The Detector

Circuit Description.—Two transistors are used in a Darlington connection to provide a high gain. When the resistance between the input terminals T1 and T2 (see fig.) is lowered the transistor collector currents increase and one coil of the remanent relay RL is energized and opens both sets of contacts. The relay remains in this state even if the coil current returns to zero. The contacts RL2 are connected in series with the battery supply to an electric clock and contacts RL1 are connected in series with the internal batteries. The unit, therefore, consumes no current except during the very short time that the relay contacts are actually changing over. When the resistance at the input terminals is raised again the contacts of the remanent relay may be closed by pressing the reset button, which switches the relay back to its resting state.

Operating Instructions.—The sensing pad is connected to push-type terminals on one side of the unit and the clock battery supply is broken through a two-pin plug. If the pad is dry the input terminal resistance is high and the clock will start when the reset button is pressed. The sensitivity control VR1 sets the terminal resistance at which the unit operates.

¹ Willington, F. L., *Gerontologica Clinica*, 1969, 2, 330.

² Willington, F. L., personal communication.

Musgrave Park Hospital, Belfast BT9 7JB

J. A. C. BALL, M.D., F.R.C.P., Consultant Physician

Short Brothers and Harland Ltd., Queens Island, Belfast

M. H. McFADDEN, B.Sc., M.I.E.E., Head of Ground Equipment, Electronics Department

Ectopic Pregnancy Despite Intrauterine Contraception: A Clue to Mode of Action of I.U.C.D.s

The mode of action of intrauterine contraceptive devices (I.U.C.D.s) remains obscure. Vessey *et al.*¹ confirmed the report by Lehfeldt *et al.*² that the proportion of ectopic nidations in cases of failed intrauterine contraception greatly exceeds that in pregnancies in the population at large. In refuting the possibility that intrauterine contraception causes ectopic pregnancy, particularly ovarian pregnancy, Lehfeldt *et al.*² stressed that it is merely more effective in preventing normal uterine implantation than ectopic implantation.

Patients

Between 1 July 1967 and 18 December 1974, 103 patients with ectopic pregnancy were admitted to hospital. There were no deaths. Fourteen of these patients had conceived an ectopic pregnancy with an I.U.C.D. in place. The sites of the pregnancies, as noted at laparotomy or laparoscopy, are shown in the fig. Those ectopic pregnancies occurring despite the use of an I.U.C.D., and accurately located, appeared to be confined to the ovary, tubal infundibulum, whence some had been extruded as tubal abortions, and tubal ampulla. Statistical evaluation is precluded by the small number of patients.

Discussion

I.U.C.D.s neither stop ovulation³ nor interfere with sperm invasion of the oviducts.^{4,5} In a study of a large series of women using I.U.C.D.s, Lehfeldt *et al.*² showed that they reduce normal uterine pregnancy by about 99.5%, tubal pregnancy by 95%, but ovarian nidation not at all. Discussing the anti-fertility effect of intrauterine contraception—maximal in the endometrial cavity, weaker in the tubes, but absent in the ovaries—these workers postulated some enzymatic or other chemical action, possibly by retrograde flow from endometrium to tubes. When this is related to the sites of the ectopic pregnancies in this series of patients fitted with an I.U.C.D. the following possibilities arise: *effective* intrauterine contraception *inhibits* ovum migration along the oviduct with the production of an anti-fertility state, though not to the absolute exclusion of an occasional ovarian pregnancy; *failed* intrauterine contraception permits essentially

Sites of 103 ectopic pregnancies noted at laparotomy or laparoscopy. ● = No I.U.C.D. in situ. + = I.U.C.D. in situ.

ally normal fertilization but with an incidence thereafter of ectopic, mainly tubal implantation by reason of *disturbed* ovum migration along the Fallopian tube. Many more patients with ectopic pregnancies despite intrauterine contraception should be studied to confirm this impression.

I thank my gynaecological and surgical consultant colleagues for access to case notes, and Miss Joy Graham for the illustration.

¹ Vessey, M. P., *et al.*, *Lancet*, 1974, 1, 495.

² Lehfeldt, H., Tietze, C., and Gorstein, F., *American Journal of Obstetrics and Gynecology*, 1970, 108, 1005.

³ Faucher, G. L., *et al.*, *American Journal of Obstetrics and Gynecology*, 1969, 104, 502.

⁴ Malkani, P. K., and Sujun, S., *American Journal of Obstetrics and Gynecology*, 1964, 88, 963.

