

## SHORT REPORTS

### High-dose oral amoxycillin for preventing endocarditis

The use of oral instead of parenteral antibiotics for preventing endocarditis and the possible advantages of amoxycillin over phenoxymethylpenicillin (penicillin V) were recently discussed.<sup>1</sup> We have reported that a single 2-g oral dose of amoxycillin gave higher and more sustained serum concentrations than an equivalent dose of phenoxymethylpenicillin and that the minimum bactericidal concentrations of amoxycillin for viridans streptococci were equal to or less than 0.12 mg/l.<sup>2</sup> A single 2-g oral dose of amoxycillin given one hour before a dental procedure, however, still fails to achieve adequate serum bactericidal concentrations for the nine-hour critical period after dental bacteraemia. We have now measured the serum amoxycillin concentrations after single oral doses of 3 g and 4 g of the drug in 13 healthy men volunteers and noted any side effects.

#### Methods and results

Amoxycillin was administered as a lemon-flavoured syrup, supplied by Bencard, dispensed as a powder and reconstituted by adding 50–65 ml water immediately before administration. Each volunteer ate a standard light breakfast one hour before taking amoxycillin and a light diet during the study. Either 3-g or 4-g doses were randomly allocated to each volunteer, and at least one week later the alternative dose was administered. Serum samples were collected from 30 minutes to 12 hours after each dose and the serum amoxycillin concentrations measured with a *Sarcina lutea* NCTC 8340 plate diffusion method.

The table shows the amoxycillin concentrations observed after each dose. Peak concentrations occurred 1½ hours after administration, and the mean peak serum concentration for the 3-g and 4-g doses were 27.8 and 34.1 mg/l amoxycillin respectively. The mean serum half life for both doses was 1½ hours. The mean area under the curve for the 4-g dose was 100.9 mg hour/l (SD 25.74), and that for the 3-g dose was 76.7 mg hour/l (SD 12.24). The difference between the areas under the curve was statistically significant ( $p < 0.01$ , paired student's  $t$  test). Although the 4-g dose had a higher total bioavailability than the 3-g dose, as indicated by the area under the curve, our results suggest that it was less well tolerated than the 3-g dose. After the 4-g dose four volunteers had diarrhoea, one developed "fruity burps," and another suffered from heartburn two hours after the dose. After the 3-g dose only two volunteers had diarrhoea and one developed nausea. In all volunteers, however, the diarrhoea was mild and resolved within 36 hours.

*Mean serum amoxycillin concentrations after oral administration of 3-g and 4-g doses to 13 healthy volunteers. Results are given as mean  $\pm$  1 SD*

Time after administration of dose (h)	Mean serum amoxycillin concentrations (mg/l)	
	3-g dose	4-g dose
0.5	8.6 ± 3.6	11.1 ± 3.6
1	16.3 ± 4.0	20.7 ± 6.7
1.5	24.4 ± 5.4	28.9 ± 8.7
2	24.2 ± 3.8	30.3 ± 4.3
2.5	17.0 ± 4.3	21.6 ± 7.3
3	11.8 ± 3.3	15.5 ± 5.4
4	7.8 ± 2.5	11.6 ± 4.8
6	3.6 ± 1.5	5.2 ± 2.5
8	1.4 ± 0.5	2.0 ± 1.2
10	0.4 ± 0.2	0.6 ± 0.3
12	0.2 ± 0.1	0.3 ± 0.2

#### Comment

The serum amoxycillin concentrations after the 3-g oral dose were well above the minimum bactericidal concentrations of amoxycillin for viridans streptococci for at least 10 hours. Bactericidal antibiotics can effectively prevent experimental streptococcal endocarditis provided that high peak serum concentrations and sustained bactericidal serum concentrations are achieved during a six-to-nine-hour critical period after bacteraemia.<sup>3,4</sup> These objectives were apparently achieved by giving a single 3-g oral dose of amoxycillin. The 4-g dose gave slightly higher serum concentrations than the 3-g dose but in our study was associated with more side effects.

There is a great need for a practical and effective oral prophylactic regimen. The 3-g "twin pack" of amoxycillin, recently introduced

for treating urinary infections, provides a highly satisfactory oral prophylaxis for endocarditis. The first 3-g dose should be given under supervision one hour before the dental procedure to provide effective cover for the critical period afterwards. Our results show that a second dose may be unnecessary; if the patient defaults on a further dose, failure of prophylaxis would seem unlikely. For the present, however, it is probably wise to suggest a safer approach and recommend that a second 3-g dose should be taken eight to nine hours after the procedure. We suggest that this oral regimen should normally be given only outside hospital, and that it is contraindicated in patients receiving general anaesthesia; patients with prosthetic heart valves require parenteral prophylaxis as recommended by the American Heart Association.<sup>5</sup>

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<sup>1</sup> Editorial. Preventing endocarditis. *Br Med J* 1979; i:290-1.

