Outcome of Unplanned Pregnancies in Trials of Progestogen-only Oral Contraceptives

Drug and Dose	Study	No. of Unplanned Pregnancies	Outcome of Unplanned Pregnancies					
			Livebirth	Stillbirth	Miscarriage	Ectopic Gestation	Termination	Unknown
Chlormadinone acetate 0.5 mg	F.P.A.	20	9	0	4	0	7	0
" " "	Yugo A ¹	4	0	0	0	1	3	0
" " "	Yugo B ²	2	0	0	0	0	2	0
Ethinodiol diacetate 0.5 mg	F.P.A.	3	0	1	1	0	0	1
Lyncestrenol 0.5 mg	F.P.A.	1	1	0	0	0	0	0
Megestrol acetate 0.5 mg	F.P.A.	8	5	0	0	0	2	1
" " 0.7 mg	Yugo B	6	0	0	0	1	5	0
Norethisterone 0.35 mg	F.P.A.	12	5	0	1	0	4	2
Norethisterone acetate 0.3 mg	F.P.A.	8	6	0	0	1	1	0
" " "	Yugo A	1	0	0	0	0	1	0
" " "	Yugo B	2	0	0	0	0	1	0
" " 0.3+0.6 mg	F.P.A.	2	1	0	0	0	1	0
" " 0.6 mg	F.P.A.	2	2	0	0	0	0	0
Norgestrel 0.05 mg	Yugo A	3	2	0	0	0	1	0
" " 0.075 mg	F.P.A.	3	1	0	1	0	1	0
" " "	Yugo B	1	0	0	0	0	1	0
Total		77	32	1	7	3	30	4

The outcome of 21 pregnancies occurring among 43 women taking megestrol acetate 0.25 mg in the Yugo A study have been omitted since this dose of the steroid was clearly a very ineffective contraceptive.

have both reported an excess of ectopic gestations among the unplanned pregnancies occurring in women using progestogen-only oral contraceptives. Their findings stimulated us to review the outcome of unplanned pregnancies occurring among the participants in the trials of progestogen-only oral contraceptives conducted by the Family Planning Association and in similar trials carried out in Ljubljana, Yugoslavia, with which one of us (M.P.V.) was associated.^{1,2} The results are shown in the table. Of the 73 pregnancies of known outcome 3 (4.1%) were extrauterine.

These data are closely similar to those that have been reported in relation to intra-uterine devices. Lehfeldt *et al.*,³ for example, found that 4.3% of pregnancies occurring with an intrauterine device in situ were ectopic, while Vessey *et al.*⁴ reported a corresponding figure of 8.9%. The implication is that progestogen-only oral contraceptives, like intrauterine devices, are much more effective at preventing uterine implantation than extrauterine. From the practical point of view we agree with Mr. Hawkins that the doctor responsible for the care of a patient who has become pregnant while using progestogen-only oral contraceptives must be on the alert in case the pregnancy is ectopic.—We are, etc.,

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- 1 Mears, E., *et al.*, *British Medical Journal*, 1969, 2, 730.
- 2 Vessey, M. P., *et al.*, *Lancet*, 1972, 1, 915.
- 3 Lehfeldt, H., Tietze, C., and Gorstein, F., *American Journal of Obstetrics and Gynecology*, 1970, 108, 1005.
- 4 Vessey, M. P., *et al.*, *Lancet*, 1974, 1, 495.

Catecholamine Excretion Levels in Neuroblastoma

SIR,—Dr. Jane V. Bond (31 August, p. 574) referred to our paper on neuroblastoma (3 August, p. 301). She pointed out that no mention was made of the use of catecholamine estimations and suggested that this might have been because in the period 1962-7 routine examinations were not being carried out. In fact, several hospitals were using these estimations as diagnostic tests and also during the follow-up of surviving

children, though the incidence of these tests increased during the later years.

Out of our total number of 639 children, we found only 109 patients who had definite reports of vanillylmandelic acid (VMA) estimations being carried out at the time of diagnosis. In 90 of these the level was raised, in 17 it was normal, and in two it was unspecified. We had records of 33 patients who were followed up over a period of time with VMA estimations being used regularly, and within the limits of our data our findings confirmed the fact that a quick return to normal levels is associated with good prognosis and vice versa. However, in view of the fact that our source material came from many different hospitals and these tests were carried out by different laboratories and under varied conditions we did not consider it worth while to publish such incomplete information in a paper largely concerned with natural history and prognostic factors.—I am, etc.,

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Status of Ward Sisters

SIR,—When the recent pay award to the nursing profession was announced there was general jubilation at this much-needed pay rise. However, when the details were made known¹ it was found that the ward sisters, who hold key positions in the nursing profession, came out badly compared with other branches of the profession. District nurses and health visitors are in Grade I and will receive a higher salary than ward sisters, who are placed in Grade II.