⁵ Morgenstern, L. L., *et al.*, *American Journal of Obstetrics and Gynecology*, 1966, 96, 114.

Hillingdon Hospital, Uxbridge, Middlesex UB8 3NN

GEORGE JONAS, F.R.C.S., F.R.C.O.G., Consultant Obstetrician and Gynaecologist

Erythrocyte Deformation in Duchenne Muscular Dystrophy

Using scanning electron microscopy Matheson and Howland¹ found an increased proportion of deformed erythrocytes (echinocytes) in patients with various forms of muscular dystrophy. Miale *et al.*,² however, were unable to repeat these results. Matheson and Howland¹ suggested that this might have been due to their small sample size and to technical differences. Since Matheson and Howland¹ stated that the deformation of erythrocytes was visible on light microscopy the present study of a much larger sample of boys with Duchenne muscular dystrophy, carriers, and controls was undertaken to determine the possible wider application of their findings to the detection of carriers. The effects of technical variations were also examined.

Methods and Results

Early morning blood samples were obtained from fasting subjects by finger-stabs. Three separate samples were obtained from each person. From each sample three slides were prepared, and from each slide 100 cells were examined in random fields. Thus 900 cells were examined from each person, from which the proportion of deformed cells was estimated. The samples were treated according to the method of Matheson and Howland.¹ After fixation, wet preparations were examined by light microscopy at $\times 625$.

Cells were considered abnormal only if they were clearly deformed as classified by Bessis⁴ as either echinocytes II or echinocytes III.

The proportion of echinocytes was not significantly affected in the controls, affected boys, or carriers by the method of blood sampling or number and duration of saline washes. In addition the purity of glutaraldehyde, osmolality, and duration of fixation had no effect. There was no relationship between age or sex and the proportion of echinocytes.

There were significant differences in the proportions of echinocytes between the controls and the affected boys ($P < 0.01$), and between the controls and the definite carriers ($P < 0.001$) (table). Nevertheless, there was considerable overlap between the controls and carriers and even between the controls and affected boys. There was no apparent correlation between the proportions of echinocytes and serum levels of creatine kinase in either the affected boys or the carriers.

Proportion of Echinocytes in Controls, Boys with Duchenne Muscular Dystrophy, and Carriers

	No.	Age Range (Years)	Percentage of Echinocytes (Mean $\pm$ S.D.)
Controls	17	10-50	3.86 $\pm$ 1.93
Boys with Duchenne muscular dystrophy	9	8-18	8.64 $\pm$ 6.12
Carriers { Definite	5	40-60	11.23 $\pm$ 8.08
{ Definite*	1	37	9.75
{ Possible	9	18-60	6.45 $\pm$ 3.66

*Manifesting carrier with severe weakness.

Comment

Though these findings to some extent confirm those of Matheson and Howland,¹ it seems unlikely that the test will prove more reliable than the estimation of serum levels of creatine kinase in detecting carriers. It might, however, prove helpful in the antenatal diagnosis of Duchenne muscular dystrophy should it prove possible to obtain samples of fetal blood in early pregnancy.

¹ Matheson, D. W., and Howland, J. L., *Science*, 1974, 184, 165.

² Miale, T. D., Frias, J. L., and Lawson, D. L., *Science*, 1975, 187, 453.

³ Matheson, D. W., and Howland, J. L., *Science*, 1975, 187, 454.

⁴ Bessis, M., *Nouvelle Revue Française d'Hématologie*, 1972, 12, 721.

University Department of Human Genetics, Western General Hospital, Edinburgh EH4 2HU

ELIZABETH M. LUMB, B.Sc., Ph.D., Research Fellow

ALAN E. H. EMERY, M.D., F.R.C.P., F.R.S.(E.), Professor

Immobilization Hypercalcaemia in Patients on Regular Haemodialysis

Immobilization of normal people causes reabsorption of calcium from bone,¹ a small rise in serum ionized calcium,² and, rarely, frank hypercalcaemia.³ The hazard is increased when patients with renal osteodystrophy are immobilized because of pathological fractures.