<sup>2</sup> Shanson DC, Cannon P, Wilks M. Amoxycillin compared with penicillin V for the prophylaxis of dental bacteraemia. *J Antimicrob Chemother* 1978; 4:431-6.

<sup>3</sup> Durack JT, Petersdorf RG. Chemotherapy of experimental streptococcal endocarditis. I. Comparison of commonly recommended prophylactic regimes. *J Clin Invest* 1973; 52:592-8.

<sup>4</sup> Pelletier LL, Durack DT, Petersdorf RG. Chemotherapy of experimental streptococcal endocarditis. IV. Further observations on prophylaxis. *J Clin Invest* 1975; 56:319-26.

<sup>5</sup> American Heart Association Committee Report. Prevention of bacterial endocarditis. *Circulation* 1977; 56:139A-43A.

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### Abuse of the mushroom *Panaeolus foenisecii*

The mushroom commonly used for hallucinogenic purposes in the United Kingdom is *Psilocybe semilanceata* (the Liberty cap).<sup>1</sup> The pharmacological effect of these mushrooms is said to be caused by 4-hydroxy-tryptamine derivatives (psilocybin and psilocin). I describe here the ingestion, for its hallucinogenic properties, of a common mushroom—*Panaeolus foenisecii*—found in lawns and parkland, often around blocks of flats in Aberdeen.

#### Case reports

Three young men (aged 16, 18, and 18 years) arrived in the casualty department, each having eaten 20 to 30 of these fresh mushrooms; they were brought by their parents after one of them had confessed to eating mushrooms after direct questioning by his mother about his excited state. In addition to euphoria the patients had experienced hallucinations of colour and speed of movement such that lawns developed patches of brilliant colours and cars and pedestrians moved frighteningly fast. Gastric lavage was performed, and the euphoria and hallucinations subsided within 12 hours without additional treatment or residual ill effects. The eldest had eaten "magic mushrooms" before. None admitted to the use of other drugs except ethanol. No anticholinergic effects were observed.

#### Comment

Reports on the presence of psilocybin and psilocin in *Panaeolus foenisecii* are confused, since both have been detected in some samples of this mushroom but not in all. It is usually considered a "latent psilocybin" mushroom, because psilocybin and psilocin may not necessarily be present in a particular specimen.<sup>2</sup>

Probable cases of *P foenisecii* intoxication have been described in children. Holden reported that a small boy became ill with tachycardia and mydriasis after eating *P foenisecii*,<sup>3</sup> but he was too young to describe adequately his subjective experience. Southcott describes a 2-year-old girl with pica who probably ate the *P foenisecii* that grew on her parents' lawn in Adelaide. She suffered from periodic attacks of hysterical behaviour with visual and tactile hallucinations; her symptoms were finally, fairly confidently, attributed to consumption of *P foenisecii*.<sup>4</sup>

Other species of Panaeolus have been recorded as being used for ritual purposes and causing accidental poisonings. In adults distortions of perception and laughing are prominent effects, but children may react more severely with convulsions.<sup>2</sup> Acute delirious and psychotic states and more prolonged "schizophrenia-like" conditions have been described after consumption of *Psilocybe semilanceata*.<sup>1</sup>

Publications exist in the United Kingdom and North America that give detailed descriptions of hallucinogenic mushrooms including *P foenisecii*. This is a common mushroom whose use for hallucinogenic and euphoric effects seems to be increasing. Furthermore, it has been suggested that this mushroom may often be collected and eaten in error for the more widely known *P semilanceata* (G Hadley, unpublished observations). It may produce acute perceptual distortions and have similar ill effects to LSD. There is also a risk of mistaking more-toxic fungi for these "magic mushrooms" and of young children eating adult doses.

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- <sup>1</sup> Hyde C, Glancy G, Omerod P, Hall D, Taylor GS. Abuse of indigenous Psilocybin mushrooms: a new fashion and some psychiatric complications. *Brit J Psychiat* 1978;132:602-4.
- <sup>2</sup> Pollock J. *Psilocybin mycetismus* with special reference to Panaeolus. *J Psychedel Drugs* 1976;8:43-7.
- <sup>3</sup> Holden M. A possible case of poisoning by *Panaeolina foenisecii*. *Bull Brit Mycol Soc* 1965;25:9-10.
- <sup>4</sup> Southcott RV. Notes on some poisoning and other clinical effects following ingestion of Australian Fungi. *S Austr Clin* 1975;6:441-78.

