TABLE 1—Anaesthetic history

Date	Procedure	Anaesthetic	Reaction
March 1966	Cautery of nose	General anaesthetic, type unknown	None
Feb 1973	Myringotomy and grommets	General anaesthetic, type unknown	None
May 1973	"	Althesin, N ₂ O/O ₂ -halothane	None
Oct 1974	Incomplete	Althesin, N ₂ O/O ₂ -halothane	Anaphylactoid
Dec 1974	Myringotomy and grommets	Methohexitone, N ₂ O/O ₂ -halothane	None
Oct 1975	"	Methohexitone, N ₂ O/O ₂ -halothane	None
Jan 1978	"	Thiopentone, suxamethonium, N ₂ O/O ₂ -halothane	Lip swelling

became weak and rapid and the systolic blood pressure fell to 50 mm Hg. After oxygen, intravenous chlorpheniramine 10 mg, and hydrocortisone 100 mg had been given his systolic blood pressure rose steadily and he slowly recovered consciousness. Angioneurotic oedema persisted for 24 hours. Skin tests showed no allergy to Althesin, though plasma studies suggested transient variations in IgE concentrations. Considerable C3 conversion, consistent with the degree of tissue oedema, was observed in his plasma (table II).

Anaesthetics were subsequently administered with no ill effects until January 1978, when the patient's upper lip began to swell considerably after administration of thiopentone 350 mg, suxamethonium 75 mg, and maintenance with an N₂O/O₂-halothane, mixture. There was no evidence of cardiovascular instability, bronchospasm, or other signs of a serious reaction, and the swelling regressed spontaneously after several hours. Nevertheless, laboratory analysis again showed C3 conversion in the patient's plasma immediately after operation. This, in contrast to the 1974 reaction, cleared rapidly.

Discussion

The laboratory findings at the time of the first reaction suggested an underlying immunopathological condition involving complement utilisation. This might have been an immune reaction to chronic infection. We have suggested that such conditions predispose towards C3 alternate pathway activation, particularly with drugs such as Althesin.^{1 2} There was

no evidence of an immune mediated response to the Althesin. Although the 1978 reaction was clinically trivial, C3 activation again occurred. So far as our records show, this was the first time that either thiopentone or suxamethonium had been given to the patient, so an immune-mediated reaction is unlikely. Although we have seen some complement-mediated reactions to thiopentone it is an unusual feature of thiopentone,^{1 2} and the patient may have reacted to suxamethonium or perhaps to the combination of the drugs.

We suggest that the curious mixture of allergic and chronic infection or secretion states in this patient made him intermittently highly susceptible to certain intravenous agents known to activate complement. We think that this case underlines a fallacy in the general interpretation of the adverse response to intravenous agents. These reactions are often described as "anaphylactoid," a term that is widely used to describe clinical manifestations (cutaneous, pulmonary, and cardiovascular) that resemble those of antibody (reagin)-mediated histamine release from mast cells. Although a reaction may be a true anaphylactic response, this assumption cannot be made on the basis of the clinical manifestations alone. We have previously emphasised the importance of simple laboratory tests to evaluate such reactions.¹⁻³ If these are not carried out then the patient may be warned that he is allergic to a particular drug and that this is not to be used again. Although this advice is basically sound, it ignores the fact that the patient may not have reacted directly to the drug. Instead the reaction may have been a non-specific effect triggered by any drug that exacerbated an underlying primary (genetic) or secondary (induced) immunopathological condition. This may explain why such a patient later reacts adversely to a totally different drug from that which was implicated in the first reaction.

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TABLE II—Plasma chemistry at time of adverse response

Incident	IgG (g/l)	IgA (g/l)	IgM (g/l)	IgE (IU/ml)	C3 (g/l)	C4 (g/l)	C1 inhibitor (g/l)	C3 conversion (%)
Anaphylactoid response Oct 1974	10.1	2.6	0.6	260	0.42	0.12	0.20	>50
Lip swelling Jan 1978	10.6	2.6	0.2	18	1.10	0.35	0.38	≤30

SIDE EFFECTS OF DRUGS

Production of ischaemic cardiac pain by nifedipine

Nifedipine (Adalat) is recommended for the treatment and prophylaxis of angina. Side effects are claimed to be rare, but transient headache, facial flushing, and dizziness may occur on starting treatment. We describe three patients treated with nifedipine in whom these side effects were accompanied by severe chest pain simulating a myocardial infarction or severe angina. This has not been described.

Case reports

Case 1—A 57-year-old woman had a myocardial infarction in 1965 with subsequent typical effort angina. Metoprolol reduced the frequency of anginal episodes but caused weakness and was discontinued. One hour after receiving nifedipine 10 mg she had facial flushing, nausea, and severe

precordial pain lasting for 30 minutes. She compared these symptoms to those accompanying her previous myocardial infarction. There was no appreciable change in pulse, blood pressure, or electrocardiogram. She felt unwell for three hours. The drug was not readministered.

Case 2—A 50-year-old man had bronchial asthma and angina. About 30 minutes after the first dose of nifedipine 10 mg, he described agonising typical ischaemic chest pain lasting an hour. This sequence occurred on two further occasions when he took nifedipine, and he consequently abandoned its use. An electrocardiogram one week later showed no fresh abnormalities.

Case 3—A 71-year-old woman with maturity onset diabetes mellitus, psoriasis, and angina was given nifedipine 10 mg. Thirty minutes after the first administration she became sweaty with facial flushing followed by severe retrosternal chest pain lasting for two hours. There was no change in pulse, blood pressure, or electrocardiogram. The drug was discontinued.

