dose might have been insufficient for a twin pregnancy), and further studies will certainly be of great interest. However, I do not think that this case supports the hypothesis of a determinative role for beta-sympathomimetic drugs in fetal lung maturation.

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PRENATAL DIAGNOSIS OF MAROTEAUX-LAMY SYNDROME

SIR,—The Maroteaux-Lamy syndrome, or mucopolysaccharidosis type VI (M.P.S. VI), is an autosomal recessive disorder characterised by severe skeletal deformities, growth retardation, and corneal opacity. The basic defect is a deficiency of the lysosomal enzyme arylsulphatase B (A.S.B.).[1] Both A.S.B deficiency[2] and an accumulation of sulphated mucopolysaccharides[3] have been demonstrated in cultured skin fibroblasts from M.P.S. VI patients. Since A.S.B activity is measurable in cultured amniotic-fluid cells[4] prenatal diagnosis should be possible.

We have investigated the second pregnancy of a woman whose first child had M.P.S. VI, established by the demonstration of A.S.B deficiency in leucocytes (Dr K. O. Liem, Free University, Amsterdam) and in cultured fibroblasts. Amniocentesis was done in the 16th week of pregnancy (Dr H. B. Rethmeyer, Sophia Hospital, Zwolle) and amniotic-fluid cells were cultured.[5] After 16 days of growth, the cells were harvested, homogenised by sonication, and analysed for A.S.B activity using a micromodification of the method of Baum et al.[6] Only 5 µl of cell homogenate (about 10^4 cells) was used per incubation with 4-nitrocatechol sulphate as the substrate; the amount of 4-nitrocatechol produced was measured in a final volume of 55 µl.[7]

ARYLSULPHATASE A AND B ACTIVITIES IN CULTURED AMNIOTIC-FLUID CELLS AND FIBROBLASTS

Cells	Arylsulphatase*	
	B	A
Amniotic-fluid cells:†		
Pregnancy at risk	8	147
Control 1	315	273
Control 2	283	235
Control range (n = 18)	182–549	103–496
Fibroblasts:†		
Index patient	52	343
Control	499	440
Control range (n =11)	345–772	321–899

*Average activity (nmol h^{-1} mg^{-1} protein of triplicate determinations).
†Cultures used in the analyses were matched for duration of cell-culture and number of subcultures.

The specific activities of A.S.B (table) showed a deficiency in the amniotic-fluid cells from the pregnancy at risk as well as in the fibroblasts from the index patient. The activities of A.S.A, measured as a control lysosomal enzyme, seemed normal. Additional evidence, demonstrating that the fetus was affected, was obtained from the study of ^{35}S-sulphate incorporation into the intracellular mucopolysaccharide pools.[8] After 4 days of incorporation, fibroblasts from the index patient and amniotic-fluid cells from the pregnancy at risk showed a threefold raised level of labelled intracellular mucopolysaccharides as compared with controls.

The parents decided on termination of pregnancy at the 20th week. Confirmatory studies were done on fetal liver and skin by separation of A.S.A and A.S.B[2] on a D.E.A.E.-column and measurement of activities with 4-methylumbelliferyl sulphate as the substrate. In a control fetal liver 58% of the total A.S. activity was found in the B peak. In contrast the A.S.B activity in the liver of the affected fetus was reduced to 8% of the total arylsulphatase activity. Similar results, confirming A.S.B deficiency in this fetus, were obtained with the fetal skin.

These results demonstrate that a reliable prenatal diagnosis of M.P.S. VI is possible and can be completed within 2–3 weeks after amniocentesis if microtechniques are used.

Dr J. J. M. van Gemund (University Hospital, Leiden), referred this family. This study was financed in part by Het Praeventiefonds, the Hague, Netherlands.

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CHOLINERGIC SIDE-EFFECTS ASSOCIATED WITH DEANOL

SIR,—The drug deanol (2-dimethylaminoethanol) has been reported to be useful in the management of several neurological problems, including learning disorders and hyperkinesis of childhood, levodopa-induced dyskinesias, Huntington's chorea, and some cases of tardive dyskinesia.[1–3] Deanol is thought to be effective in these conditions through its conversion in vivo to choline and acetylcholine. High doses (above 1 g per day in adults) given for at least 3 weeks are required before the efficacy of the drug can be determined.[1] Side-effects have not been prominent with this drug. We wish to report the occurrence of serious cholinergic side-effects in one patient.