All nurses in training are influenced by the standards of ward sisters, patient care depends directly on their competence, and the entire organization of the ward is their responsibility. I feel these important factors have been neglected by the Halsbury Committee. It has downgraded the ward sister's position so that it becomes quite intolerable for skilled nurses to continue as ward sisters and they are being forced out of the wards, and in some cases they are leaving the profession altogether.

This lack of recognition of the ward sister's value is also seen in the limitation of the salary increments to six, which forces

nurses into nursing administration when their interest is still patient care.—I am, etc.,

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¹ Report of the Committee of Inquiry into the Pay and Related Conditions of Service of Nurses and Midwives. London, H.M.S.O., 1974.

Tissue for Transplantation

SIR,—While I am unable to accept many of Mr. J. R. Salaman's conclusions in his frank if somewhat despondent communication (21 September, p. 736), he makes one very germane point.

There is a great and, as Mr. Salaman suggests, misplaced reluctance within the nephrological and renal transplant spheres to approach close relatives of patients in terminal renal failure to obtain live donor kidneys. The advantages of transplanting a kidney which functions immediately are considerable apart from the expected greater long-term viability. The procedure of removing a kidney from a healthy donor is very safe (18 May, p. 344).—I am, etc.,

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SIR,—Many persons are willing to donate kidneys (or any of their organs) for transplant surgery.

Some time ago a patient told me she wished to donate her eyes. She had informed her solicitor. Her medical record file had been accordingly endorsed. She was killed in a road accident. Neither her solicitor nor I heard of her death for some considerable time. Similar happenings must be quite frequent.

Why not an internationally agreed symbol tattooed, say, in the mid-lumbar region, indicating willingness to donate one or any organ?—I am, etc.,

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Gilbert's Disease and Postanaesthetic Jaundice

SIR,—Further to the discussion of the role of halothane in postanaesthetic jaundice I

would like to add one more consideration. I have recently observed two cases of post-anaesthetic jaundice in which halothane was employed. On careful investigation these were proved to be due to Gilbert's disease (congenital hyperbilirubinaemia). Starvation precipitates icterus in these cases, causing a raised plasma unconjugated bilirubin level, usually within 48 hours. The incidence of Gilbert's disease may be as high as 5% and it should therefore be a consideration in the differential diagnosis of cases of post-anaesthetic jaundice.—I am, etc.,

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Gonorrhoea in Obstetrics and Gynaecology

SIR,—Dr. R. S. Morton's letter (27 July, p. 253) raises some very interesting and important points.

The approval by the Royal College of Obstetricians and Gynaecology of a post in venereology during the elective year preceding the M.R.C.O.G. examination is most welcome, as it would enlighten the holders of such a post that venereology is a much more complex subject than is generally thought. However, I fail to follow Dr. Morton's reasoning that "the emphasis in the specialty of venereology is nowadays very much on what might be called medical gynaecology" and that the "future lies with holders of the M.R.C.O.G." If this were true it would have a disastrous effect on the recruitment of junior medical staff. While solving an immediate situation, it would in the long term aggravate a condition which is becoming more and more acute. In my opinion the specialty of venereology is in danger of collapse unless we sell the image of the specialty as it really is—one of importance and not one to be ignored, as is shown by the increasing number of patients and the more complex diagnostic tests.

A major factor in the deterioration of recruitment to the specialty is outlined in the letter from Dr. S. Mehta and others (14 September, p. 690). Though they did not name it, venereology is in the very worst position in that few if any consultants receive more than the basic salary. If this cause were removed it would obviate the necessity for back-door recruitment.—I am, etc.,

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Plagiarism in Medicine

SIR,—Professor Douglas Hubble's Personal View (7 September, p. 623) has proved too great a temptation for me to resist confessing the "rare excitement" I felt when I thought I was the first to find that Lord Lister had not introduced antiseptic surgery. While preparing my M.D. thesis I read that of the French physiologist Paul Bert, which was published in 1863. While considering the influence of various agents on the survival of skin grafts he wondered if "*la présence d'acide phénique si propre à arrêter les transformations putrides*" offered an advantage or disadvantage.¹

To avoid the accusation that "eagerness to declare" my discovery might shamefully distort [my] historical judgement² I looked up Lister's original communication³ in which he stated that "in the course of the year 1864 I was much struck with the account of the remarkable effects produced by carbolic acid upon the sewage of Carlisle . . . and the applicability of carbolic acid for the treatment of compound fractures naturally occurred to me." Six months later, in a leading article, the *Lancet*⁴ revealed that Dr. Lemaire of Paris had already published a book on the use of carbolic acid in medical and surgical diseases but credited Lister with having made the agent extensively known in this country. This provoked a spirited reply from Lister⁵ who, to quote Professor Hubble "introduced some explanation, which, in his own view at least, diminished the fault." He admitted that he did not claim the introduction of carbolic acid to surgery but claimed originality "for its employment with the view of protecting the reparatory processes from disturbance by external agency." A broadside was then delivered by Sir James Young Simpson in the form of an article⁶ giving very detailed evidence that "Mr. Lister has been most undoubtedly preceded by other authors in all his leading theories and uses in connexion with this subject." The earliest use of carbolic acid that he quoted was as a dressing to wounds by Cruveilhier, Follet, and Rigault in 1859, followed by the treatment of compound fractures by MM. Darrican and Petit in 1860. After this Lister retired as gracefully as possible "having already endeavoured to place the matter in its true light without doing injustice to anyone."⁶

