detection. This study showed that questioning patients about their drinking habits was not perceived by doctors as a priority. Many patients who drink to excess therefore remain unidentified and a major reducible cause of disease and death is ignored.

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- 1 Lloyd G, Chick J, Crombie E, Anderson S. Problem drinkers in medical wards: consumption patterns and the disabilities in newly identified male cases. *Br J Addict* 1986;81:789-95.
- 2 Barrison IG, Viola L, Murray-Lyon IM. Do housemen take an adequate drinking history? *Br Med J* 1980;281:1040.
- 3 Babor TF, Ritson EB, Hodgson RJ. Alcohol related problems in the primary health care setting: a review of early intervention strategies. *Br J Addict* 1986;81:23-46.
- 4 Mayfield D, McLeod G, Hall P. The CAGE questionnaire: validation of a new alcoholism screening instrument. *Am J Psychiatry* 1974;131:1121-3.
- 5 Health Education Council. *That's the limit*. London: Health Education Council, 1986.

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Centre for Health Economics, University of York, York YO1 5DD

N ROWLAND, BA, DIPCONS, research fellow
A MAYNARD, BA, BPHIL, professor of economics

Booth Park Hospital, York

A BEVERIDGE, MRCPsych, MPhil, senior registrar in psychiatry
P KENNEDY, MD, FRCPsych, consultant psychiatrist
W WINTERSGILL, FFCM, MRCP, community physician

District Hospital, York YO3 7HE

W STONE, FRCP, consultant physician

Correspondence to: Ms Rowland.

Successful treatment of infertility due to polycystic ovary disease using a combination of luteinising hormone releasing hormone agonist and low dosage menotrophin

Infertility and early loss of pregnancy in women with polycystic ovary disease may be caused by excessively high concentrations of luteinising hormone during follicular development.¹ Different regimens have been suggested to improve the poor outlook for these patients,² including the use of "pure" follicle stimulating hormone (Metrodin)³ and suppression of endogenous luteinising hormone production by treatment with a luteinising hormone releasing hormone agonist before stimulation of the ovaries.⁴ Luteinising hormone releasing hormone agonists, given continuously rather than cyclically, reduce gonadotrophin concentrations to prepubertal values. We describe the successful treatment of a patient with polycystic ovary disease and primary infertility of five years duration using a "block and replace" approach.

Case report

A woman started taking the contraceptive pill at the age of 18 because of irregular menstrual cycles and menorrhagia and stopped taking it at the age of 23 because she wished to become pregnant. Her cycles were irregular for 18 months, and a gynaecological opinion was sought. Examination showed that she was slim and non-hirsute. Investigations showed a testosterone concentration of 6.0 nmol/l (normal range in women <2.5 nmol/l), and luteinising hormone was raised throughout the menstrual cycle (37, 45, >50, 24, >50 IU/l); Prolactin concentration was normal, but serial mid-luteal progesterone was <3 nmol/l, confirming non-ovulatory cycles. Clomiphene citrate 50 mg taken on days 2-6 induced regular cycles, but persistently low progesterone values showed that they were non-ovulatory.

Ultrasound examination showed the classic appearance of polycystic ovaries, which were confirmed histologically. Laparoscopy and injection of dye showed that the uterus and fallopian tubes were normal. Clomiphene citrate 100 mg taken on days 2-6 induced an increase in oestradiol concentration to 830 pmol/l with a dominant follicle 17 mm in diameter; however, mid-luteal progesterone concentration remained poor at 15 nmol/l, despite intramuscular injection of human chorionic gonadotrophin 10 000 IU. Treatment with menotrophin (Pergonal), as directed by the manufacturers, was started, but after three ampoules (225 IU follicle stimulating hormone and 225 IU luteinising hormone) on days 3, 5, and 7 oestradiol concentration rose to 2760 nmol/l. Ultrasound examination confirmed moderate hyperstimulation with three to four follicles in each ovary.

