

BRITISH MEDICAL JOURNAL

SATURDAY 1 SEPTEMBER 1979

LEADING ARTICLES

Vasodilators in senile dementia.....	511	Plasma concentrations of psychotropic drugs.....	513
Gastric ulceration after burns.....	512	Bladder cancer.....	514
Acquired pulmonary stenosis.....	512		

PAPERS AND ORIGINALS

Large-bowel obstruction caused by cancer: a prospective study L P FIELDING, SARAH STEWART-BROWN, LYNDY BLESOVSKY....	515
Effect of beta-blockers on arrhythmias during six weeks after suspected myocardial infarction J M ROLAND, R G WILCOX, D C BANKS, B EDWARDS, P H FENTEM, J R HAMPTON.....	518
Decreased serum 24,25-dihydroxy vitamin D concentrations in children receiving chronic anticonvulsant therapy Y WEISMAN, A FATTAL, Z EISENBERG, S HAREL, Z SPIRER, A HARELL.....	521
High-carbohydrate diets and insulin-dependent diabetics R W SIMPSON, J I MANN, J EATON, R D CARTER, T D R HOCKADAY....	523
Failed laparoscopic clip sterilisation A KENNEY, R D DE VERE, J R JASS.....	526
Effects of the media on attitudes to electric convulsion therapy J M BIRD.....	526
Pathological fracture of tibia in patient with corticosteroid-dependent psoriasis treated by functional bracing N M P CLARKE, D N SMITH, C J PAUL.....	527
Use of ethamsylate in vaginal surgery and deep-vein thrombosis M F VERE, S M SELLERS, D N JOYCE, G E STADDON.....	528

MEDICAL PRACTICE

Design of forms for clinical trials (1) PATRICIA WRIGHT, JOHN HAYBITTLE.....	529
Social factors and marital pathology J DOMINIAN.....	531
Vitamin B ₁₂ : an area of darkness D M MATTHEWS, J C LINNELL.....	533
In My Own Time: Osteosarcoma RODNEY SWEETNAM.....	536
Classes in literature W L BURROWES.....	538
Words.....	537
Any Questions?.....	530, 532, 539
Materia Non Medica—Contributions from J C HAWKSLEY, J P COLQUHOUN, ARTHUR SUTHERLAND.....	535
Medicine and Books.....	540
Personal View V BASNAYAKE.....	545

NEWS AND NOTES

Views.....	559
Medical News.....	560
BMA Notices.....	560

CORRESPONDENCE—List of Contents.....

546

OBITUARY.....

556

CORRESPONDENCE

Post-marketing surveillance of drugs D H Lawson, MD.....	546	Blindness after treatment for malignant hypertension J H Wetherill, MRCP.....	550	Smoking and anaesthetics S McKechnie, FFARCS.....	553
Drug information and cost effectiveness A K Maynard, BPHIL.....	546	Maturity-onset diabetes R H Lloyd-Mostyn, MRCP, and R M Goodfellow, PHD.....	550	Fetal malnutrition—the price of upright posture? P L C Diggory, FRCOG.....	553
Heatstroke in a “run for fun” T J Bassler, MD.....	547	Serum free thyroxine in pregnancy A Margot B Boss, BSC, and D Kingstone; A B Kurtz, MRCP, and others.....	550	Yersinia arthritis D L Walker, BSC, and T J Coleman, MRCPATH.....	553
The haematuria of the long-distance runner T Heide, MD.....	547	General practitioners’ advice against smoking G H Fowler, FRCGP.....	551	The case against neonatal circumcision P M Fleiss, MD, and J Douglass, MD.....	554
Alcohol-dependent doctors M Rosen, FFARCS; G V Lewis, MRCS, and P J Rawlinson, MB.....	547	Comparison of buprenorphine and diamorphine in suspected myocardial infarction H C R Simpson, MRCP.....	551	Destroying the whole-time option P W Fisher, FRCP.....	554
Extracranial-intracranial anastomoses Carys M Bannister, FRCS(ED).....	547	Interstitial fibrosis in a patient treated with 5-fluorouracil and mitomycin C J W L Fielding, FRCS, and others.....	551	The “Radcliffe” hospitals, Oxford M H Gough, FRCS.....	554
On-demand analgesia equipment T Lind, MRCP, and others.....	548	Practical problems with the Clinitest P A Aspinall, PHD, and A R Hill, PHD.....	552	Survival of the fittest? T J Daymond, MRCP.....	554
Splenectomy for massive splenomegaly D Shaw, MD, and G R Tudhope, FRCP; P J Toghill, FRCP.....	548	The grumbling appendix I Lewis, FRCS.....	552	Points Unfit for holiday (W I Martin, MB); Fifty years of penicillin (H S Fraser, MRCP, and Iris Bannochie); How to use an overhead projector (C F Hawkins, FRCP); Handicapped Children’s Pilgrimage Trust (P A Trafford, MB); Exercise testing in patients with angina pectoris (P F Meyer, MD); Free treatment for foreigners (J M F Clarke, FRCS); “To fart” (P D Welsby, MRCP; P J E Wilson, FRCS); Chlamydia (G L Ridgway, MD, and J D Oriel, MD); Single trainees (E J Webb, MB); Easy-rider sling (J R Gillespie, MB); The grumbling appendix (J W Maltby, FRCS); Penicillamine causing acute colitis (G B Grant, FRCGP).....	554
Suicide and attempted suicide F D Hart, FRCP.....	549	Doctors and children’s teeth I P D Stocker.....	552		
Wernicke’s encephalopathy G H Jones, MRCPsych; D S McLaren, MD, and D H A Boyd, FRCPED.....	549	Disposable insulin syringes M R Phillips, MB, and others.....	552		
Herpetic proctitis and sacral radiculomyelopathy in homosexual men D Goldmeier, MD.....	549	Lupus-like autoimmune syndrome after levodopa and benserazide G Massarotti, MD, and others.....	553		
Relation between herpes simplex virus and carcinoma M G Davies, MRCP.....	549				

