Maternity Hospital, Dublin, could be staffed in many of them. You, Sir, in your leading article (9 August, p. 315) suggest that "the excellent results reported by O'Driscoll may be due as much to the high standards of supervision as to the active policies adopted," and with this observation many of your readers will agree. The fact that 796 out of 915 primigravidae in labour proceeded in normal labour without either amniotomy or oxytocin highlights the essential difference between the several groups. It is reasonably certain that endogenous oxytocin does not put a woman into labour but rather that physico-chemical changes in and around the myometrial cells sensitize the human myometrium to the amounts of oxytocin which normally circulate in the blood and which probably never reach 2 microunits/ml. blood.⁵

The real problem is why the uterus tolerates the foetus, and when that is understood it may be possible to use physiological means to induce labour-readiness measured by myometrial sensitivity to oxytocin. Having

the privilege of knowing Mr. O'Driscoll, I am convinced that he would be the last person to encourage harassed, inadequately equipped, and understaffed hospitals to conduct labour with a stop-watch in hand and to venture on the use of a hormone as a drug in order to achieve chemical *accouchement forcé*.—I am, etc.,

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SIR,—Mr. K. O'Driscoll and others (24 May (p. 477) have reported the use of pharmacological concentrations of intravenous oxytocin (3.1 mU–50 mU/min.) in preventing prolonged labour, and you have commented on this in a leading article (9 August, p. 315).

In Southampton the regimen of oxytocin therapy advocated by Mr. O'Driscoll has been used since late May of this year in 40 patients. Of these patients 19 were primigravidae and 21 were multigravidae. In this series there has been no evidence of uterine or foetal damage. The results support Mr. O'Driscoll's observations that delivery can generally be expected within six hours of setting up the drip. However, two patients were delivered by caesarean section on account of foetal heart irregularity early in labour. It may be significant that both these were elderly primigravidae with "precious babies," and it was felt abdominal delivery was conservative in the absence of sophisticated means for assessing foetal wellbeing.

This series has mainly been confined to patients having amniotomy as a means of inducing labour, indicated by abnormal glucose tolerance, apparent prolonged pregnancy, and pre-eclampsia. In addition, five patients with already prolonged labour were treated.

In a group of seven patients with evidence of pre-eclampsia we combined oxytocin-promoted labour with lumbar epidural block anaesthesia. This combination has the advantage of lower levels of blood pressure and absence of painful stimuli, both desirable in the pre-eclamptic. The oxytocin concentrations advocated by Mr. O'Driscoll do seem to raise the level of blood pressure in labour, and conduction anaesthesia may remove this possible objection to their use.

It is felt that this experience in a busy provincial centre in England might be relevant to the discussion on active management obstetrics. Though the policies advocated by Mr. O'Driscoll involve closer attention by both doctors and midwives, this further step towards planned obstetrics has considerable advantages in the busy city maternity units characteristic of Britain.—I am, etc.,

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Oral Contraceptives and Thromboembolism

SIR,—Although Drs. M. P. Vessey and Richard Doll (14 June, p. 651) have found that the incidence of thromboembolism in patients admitted to hospital does not vary greatly with age or parity, this is not so for all patients with thromboembolism brought to general practitioners and from which hospital admissions are selected. In the communication of the Royal College of General Practitioners' Research Unit, 1967,¹ in which the relationship between thromboembolism and use of oral contraceptives was first established at a significant level, it was shown that rates per 1,000 population at risk increased with age and with parity. The Table gives the estimated rates for married women between the ages of 15 and 50 using the data collected in the above-mentioned study. Results are given separately for patients with venous thromboemboli: (1) seen during pregnancy and the puerperium, (2) using oral contraceptives, and (3) all others. The respective populations at risk were estimated by applying to the total population of the practices concerned in the study (1) national birth rates by age, and parity (Registrar General's *Statistical Review*, 1966), and (2) information about oral contraceptive usage during 1965–6 obtained from various papers quoted as references in the paper under discussion.

Age Group	Population at Risk (Married Women)	Patients with Venous Thromboembolism (Rates per 1,000 Population)		
		Pregnant or Puerperal	Oral Contraceptive Users	Others
15–29	12748	3.9 (14)	2.1 (2)	0.6 (5)
30–39	15756	8.8 (11)	5.9 (7)	1.1 (15)
40–49	15811	32.5 (4)	14.7 (7)	3.4 (52)
N.K.		(1)		(3)
All ages	44315	6.1 (30)	6.1 (16)	2.0 (75)

The numbers of patients are shown in parentheses.

For each group of patients rates increase with age, although it must be admitted that some of the numbers of patients concerned are small. The numbers of married women aged 15–49 in each parity group have also been estimated, and the following rates were obtained for those who were neither pregnant during a 12-month period nor using oral contraceptives; the numbers of cases are shown in brackets. An increasing trend in the rates with increasing parity is evident.

Drs. Vessey and Doll found that five married women per 100,000 at risk in the age group 15–40 were admitted to hospital with thromboembolic disorders without evident cause. We have assumed that this is equivalent to our category: not pregnant or puerperal, and not on oral contraceptives. We estimate the total in this group to be 93 per 100,000 at risk. The equivalent figures for married women on oral contraceptives are 57 per 100,000 admitted to hospital in the Vessey and Doll study, and our estimated total of 424 per 100,000 at risk. There would therefore seem to be a bias of 2.5 to 1 in favour of a woman with thromboembolism and taking oral contraceptives being admitted to hospital compared with women who are not using oral contraceptives.

The relative risk of hospital admission estimated by Drs. Vessey and Doll, using a direct comparison of affected and control patients, was 6.3 to 1, with 95% confidence levels between 3.4 and 11.6 to 1, and they state that "other evidence suggests that the true risk