Case Reports

Case 1.—A man aged 27 with obstructive uropathy from childhood who had been on regular haemodialysis for six years developed renal osteodystrophy despite prolonged treatment with vitamin D, changed in October 1972 to dihydrotachysterol (DHT) with aluminium hydroxide 30 ml/d for indigestion. In May 1973 he sustained a fracture of the femoral shaft after minor trauma and was immobilized in a Thomas splint. Two weeks later conjunctivitis with corneal calcification developed and the serum calcium reached 3.9 mmol/l (15.8 mg/100 ml) (fig.). DHT was stopped and the dialysate calcium reduced to 1.0 mmol/l (4 mg/100 ml). Despite these measures the serum calcium fell slowly and was still 3.6 mmol/l (14.6 mg/100 ml) after 30 days. The conjunctivitis persisted for two months.

Case 2.—A 46-year-old woman with chronic pyelonephritis started regular haemodialysis in January 1973 after a uraemic fit in which she fractured her right femur. This was treated by pin and plate, and bone biopsy confirmed

Case 1 Serum Alkaline, phosphate, and Alkaline phosphatase levels and treatment used.

renal osteodystrophy. She was given daily doses of DHT 0.25 mg and aluminium hydroxide gel 30 ml until February 1975, when DHT was changed to 1- α -hydroxycholecalciferol (OHCC) 2 μ g/d because of the persistence of histological osteitis fibrosa and osteomalacia. In March the pin and plate had worked loose, and since the fracture was still ununited she was admitted for bone grafting. OHCC was stopped on admission but after 16 days of immobilization her serum calcium had risen to 3.3 mmol/l (13.4 mg/100 ml). Ten days after she was mobilized the serum calcium was 2.9 mmol/l (11.8 mg/100 ml).

Case 3.—A 19-year-old man with medullary cystic disease presented five years previously with growth retardation, myopathy, and severe osteitis fibrosa. Bone disease persisted despite treatment with vitamin D and subsequently daily doses of DHT 0.5 mg and aluminium hydroxide gel 60 ml. In September 1974 he started regular haemodialysis, and in the November, DHT was changed to 1,25-dihydroxycholecalciferol ((OH)₂CC) 1 μ g/d. On 3 February 1975 he was admitted for pinning of a slipped femoral epiphysis and (OH)₂CC was stopped. By 18 February the serum calcium had risen from 2.6 to 3.7 mmol/l (10.5 to 14.9 mg/100 ml). He was mobilized on 25 February, and by 5 March his serum calcium had fallen to 3.0 mmol/l (12.2 mg/100 ml). This fall towards normal continued.

Case 4.—A man aged 31 with obstructive uropathy since birth and old renal rickets started regular haemodialysis 15 months previously. He had histological evidence of osteitis fibrosa and osteomalacia for which he received calcium carbonate 6 g/d for seven months, aluminium hydroxide gel 30 ml/d for five months, and DHT 0.25 mg on alternate days for two months. All drugs were stopped on admission but reinstituted 18 days later, DHT in a dose of 0.75 mg/d. Three days later his serum calcium had risen from 2.5 mmol/l (10.2 mg/100 ml) on admission to 2.9 mmol/l (11.6 mg/100 ml) and it continued to rise to 4.5 mmol/l (18.2 mg/100 ml), when he developed confusion, nausea, and vomiting despite stopping the DHT. Serum calcium fell slowly to 2.6 mmol/l (10.6 mg/100 ml) after two months.

Discussion

Immobilization was apparently the main cause of the hypercalcaemia in cases 1 to 3 and a contributory cause in case 4, in which the patient also received DHT and calcium carbonate⁴ at the crucial time. Fluctuations in plasma phosphatase due to variable adherence to the prescribed dose of aluminium hydroxide⁵ may also have contributed in two cases. A critical review of all treatment is necessary when patients with renal bone disease are immobilized, and careful monitoring of serum calcium and phosphate is mandatory.

References

- Hantman, D. A., et al., *Journal of Clinical Endocrinology and Metabolism*, 1973, 56, 845.
- Heath, H., et al., *Metabolism*, 1972, 21, 633.
- Lawrence, G. D., et al., *Journal of Bone and Joint Surgery*, 1973, 55A, 87.
- Ginsburg, D. S., Kaplan, E. L., and Katz, A. I., *Lancet*, 1973, 2, 1271.
- Baker, L. R. I., et al., *British Medical Journal*, 1974, 3, 150.

University Department of Medicine, Newcastle upon Tyne NE1 4LP

GEORGE DRIVAS, M.D., Research Associate

MICHAEL WARD, M.B., M.R.C.P., Lecturer

DAVID KERR, M.Sc., F.R.C.P., Professor