The fact remains that Lister had claimed to have introduced carbolic acid to "protect the reparatory processes from external agency" in 1864, while in 1863 Bert was of the opinion that *acide phénique* was essential to arrest putrid transformation. I think we may safely say with Sir Walter Langdon-Brown that "while there was no real claim to priority, there was no wilful plagiarism with intent to deceive."—I am, etc.,

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- 1 Bert, P., *De la greffe animale*. Paris, Baillière, 1863.
- 2 Lister, J., *Lancet*, 1867, 1, 326.
- 3 *Lancet*, 1867, 2, 412.
- 4 Lister, J., *Lancet*, 1867, 2, 444.
- 5 Simpson, J. Y., *Lancet*, 1867, 2, 546.
- 6 Lister, J., *Lancet*, 1867, 2, 595.

Sexual Dysfunction Due to Methyldopa

SIR,—It is now widely held that methyldopa is a drug which can control systemic hypertension with relatively few unwanted side effects. Disorders of sexual function are known to occur, but apart from reports saying that they are "rare"¹ or met with "seldom"² or "infrequently"³ their exact incidence has been poorly documented. Papers reporting a 2% incidence of methyldopa-induced impotence have been published⁴ as well as others which report no significant change in libido, potency, or ejaculation.^{5,6} We are of the opinion that disorders of sexual function occur in approximately one-third of males so treated and append the following information.

Twenty-seven male patients being treated

with methyldopa for essential hypertension were seen in our medical outpatient clinic at the Veterans Administration Hospital, Northport, New York, in the month of July 1974. These patients were taking 500-2,000 mg a day in divided oral doses and were aged 43-64 years. Close interrogation revealed that seven were experiencing some disorder of sexual function which had started within a few days of commencing therapy. These included a decrease in libido, an inability to maintain an erection, and difficulty in ejaculation. Within two weeks of discontinuing the drug and instituting a regimen of propranolol and hydralazine these undesirable side effects had disappeared. Sexual dysfunction was not noted in a comparable group of 22 hypertensive males treated with a thiazide diuretic alone.

In view of the fact that aberrations of sexual function were not related to age or daily dose of the drug we would urge physicians to inquire specifically about the side effects experienced by patients being treated with methyldopa.—We are, etc.,

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- 1 Wilson, G. M., *Practitioner*, 1965, 194, 51.
- 2 Bock, K. D., von., *Zeitschrift für Allgemeinmedizin*, 1970, 46, 1287.
- 3 Evans, B., *Practitioner*, 1963, 191, 96.
- 4 Johnson, P., et al., *British Medical Journal*, 1966, 1, 133.
- 5 Bauer, G. E., et al., *Medical Journal of Australia*, 1973, 1, 930.
- 6 Bulpitt, C. J., and Dollery, C. T., *British Medical Journal*, 1973, 3, 485.

Swelling of Arm in Patients with Arteriovenous Fistula

SIR,—We were most interested in the recent case report by Drs. J. Göthlin and E. Lindstedt (7 September, p. 629) and have recently completed formal studies of hand volume in patients on intermittent dialysis using an arteriovenous fistula. We found that the volume of the dominant hand was 5.1% greater than that of the non-dominant hand ($P < 0.001$) in 28 normal subjects but that the volume of the non-dominant (fistula) hand was greater in age- and sex-matched male (18%, $n = 23$, $P < 0.001$) and female (21%, $n = 5$, $P < 0.01$) dialysis patients.

We found that 23 out of 36 patients developed pain, numbness, or paraesthesiae on dialysis, these symptoms being confined to the distribution of the median nerve in the fistula hand. In six patients with severe symptoms the volume of the fistula hand increased by 15% on dialysis ($P < 0.05$), whereas the volume of the non-fistula hand increased by 4% ($P > 0.10$). Predialysis venous pressure in the dorsum of the fistula hand was 21 ± 4 cm H₂O higher than in the non-fistula hand. Because of severe symptoms two patients have required carpal tunnel decompression.

We conclude that oedema of the fistula hand is common in dialysis patients, though it may be undetectable on physical examination. The oedema is probably a consequence of high venous pressure and exacerbated by immobility during dialysis. Construction of an end-to-side anastomosis