The patient was a 37-year-old woman who had tardive dyskinesia of 4 years' duration, which had not responded to other drugs. She had grotesque oral, lingual, and buccal movements which had caused her to break several teeth and to bite her tongue occasionally. These movements would cease temporarily upon voluntary actions such as forced protrusion of the tongue, but she experienced difficulty with chewing and swallowing, and she would frequently spit rather than swallow her saliva. Deanol was given for 19 days in increasing doses. After 17 days, while receiving 1500 mg per day, the patient began to have increased nasal and oral secretions. Within 2 more days she complained of dyspnœa and was having obvious respiratory difficulty. Examination disclosed rhinorrhœa, sialorrhœa, a respiratory-rate of 25/min, a pulse-rate of 100/min, and unchanged blood-pressure. Diffuse rhonchi and moderate expiratory wheezing were heard in both lung fields; many upper airway sounds also were present. She was afebrile, and a blood-count revealed no evidence of infection. A chest film taken at the time showed only changes consistent with chronic obstructive pulmonary disease (the woman was a heavy smoker). Deanol was discontinued, and within 16 h the patient reported improvement in her symptoms; objectively the lungs had cleared considerably. By the second day after the drug was stopped the lungs were clear, the rhinorrhœa and sialorrhœa had stopped, and the patient had returned to her previous status.

These side-effects of a cholinergic nature suggest that deanol may indeed act in man by conversion to choline and

1. Stumpf, D. A., Austin, J. H., Crocker, A. C., LaFrance, M. *Am. J. Dis. Child.* 1973, **126**, 747.
2. Fluharty, A. L., Stevens, R. L., Sanders, D L., Kihara, H. *Biochim. biophys. Res. Commun.* 1974, **59**, 455.
3 Barton, R. W., Nuefeld, E. F. *J. Pediatrics*, 1972, **80**, 114.
4. Beratis, N. G., Turner, B. M., Weiss, R., Hirschhorn, K. *Pediat. Res.* 1975, **9**, 475.
5. Niermeijer, M. F., Koster, J. F., Jahodova, M., Fernandes, J., Heukels-Dully, M. J., Galjaard, H. *ibid.* 1975, **9**, 498.
6 Baum, H., Dodgson, K. S., Spencer, B. *Clinica. Chim. Acta*, 1959, **4**, 453.
7. Galjaard, H., Hoogstraten, J. J. van, de Josselin de Jong, J. E., Mulder, M. P. *Histochem. J.* 1974, **6**, 409.
8. Fratantoni, J. C., Hall, C. W., Neufeld, E. F. *Proc. natn. Acad. Sci. U.S.A.* 1969, **64**, 360.

1. Re, O. *Curr. ther. Res.* 1974, **16**, 1238.
2. Miller, E. M. *New Engl. J. Med.* 1974, **291**, 796.
3. Escobar, J. I., Kemp, J. F. *ibid.* 1975, **292**, 317.

acetylcholine. The clinical picture was thought initially to be one of bronchopneumonia; this was not the case but bronchopneumonia might well have developed had the drug been continued.

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ACRODERMATITIS ENTEROPATHICA AND NERVE DAMAGE

SIR,—Several reports have been published in *The Lancet* on the ætiology,[1] symptoms, [2 3] and treatment[4] of acrodermatitis enteropathica. Clearly long-term treatment with oxyquinoline derivatives may be very dangerous because of damage to the optic nerve. Its replacement by zinc leads to a complete and quick recovery, because—according to our present knowledge—the disease is caused by zinc malabsorption.

In our experience in five patients biochemical investigations and clinical observations confirm that zinc treatment is effective and safe. These patients had been on oxyquinolines 'Enteroseptol' for months or even years, and none had optic-nerve damage. But we did find hypoacusis in two of our patients during the treatment(one of them had had an antrotomy operation as a baby). This might mean that the neurotoxic effect of oxyquinoline products affects not only the optic nerve but also the acoustic (cochlear) nerve. Fortunately the zinc treatment suggested by Dr E. J. Moynahan eliminates this risk too.

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EFFECT OF SPIRONOLACTONE ON BLOOD BILE-ACID LEVELS

SIR,—Patients with liver and bileduct diseases often have raised blood bile-acid levels and consequent symptoms such as pruritus. Treatment with cholestyramine, neomycin, or a barbiturate may lower the high plasma bile-acid concentration, but their application is limited by side-effects. Cholestyramine, the anion exchange resin, which decreases bile-acid levels by accelerating fæcal excretion,[5] may cause diarrhœa, steatorrhœa, and loss of fat-soluble vitamins. Polybasic antibiotics, such as neomycin, which lower bile-acid levels by the formation of insoluble precipitates,[6] may induce a malabsorption syndrome with mucosal changes in the bowel. Phenobarbitone in large doses reduces plasma bile-acid concentration, possibly through enzyme inductive effects,[7] but many patients suffer from excessive sedation.