After the follicles had regressed a low dosage regimen of menotrophin was introduced using one ampoule (75 IU follicle stimulating hormone and 75 IU luteinising hormone) daily and increasing by half an ampoule each week until a dominant follicle developed. On day 14 there was a single follicle 22 mm in diameter, and oestradiol concentration was 2340 pmol/l. Human chorionic gonadotrophin 5000 IU was given intramuscularly to provide a surge in luteinising hormone, and seven days later the progesterone concentration was 68 nmol/l, suggesting ovulation. Ultrasound examination, however, showed hyperstimulation, with eight cysts 20-30 mm in diameter on the right ovary and four cysts on the left ovary. A similar regimen in the next cycle resulted in a single follicle 18 mm in diameter on day 14; this time no human chorionic gonadotrophin was given. Mid-luteal progesterone concentration was 11 nmol/l, and the follicle regressed. Thus low dose menotrophin treatment induced normal follicular development but no spontaneous ovulation, and human chorionic gonadotrophin induced hyperstimulation.

Suppression of the persistently high luteinising hormone concentrations with a luteinising hormone releasing hormone agonist was attempted. Buserelin was given intranasally four times daily (total daily dose 1200 µg), and luteinising hormone, follicle stimulating hormone, and oestradiol concentrations were monitored. The table shows the rise in oestradiol concentration with initial stimulation and subsequent suppression of gonadotrophins and oestradiol. After one ampoule of menotrophin given intramuscularly each day for 10 days oestradiol concentration was 1840 pmol/l and two follicles, 17 and 20 mm in diameter, were seen on ultrasound examination. Human chorionic gonadotrophin 5000 IU was given intramuscularly, but ultrasound examination confirmed failure of ovulation, with cyst formation (42 and 50 mm in diameter) and a progesterone concentration of 24 nmol/l associated with theca cell luteinisation. This regimen was repeated. On day 11 the oestradiol concentration was 1800 pmol/l, and ultrasound examination showed one follicle 18 mm in diameter and three follicles 10-12 mm in diameter. Human chorionic gonadotrophin 7500 IU was given intramuscularly, and seven days later the progesterone concentration was very high (>100 nmol/l), suggesting conception. Buserelin was withdrawn and a singleton pregnancy was confirmed on ultrasound examination. At the time of writing the pregnancy had reached 30 weeks gestation and was progressing normally.

Concentrations of oestradiol, follicle stimulating hormone, and luteinising hormone before and after treatment with buserelin

	Oestradiol (pmol/l)	Follicle stimulating hormone (IU/l)	Luteinising hormone (IU/l)
Before treatment with buserelin	170	5.3	37
After treatment with buserelin:			
1 week	450	2.9	26
2 weeks	880	0.7	7.1
3 weeks	70	0.8	3.2
6 weeks	80	3.2	2.0

Comment

Our patient's treatment was hampered by her tendency to hyperstimulate with pronounced cyst formation, probably related to her persistently raised luteinising hormone concentration. The combination of suppression of endogenous luteinising hormone production and low dose menotrophin treatment resulted in conception in the second cycle of treatment. This regimen, or one using a long acting luteinising hormone releasing hormone analogue,⁵ may be helpful in other patients with polycystic ovary disease.

- 1 Howles CM, Macnamee CM, Edwards RG, Goswamy R, Steptoe PC. Effect of high tonic levels of luteinising hormone on outcome of in-vitro fertilisation. *Lancet* 1986;ii:521-2.
- 2 Franks S, Adams J, Mason H, Polson D. Ovulatory disorders in women with polycystic ovary syndrome. *Clin Obstet Gynaecol* 1985;12:605-32.
- 3 Ginsburg J, Sallam H, Scammell G, et al. Ovulation and pregnancy after pure FSH therapy in sclerocystic ovarian change. In: Ludwig G, Thompson K, eds. *Archives of gynaecology*. Berlin: Springer Verlag, 1986.
- 4 Fleming R, Haxton MJ, Hamilton MPR, et al. Successful treatment of infertile women with oligomenorrhoea using a combination of an LHRH agonist and exogenous gonadotrophins. *Br J Obstet Gynaecol* 1985;92:369-73.
- 5 Thomas EJ, Jenkins J, Lenton EA, Cooke ID. Endocrine effects of goserelin, a new depot luteinising hormone releasing hormone agonist. *Br Med J* 1986;293:1407-8.

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Endocrine Section, Department of Medicine II, Southampton General Hospital, Southampton SO9 4XY

MARY ARMITAGE, BSC, MRCP, senior registrar
TERENCE WILKIN, MD, MRCP, senior lecturer

Department of Radiology, Southampton General Hospital, Southampton SO9 4XY

KEITH DEWBURY, FRCP, MB, consultant radiologist

Correspondence to: Dr Mary Armitage, Medicine II, Level D, South Block, Southampton General Hospital, Southampton SO9 4XY.