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## Does increased movement protect smokers from postoperative deep vein thrombosis?

Clayton *et al* have shown that cigarette smoking is associated with a decreased incidence of postoperative deep venous thrombosis.<sup>1</sup> Pollock and Evans<sup>2</sup> have reported that among surgical patients cigarette smokers are younger and thinner than non-smokers and therefore less likely to suffer from postoperative deep venous thrombosis, but they concluded that this is certainly not the whole explanation. Coagulation studies have shown no difference between the blood of the smoker and the non-smoker.<sup>3</sup> We postulated that patients who are smokers may be protected postoperatively against deep venous thrombosis because they move more—possibly for a surreptitious cigarette in the bathroom.

### Patients, methods, and results

We tested this theory in 40 patients undergoing inguinal herniorrhaphy. We recorded their movement with a sensitive pedometer worn in their pyjama-coat pocket. All patients undergoing the operation wore the pedometer for 24 hours preoperatively and until the fourth day after operation. The patients were divided into smokers and non-smokers and their ages recorded. The median age of the non-smokers was 54·5 years (range 48-65), whereas that of the smokers was 47 years (range 33·5-53·5). This difference was significant ( $p < 0·025$ ). Smokers smoked an average of 22 cigarettes a day.

For the 24 hours before operation the median distance moved by the smokers was 2·01 km (range 1·77-2·25) and by the non-smokers 1·93 km (range 1·28-2·9). This difference was not significant ( $p = 0·52$ ). On the fourth postoperative day the smokers had walked 3·06 km (range 2·09-4·51) since the operation and the non-smokers 2·41 km (range 1·61-4·42). Again this difference was not significant ( $p = 0·68$ ).

### Comment

We conclude that there is no difference between the movements of smokers and non-smokers after operation and therefore that smokers are not protected from deep venous thrombosis by increased movement. The reason for the decreased incidence of thrombosis in smokers remains a mystery.

<sup>1</sup> Clayton JK, Anderson JA, McNicol GP. Effect of cigarette smoking on subsequent postoperative thromboembolic disease in gynaecological patients. *Br Med J* 1978;ii:402.

<sup>2</sup> Pollock AV, Evans M. Cigarette smoking and postoperative deep venous thrombosis. *Br Med J* 1978;ii:637.

<sup>3</sup> Clayton JK, Anderson JA, McNicol GP. Preoperative prediction of postoperative deep venous thrombosis. *Br Med J* 1976;ii:910-12.

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## Outcome of pregnancy after spontaneous abortion

A recent report from Liverpool<sup>1</sup> suggested that there may be a four-fold increase in congenital malformations in the pregnancy after a spontaneous abortion. Only a few cases were studied, and the authors called for studies from elsewhere. It has been generally accepted that a history of abortion, stillbirth, or neonatal death indicates an increased risk of subsequent obstetric problems.<sup>2</sup> In certain patients—for example, a woman who aborted a fetus with anencephaly—one would expect an increased risk of a further neural tube defect in subsequent pregnancies. No one to our knowledge, however, has suggested a risk of malformations in general on the scale found in the Liverpool study, and we thought that this warranted further investigation in a slightly different way.

### Patients, methods, and results

We studied the case notes of women who had delivered a baby at the old Bristol Maternity Hospital. The notes at the old hospital were conveniently filed according to the year of the mother's most recent delivery, and we selected a group of women whose final delivery was in either 1969 or 1970.

We excluded as malformations the following: clicking and dislocated hips, talipes, innocent systolic murmur, and undescended testicle. We included chromosome abnormalities, sacral dimples and sinuses, and hydroceles, so that our figures could be more easily compared with those of the Liverpool group.

We examined the records of 2633 pregnancies to see whether the outcome

*Outcome of index pregnancy and outcome of subsequent pregnancy in 2633 patients. Results are given as number of cases with percentages in parentheses*

Outcome of index pregnancy	No	Outcome of subsequent pregnancy			
		Normal	Spontaneous abortion	Malformation†	Anatomically normal stillbirths
Normal	2107	1824 (86·6)	213 (10·1)	51 (2·4)	19 (0·9)
Spontaneous abortion	440	304 (69·1)	120 (27·3)	10 (2·3)	6 (1·4)
Stillbirth	45	37 (82·2)	5 (11·1)	3 (6·7)	0
Major malformation*	41	30 (73·2)	9 (22·0)	1 (2·4)	1 (2·4)
Total	2633	2195	347	65	26

\*Major malformation included cases of spina bifida, hydrocephalus, anencephalus, congenital heart disease, malformations of the gut, and cleft palate.

†Live-born and stillborn babies were included in this category.