Solymoss et al.[8] and Szeberényi and Fekete[9] have shown that spironolactone is a potent microsomal enzyme inducer and can accelerate the metabolism of various drugs. We therefore suggested that spironolactone might also reduce raised bile-acid levels and might do so without serious side-effects.

Eleven patients with a diagnosis of liver cirrhosis and four with various forms of bileduct obstruction received spironolactone ('Verospiron', Richter, Budapest) 200 mg/d by mouth for 4 to 14 days. Levels of cholic, chenodeoxycholic, and deoxycholic acids were determined by our spectrofluorimetric method[6] before and on the last day of treatment. The sum of the values of the metabolites were recorded (see accompanying table). The normal fasting bile-acid level in our previous study[10] was between 89 and 157 (average 116), μg/dl. After spironolactone a sharp fall from 545 to 240 μg/dl was observed in patients with hepatobiliary diseases. Spironolactone did not affect the normal plasma bile-acid level of 8 control subjects.

EFFECT OF SPIRONOLACTONE ON PLASMA BILE-ACID LEVELS IN LIVER AND BILEDUCT DISEASES

Subjects	No.	Cholic+chenodeoxycholic+deoxycholic (μg/dl) (±S.E.)
Liver cirrhosis or bileduct obstruction	15	545±108* 240± 47† $P<0.01$
Controls	8	145± 14* 137± 14†

*Before spironolactone.
† After spironolactone.

Patients with liver disease, mostly those with cirrhosis, often receive spironolactone as a diuretic. Our observations suggest that spironolactone is indicated for patients with cirrhosis who are not already on it and have raised plasma bile-acid concentrations. Spironolactone also seems to be indicated in intrahepatic cholestasis and possibly in other hepatobiliary diseases with high plasma bile-acid levels.

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A. TANKÓ

1. Kay, R. G., Tasman-Jones, C. *Lancet*, 1975, ii, 605.
2. *ibid.* 1975, ii, 351.
3. Moynahan, E. J. *ibid.* 1976, i, 91.
4. Moynahan, E. J. *ibid.* 1974, ii, 399.
5. Moore, R. B., Crane, C. A., Frantz, I. D., Jr. *J. clin. Invest.* 1968, **47**, 1664.
6. Eyssen, H., Evrard, E., Vanderhaeghe, H. *J. Lab. clin. Med.* 1966, **68**, 753.
7. Redringer, R. N., Small, D. M. *J. clin. Invest.* 1973, **52**, 161.
8. Solymouss, B., Classen, H. G., Varga, S. *Proc. Soc. exp. Biol. Med.* 1969, **132**, 940.
9. Szeberényi, S., Fekete, G. *Expta. med. Int. Congr. Ser.* 1970, no. 210, p. 182.
10. Fehér, T., Papp, J., Kazik, H. M. *Clinica. chim. Acta*, 1973, **44**, 409.

Obituary

STEPHEN HENRY BRUNTON BLAIKIE

T.D., M.B.Edin., F.R.C.P.E.

Dr Stephen Blaikie, who had been in general practice in Knightsbridge for the past 25 years, died on June 4 at the age of 59.

After Uppingham, he started his medical training at the University of Edinburgh, but before it was completed he left to join the Royal Scots, later transferring to the Parachute Regiment, of which he came to command the 4th Battalion. Wounded in Italy, he was invalided home and resumed his training at Edinburgh. He rapidly qualified and after house-appointments at the Royal Infirmary, in 1947 he became M.R.C.P.E. and started in general practice in London. His father, who had been a well-known and much-loved general practitioner in Brook Street, died before his son had qualified. There was, therefore, no direct succession, and Stephen Blaikie's early years in London were spent as an assistant to Dr John Hunt (now Lord Hunt of Fawley). He became F.R.C.P.E. in 1972.

Stephen Blaikie's grace and distinction, combined with his formidable professional attainments, ensured his immediate success in general practice. For over a quarter of a century he held a leading place amongst the family doctors of the West End of London. His charm, his compassion, and his gaiety won the devotion of the numberless patients who entrusted themselves to his care. His scrupulous professional standards and his outstanding ability endeared him to his colleagues, both general practitioners and consultants, He exemplified all that was best of the traditional British family doctor. There will be many patients who feel not only a sense of personal bereavement at his passing but also an irreparable loss at being