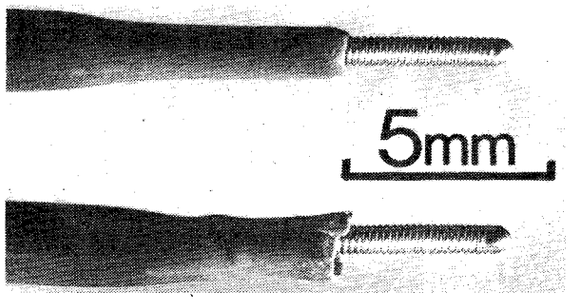
SIR,—During the past decade silicone elastomer ('Silastic') catheters have largely replaced the more rigid 'Teflon' and polypropylene catheters for long-term parenteral nutrition. Given a safe and effective means of placement,[1] our experience now is of very few mechanical or thrombotic problems.

The recent correspondence regarding thrombosis of the superior cava related to the tip of central venous catheters has highlighted the association of this complication with rigid catheters, especially those used for haemodialysis. Since 1980 we have been using 'Vas-cath' (Gambro) catheters for short-term haemodialysis. Seventy catheters have been placed de novo in 65 patients. Poor flow has been infrequent and usually corrected by catheter change over a guidewire. Since none of our patients has been investigated by venography we cannot exclude the possibility of superior vena caval thrombosis around the catheter tip.

An assumption that intimal damage to the superior vena cava is important in the genesis of this complication explains the association with rigid catheters. However, I believe that the tips of these catheters can become seriously damaged during insertion over the guidewire. Such a damaged tip (figure) can have sharp everted



Damaged tip of vas-cath following insertion over guidewire without dilator (above, an unused catheter for comparison).

edges which will, I suggest, lead to intimal damage of the cava.

In view of this I have now changed our technique of insertion.[2] Whereas we used to dilate the track and the tunnel separately with the catheter itself, we now do this with a disposable dilator; passage of the vas-cath itself is now not attended by any snagging or the need for excessive pushing and twisting.

Until softer more pliable catheters are available I would strongly recommend the use of a dilator to avoid catheter tip damage.

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MATERNAL VALPROIC ACID AND CONGENITAL NEURAL TUBE DEFECTS

SIR,—Our birth defects monitoring system for the Rhône-Alpes region of France, where there are about 72 000 births a year, operates with the collaboration of all paediatricians and obstetricians. We participate in the international clearing house for birth defects monitoring.[3] We collected, between Aug. 11, 1979, and Aug. 10, 1982, 72 case-records of infants born with lumbosacral neural tube defects (NTD) alone or associated with other malformations. 9 were infants born to epileptic mothers who had taken valproate during pregnancy. Gomez' letter[4] prompted us to describe these cases (see table).

We have no case of association of valproic acid with anencephaly (among the 17 cases of anencephaly collected during the same period), but our monitoring system is imperfect for stillbirths and for therapeutic abortions.

DETAILS OF NINE CASES OF NTD IN INFANTS BORN TO MOTHERS WHO HAD TAKEN VALPROATE DURING PREGNANCY

Case (and date of birth)	Valproate* (mg/day)	Defect(s)	Family history
1 (Nov. 8, 1979)	1500	LMS	Father's brother. SBA, died at 6 mo First cousin: mucoviscidosis
2 (June 28, 1980)	1500	Sacral meningocele	None
3 (March 6, 1981)	400	LSM + hydrocephaly and microcephaly	None
4 (April 5, 1981)	2000	Lumbar SBA	Grandmother's sister: trisomy 21 Second cousin: DMD Maternal grandmother and maternal second cousin: epilepsy
5 (Aug. 12, 1981)	1200	Epidermised lumbar SBA* + hydrocephaly	Second cousin: SBA First cousin: late enuresis
6 (Nov. 19, 1981)	1000	LSM + complex congenital cardiopathy + hypospadias (karyotype normal)	Mother's sister: SBO + late enuresis
7 (March 2, 1982)	1000	Sacral meningocele	None
8 (March 18, 1982)	750	Lumbar SBA	None
9 (Aug. 10, 1982)	1500	Sacral open meningocele	None

SBO = spina bifida occulta; SBA = spina bifida aperta; DMD = Duchenne muscular dystrophy; LSM = lumbar myelomeningocele

*Throughout pregnancy except in case 2 (first trimester), other anticonvulsants (and daily doses in mg) were: phenobarbitone 50 (case 1), phenobarbitone 200 (case 2), phenobarbitone 200 + primidone 250 (case 3), and clonazepam 2 (case 9).

2 of the 9 cases had another case of severe NTD in their family, a larger than expected proportion.

All 9 cases required surgery, and 1 died (no. 6). Only one mother (no. 2) had non-stabilised epilepsy: she had had four epileptic seizures during the first trimester of pregnancy.

Valproic acid was given alone (5 cases) or with phenobarbitone (3 cases), or clonazepam (1 case). The doses of valproic acid were high, over 1 g daily in 7 cases. Blood concentrations of valproate in these women will be measured while they are on the same treatment.

We suspect that valproate may be teratogenic and have started a case-control study in collaboration with some other members of the International Clearinghouse.

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**In France and in West Germany, where the equivalents of data sheet compendia are readily available to the public, warnings about the possible teratogenicity of sodium valproate are low key, but in the U.K., U.S.A. and elsewhere the product information warnings are specific and refer to animal evidence. Besides Gomez' report there are other human data that warrant caution.—ED. L.

POLYCYSTIC OVARIES DISEASE: ONE OVARY TOO MANY?

SIR,—The Stein-Leventhal syndrome—consisting of hirsutism, oligomenorrhoea or amenorrhoea, and obesity combined with polycystic ovaries, and nowadays called the "polycystic ovaries syndrome" (PCO)—still has an uncertain aetiology. The primary lesion can (but generally does not) originate in the adrenal glands. In most cases it remains unclear whether one or both ovaries or hypothalamic-hypophyseal dysfunction is predominantly involved in the disease. However, it is well established that androgen production from ovaries and/or adrenal glands is increased and that continuous oestrogen release contributes to the syndrome.

There is a tendency to the view that PCO should not be left untreated. The androgen excess, it is argued, can cause hirsutism (or even virilism) and overweight because of the anabolic effects of androgens and the increased appetite while the continuous release of unopposed oestrogen could increase the risk of endometrial and mammary cancer.

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3. Flynt JW, Hay S. International Clearinghouse for Birth Defects Monitoring system. *Contr Epidemiol Biostat* 1979; **1:** 44–52
4 Gomez M. Possible teratogenicity of valproic acid. *J Pediatr* 1981; **98:** 508.