We may return unduly long letters to the author for shortening so that we can offer readers as wide a selection as possible. We receive so many letters each week that we have to omit some of them. Letters must be signed personally by all their authors. We cannot acknowledge their receipt unless a stamped addressed envelope or an international reply coupon is enclosed.

Post-marketing surveillance of drugs

SIR,—I read the article by Dr A W H Marcus and his colleagues (21 July, p 163) with interest. These workers have shown that at the instance of the Committee on Safety of Medicines it is possible for a pharmaceutical company to identify a selected cohort of over 9000 hospitalised recipients of a new injectable drug and record brief details of its efficacy and toxicity for periods of several hours after the injection. Regrettably they did not give full details of the cost of the study, but from the information given it would seem unlikely to be less than £50 000. Thus, as a pilot study for a post-marketing surveillance programme of a new compound, this project seems to have been successful in its limited aims. It is important, however, to emphasise that it does not give much useful information on what is seen to be the main problem with new drugs—that of detecting reasonably common delayed adverse drug effects or effects arising only after long-term use of the new compound. For this purpose one requires to look to some of the proposed developments recently discussed in the *British Medical Journal* and elsewhere.¹⁻³ These studies all aim to identify a large cohort

of patients receiving a new drug and follow them for periods of up to one or two years. As yet none of the pilot studies currently under way have reported their results. Until they do it is important not to conclude, as Dr H Marcus does, that post-marketing surveillance studies are unlikely to add much to the knowledge and understanding of new drugs already gained from preregistration clinical trials.

Finally, I would take issue with Dr H Marcus and his colleagues when they state that “monitored release, however large the cohort size, without a suitable (randomised?) control group is a methodological impasse when rare effects are considered.” The objective of the proposed studies is to look for common (up to 1 in 500 recipients) serious events which may be drug related.⁴ If such events are noted in an uncontrolled screening programme such as carried out by Dr H Marcus then more detailed studies with different methods and incorporating appropriate controls are required to elucidate whether the event is truly drug related or not. The original screening studies can only be hypothesis-generating projects which, if successful, will require further

detailed studies before any outcome is accepted as being truly drug related.

D H LAWSON

Department of Clinical Pharmacology,
Royal Infirmary,
Glasgow G4 0SF

- ¹ Inman, W H W, in *Drug Monitoring*, ed M Gross and W H W Inman. New York, Academic Press, 1977.
- ² Dollery, C T, and Rawlins, M D, *British Medical Journal*, 1977, 1, 96.
- ³ Lawson, D H, and Henry, D A, *British Medical Journal*, 1977, 1, 691.
- ⁴ Lawson, D H, *British Journal of Clinical Pharmacology*, 1979, 7, 713.

Drug information and cost effectiveness

SIR,—The randomised controlled trial analysing the relative merits of buprenorphine and diamorphine by Dr M J Hayes and others (4 August, p 300) for the treatment of chest pain in suspected myocardial infarction is most interesting, but incomplete.

It is unfortunate that the authors of the study did not complement their careful analysis with an appraisal of the full economic costs of the different drugs. Buprenorphine is uncontrolled but more expensive to buy. The full costs of controlled and uncontrolled drugs can be estimated—see, for example, Culyer and Maynard’s analysis of the cost effectiveness of Fortral and morphine¹—and doctor decision makers should be given evidence not only of clinical efficacy but also of costs if we