members who are not day to day colleagues as well as the statutory lay member or two. Obtaining the necessarily robust approach needed for the task of assessing protocols is not easy if the set up is too locally based.

Fourthly, ethical committees should not only vet applications; they should monitor the projects in action to ensure standards are adhered to and procedures correctly followed. Far too often there is an attitude of "it's too difficult, we are all busy people, and anyway the drug houses do that."

Finally, the whole question of accountability and indemnification needs to be examined and tightened up. The Association of the British Pharmaceutical Industry guidelines on compensation for medicine induced injury in clinical trials are, in the words of a barrister friend, legally not worth the paper they are written on. Usually the consultant in charge is named, but rarely is provision made for the owners of the premises where the work takes place. There does not seem to be any time limit set nor is it clear what happens if the named person leaves in the middle of a project; is the successor automatically covered? Does anyone inquire into the insurance cover carried by the drug houses offering, say, £5m indemnity to a project organiser? Are we necessarily right to assume that a well known organisation must be adequately covered itself?

With ever increasing compensation payments being awarded it behoves the profession and hospital managers to be more aware of the potential risks.

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1 Korlipara K. A national ethical committee. *Br Med J* 1989;**298**: 386. (11 February.)
2 Warnock M. A national ethical committee. *Br Med J* 1988;**297**: 1626-7.

Drug Points

Profound bradycardia after the addition of diltiazem to a β blocker

Drs A B HASSELL and J E CREAMER (Department of Medicine, University of South Manchester, Manchester M20 8LR) write: The combination of a β blocker and diltiazem is effective in treating angina.[1 2] We report two cases in which this combination induced profound bradycardia with serious haemodynamic effects.

Case 1—A 68 year old woman was treated with sotalol 160 mg twice daily for palpitation due to episodes of supraventricular tachycardia and salvos of ventricular premature beats. In November 1987 she suffered an uncomplicated anterior myocardial infarction. Diltiazem 60 mg thrice daily was added for angina just before discharge. Two days later she was admitted unconscious with a pulse rate of 15 beats/minute. Blood pressure was unrecordable. Electrocardiography showed sinus bradycardia. There was no response to atropine 2 mg intravenously. Temporary transvenous ventricular pacing was started and within 10 minutes she regained consciousness. Additional inotropic support was needed initially, but after four hours sinus rhythm returned and subsequent recovery was uneventful. There was no evidence of further myocardial infarction or of self poisoning, and later treatment with sotalol alone did not produce bradycardia.

Case 2—A 77 year old woman had stable angina controlled by pindolol 10 mg thrice daily. In August 1986 her angina became more frequent and diltiazem was added. Two hours after taking the first 60 mg tablet she felt cold and dizzy. Physical examination at home showed a pulse of 26 beats/minute and systolic blood pressure 70 mm Hg. The electrocardiogram in hospital showed sinus bradycardia. Over the following hour her pulse returned to 60 beats/minute and blood pressure to 150/70 mm Hg. Serial electrocardiograms and cardiac enzyme activities were normal. Pindolol was subsequently well tolerated.

Both verapamil and diltiazem delay conduction through the atrioventricular node, and diltiazem alone may cause sinus bradycardia.[3] A combination of diltiazem with a β blocker might be expected to cause bradyarrhythmias and this has been shown in combinations with propranolol.[4 5] Nevertheless, several trials have found no important bradycardias with such combination treatment[1 2] and it is now widely prescribed. We suggest that both our patients had serious bradycardia as a result of adding diltiazem to pindolol or sotalol in the absence of overt pre-existing sinoatrial disease. In view of the sudden collapse of the second patient after a single tablet we suggest that diltiazem should be avoided in patients taking β blockers and that nifedipine or nicardipine should be preferred.

We thank Dr J C Leonard for allowing us to report on these patients under his care and for his helpful comments.

1 Kostuk WJ, Pflugfelder P. Comparative effects of calcium entry-blocking drugs, beta blocking drugs, and their combination in patients with chronic stable angina. *Circulation* 1987;**75** (suppl):V114-21.
2 Humen DP, O'Brien P, Purves P, Johnson D, Kostuk WJ. Effort angina with adequate beta-receptor blockade: comparison with diltiazem alone and in combination. *J Am Coll Cardiol* 1986;**7**:329-35.
3 Belanger LG, Charbonneau M, Lavallee JP, Lenis J, Ouellet AC. Treatment of stable angina pectoris with calcium antagonists alone or combined with beta-blocking agents: a review of the literature. *Can J Cardiol* 1986;**2**:212-7.
4 O'Hara MJ, Khurmi NS, Bowles MJ, Raftery BB. Diltiazem and propranolol combination for the treatment of chronic stable angina pectoris. *Clin Cardiol* 1987;**10**:115-23.
5 Hung J, Lamb IH, Connolly SJ, Jutzy KR, Goris ML, Schroeder JS. The effect of diltiazem and propranolol, alone and in combination, on exercise performance and left ventricular function in patients with stable effort angina: a double-blind, randomized, and placebo-controlled study. *Circulation* 1983; **68**:560-7.