Comment

In two recent studies,^{1 2} which covered 31 patients, nifedipine produced no serious side effects. Our patients described facial flushing

and chest pain simulating prolonged angina or a myocardial infarction which occurred about 30 minutes after taking the drug. These symptoms lasted for up to three hours and did not recur when the drug was withdrawn. We considered the chest pain to be a direct effect of nifedipine treatment. Nifedipine increases the myocardial blood supply and reduces coronary sinus lactate concentrations.³ It also tends to increase cardiac output and heart rate and to reduce peripheral resistance.^{4,5} These effects possibly caused the cardiac pain in our patients. We suggest that patients starting treatment with nifedipine should be warned to discontinue the drug immediately if they experience these side effects.

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- ² McIlwraith, G, in *New Therapy of Ischaemic Heart Disease*, ed W Lochner, W Braasch, G Knoneberg. Berlin, Springer-Verlag, 1976.
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Visual hallucinations and illusions with propranolol

Disorders of visual perception are known to occur, in the absence of confusion, in hypertensive patients treated with β -adrenoceptor blockers including propranolol, sotalol, and pindolol. This study, in which patients treated with propranolol were subjected to a semi-structured interview, shows a much higher incidence (17.5%) than has been recorded in reviews of clinical trials (0.3-0.6%).^{1,2}

Patients, methods, and results

A total of 115 patients attending a hypertension clinic were treated with propranolol with or without other antihypertensives: 77 patients were taking propranolol either alone or with diuretics. Of these 63 (27 women; 36 men) were systematically studied by a semi-structured interview including a check list for 55 psychological and somatic symptoms. The average age of these patients was 51 years (range 25-70 years), and their average daily dose of propranolol was 200 mg (range 60-640 mg).

Eleven of these patients (see table) were found to have recurrent visual perceptual disorders—an incidence of 17.5%. (The lowest possible incidence for the whole group of 77, given that no other patient had similar symptoms, would be 14.3%.) Visual hallucinations were recurrent in six patients but had occurred as isolated instances in a further two, who thought they might be dreaming. Although lacking in colour, hallucinations were so vivid that two patients were frightened: two patients, however, were aware that their

hallucinations lacked reality. Recurrent visual illusions—for example, furniture and clothes appearing to change into animals and people—occurred in 10 patients; distortions of spatial allocation and perspective also occurred with displacement of furniture or opening of doors. The following cases illustrate the type of disorders experienced.

Case 1—This man saw a dead body in a lighted niche by his bed turning towards him; his pillow was made of spiders. Furniture and doors moved, opening on to strange rooms.

Case 2—This patient repeatedly saw a scarred man coming to his bedside, and would lash out at him.

Case 3—A helmeted coalminer appeared at the window of this patient. His clothes turned into people sitting on chairs.

Case 4—This man saw his alarm clock turn into an owl and his dressing-gown into a man, who came to his bedside.

All episodes of visual perceptual disorder occurred in either hypnagogic or hypnopompic states and were abolished by complete wakefulness. During interviews all patients were in clear consciousness with no evidence of psychiatric abnormality, although two complained of drowsiness and mild dysphoria. The onset of hallucinations occurred in four patients within a week of an increase in dose. Hallucinations stopped a few days after the drug was withdrawn in four patients who found them intolerable. The four patients who had the most vivid hallucinations regularly consumed alcohol. Withdrawal from the drug, but not from alcohol, abolished the symptoms.

Comment

The results of this study, in which symptoms were systematically sought in a semi-structured interview, show that it is important to realise that visual perceptual disorders may occur in patients receiving propranolol in modest doses (average dose 254 mg daily) for hypertension. Patients may not complain of these spontaneously because they fail to connect the symptoms with the drug and may be embarrassed to discuss possible mental illness or excessive use of alcohol. They may also attribute hallucinations to dreaming, and some of the nightmares and bizarre dreams described as side effects^{1,2} may in fact be hypnagogic hallucinations.

The reported low incidence of visual hallucinations has been offered as evidence that propranolol has little central action in man,³ although it is now known that it crosses the blood-brain barrier and is concentrated in the brain of man.⁴ Recent work on the treatment of schizophrenia with propranolol,⁵ however, suggests that the drug has central psychotropic properties. The present findings add further support for this, and show that central effects may develop at doses commonly used to treat hypertension.

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¹ Stephen, S A, *American Journal of Cardiology*, 1966, **18**, 463.

² Conway, J, *Modern Trends in Cardiology*, 1975, **3**, 376.

³ *Lancet*, 1976, **2**, 611.

⁴ Myers, M G, *et al*, *Journal of Pharmacology and Experimental Therapeutics*, 1975, **192**, 327.

⁵ Yorkston, N J, *et al*, *Lancet*, 1977, **2**, 575.

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Visual hallucinations and illusions: side effects of propranolol

Case No	Age and sex	Critical dose of propranolol (mg/day) (previous dose)	Symptoms intolerable, necessitating withdrawal	Alcohol*	Relation of disorders to sleep	Hallucinations	Illusions
1	55 M	240 (120)	Yes	++	After	Yes	Yes
2	38 M	240 (120)	Yes	++	Before	Yes	Yes
3	37 M	320	Yes	+++	After	Yes	Yes
4	43 M	160 (80)	Yes	++	After	Yes	Yes
5	60 M	160		+	After	Yes	No
6	42 M	320 (160)		+	After	No	Yes
7	59 M	320 (160)		++	Before	No	Yes
8	57 F	320 (240)		+	Before	No	Yes
9	52 M	320		-	Before	Yes	Yes
10	44 M	320 (150)		Unknown	After	No	Yes
11	61 F	80		+	After	No	Yes

Average age 50 years; average daily dose = 254 mg.

* - = None; + = rare; ++ = moderate; +++ = excessive.