Remission of alopecia universalis during sulphasalazine treatment for rheumatoid arthritis

Drs A S M JAWAD and D G I SCOTT (Department of Rheumatology, Norfolk and Norwich Hospital, Norwich NR1 3SR) write: Alopecia areata and its variants, totalis and universalis, are thought to be immune mediated diseases and have an increased incidence in patients with diseases such as Addison's disease, diabetes mellitus, and vitiligo. Although alopecia may remit spontaneously, the longer the history and the more extensive it is the less likely the remission. We describe a 34 year old woman with a 30 year history of alopecia universalis whose hair started regrowing during sulphasalazine treatment for rheumatoid arthritis.

This woman, born in 1954, had been suffering from alopecia universalis since she was 3. She had no history of any atopic diathesis. She was first seen in the rheumatology clinic in 1980 at the age of 26 suffering from palindromic rheumatism. Repeated erythrocyte sedimentation rate and rheumatoid factor estimations were negative. She was treated with hydroxychloroquine with an excellent response and had no further attacks.

In March 1982, two months after the hydroxychloroquine was stopped, she developed polyarthritis of the proximal interphalangeal, metacarpophalangeal, wrist, knee, and metatarsophalangeal joints. Her arthritis completely settled, however, when she became pregnant three months later.

In May 1987 the polyarthritis recurred. Investigations showed: haemoglobin 106 g/l, erythrocyte sedimentation rate 45 mm in the first hour, rheumatoid factor positive (titre 1/320); radiographs of her hands and feet showed marginal erosions at several metacarpophalangeal and metatarsophalangeal joints. She was treated with indomethacin 25 mg three times a day and sulphasalazine up to 0·5 g three times a day. Within four months her arthritis settled and her erythrocyte sedimentation rate dropped to 9 mm in the first hour and her haemoglobin rose to 129 g/l. Simultaneously, for the first time in 30 years, her eyebrows, eyelashes, and scalp, axillary, and pubic hair started growing. A year later she was able to abandon her wig.

Sulphasalazine is of therapeutic value in immune mediated disease, such as rheumatoid arthritis[1 2] and inflammatory bowel disease,[3] but its mechanism of action is not fully understood. Our patient's hair regrowth coincided with the response of her arthritis to sulphasalazine. Although this might have been coincidental, there was a strong temporal relation between the introduction of sulphasalazine, the remission of the arthritis, and the hair regrowth. The possible beneficial effect of sulphasalazine in patients with alopecia areata should be examined in a prospective study.

1 Neumann VC, Grindulis KA, Hubball S, McConkey B, Wright V. Comparison between penicillamine and sulphasalazine in rheumatoid arthritis. *Br Med J* 1985;**44**:194-8.
2 Pullar T, Hunter JA, Capell HA. Sulphasalazine with placebo and sodium aurothiomalate. *Br Med J* 1983;**287**:1102-4.
3 Lennard-Jones JE, Longmore AJ, Newell AC, Wilson CWE, Avery JF. An assessment of prednisolone, Salazopyrin and topical hydrocortisone hemisuccinate used as outpatient treatment for ulcerative colitis. *Gut* 1960;**1**:217-22.

Drug induced hair loss

Drs JULIAN H BARTH and RODNEY P R DAWBER (Department of Dermatology, Slade Hospital, Oxford OX3 7JH) write: There are many reports of drug induced hair loss. Most include sparse clinical details and it is not possible to make a diagnosis. The case reported by Dr D A C Barter, however, gives enough detail to exonerate naproxen as the cause of hair loss.[1]

The physiology of hair growth is now quite well understood. There is a growth phase (anagen) followed by a resting phase (telogen). The telogen phase is followed by the shedding of the hair shaft as the new hair emerges from the same follicle. Hairs on the scalp have an anagen phase which lasts roughly three years and a telogen phase of roughly three months (which may be shorter in children).[2] The growth of human head hair, unlike that of animals, is not synchronised and no moulting occurs but there is a steady daily loss of 70-150 hairs.[4]

Toxic hair fall may be classified into those forms associated with loss of hair in the anagen phase and those in the telogen phase. Anagen hair loss is associated only with cytotoxic and radiation treatment and is characterised by hair loss at the time of the toxic insult. Telogen hair loss differs. It is due to a pathological and widespread conversion of the hair roots to telogen by a toxic event, such as childbirth, fever, haemorrhage, etc. This trigger event is often forgotten as the dramatic loss of telogen hair is delayed by three months, during which the telogen hair root is retained in the follicle.[3] As the hair root is not damaged by the process regrowth of hair spontaneously follows. The case of hair loss described by Dr Barter clearly describes hair loss occurring 11 weeks after the onset of an inflammatory disease and should therefore have been diagnosed as a toxic telogen effluvium.

1 Barter DAC. Hair loss in a child associated with naproxen. *Br Med J* 1988;**298**:325. (4 February.)
2 Barth JH. Normal hair growth in children. *Pediatr Dermatol* 1987;**4**:173-84.
3 Kligman AM. Pathologic dynamics of human hair loss. 1. Telogen effluvium. *Arch Dermatol* 1961;**83**:175-98.