TABLE 11—Outcome after one year

	Dead	Refused or no contact	Blood tests incomplete	Blood tests complete	
				Definitely improved	Not definitely improved
Patients given counselling (n = 78)	1	8	4	34*	31*
Controls (n = 78)	2	12	5	20	39

*Patients given counselling v controls: $\chi^2 = 4.26$, $p = 0.038$.

counselling and 15 (23%) of the controls were admitted to hospital during the follow up period; four (6%) and 11 (17%), respectively, were admitted for eight days or more.

Discussion

Many patients showed a substantial improvement during the 12 months after the index admission to hospital. The experience of being ill, advice from various doctors treating them, and increases in the price of alcohol⁸ may all have had a beneficial effect. There may also have been a "regression to the mean" effect: some patients were admitted with illnesses related to alcohol after a period of heavy drinking, and it is to be expected that at an arbitrary point in the future the consumption and associated problems of such patients would be reduced. Nevertheless, those who received additional counselling achieved a significantly greater improvement than those who received only routine medical care.

In defining outcome we gave precedence to improvements in self reported problems related to alcohol over improvements in self reported consumption because we believe that it is harder for a man to prevaricate about whether he has lost a job through drinking, for example, than about how much he drank in the previous week or in a typical week. Furthermore, our strategy of treatment was aimed at helping men achieve problem free drinking and not necessarily complete abstinence.

Our groups were not matched for the number of alcohol related problems at intake, though they were matched on every other variable at intake that we measured. We believe that this lack of matching can only have occurred by chance. In view of the difference in alcohol related problems we specified definite improvement as complete freedom from problems at follow up. This might have weighted our analysis against finding an

effect of counselling because it would be harder for patients with several problems related to alcohol (of whom there were more in the counselling group) to become completely free of them than for patients with few problems.

The effectiveness of treatment for established alcoholics continues to be a matter of debate. A controlled study of intervention in early cases has yielded promising results⁹; even self help booklets, such as *Drinking Problems: Information and Advice for the Individual, Family and Friends*,¹⁰ have proved successful.¹¹ The effect of treatment may well persist if brief intervention is repeated at intervals.⁹ Our study shows how important early detection is, and our results are sufficiently encouraging for us to recommend that similar studies should be conducted in other general hospitals with inpatients or outpatients. Patients may be especially receptive to counselling when recovering from a medical illness. Screening for alcohol problems should become a routine part of nursing assessment and the medical history so that advice can be given before irreversible physical or psychosocial problems have developed.

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SHORT REPORTS

Paecilomyces varioti pneumonia complicating hairy cell leukaemia

Infection is the major cause of morbidity and death in patients with hairy cell leukaemia.¹ Aspergillosis and candidiasis are common mycotic infections in such patients, and histoplasmosis and cryptococcosis have been described,² but pneumonia due to *Paecilomyces varioti* has not been reported. We report on a patient with hairy cell leukaemia who developed such pneumonia.

Case report

A 64 year old woman with hairy cell leukaemia presented with a history of cough accompanied by small amounts of greyish sputum of five weeks' duration. Hairy cell leukaemia had been diagnosed six years previously when she presented with Gram negative septicaemia. Her white cell count then had been $2.7 \times 10^9/l$ with 90% hairy cells in the peripheral blood. Aspiration of bone marrow and trephine biopsy had confirmed the diagnosis. Initial treatment with steroids, chlorambucil, and cyclophosphamide had been followed by splenectomy. Recurrent attacks of pneumonia had occurred over the next few years but responded to treatment with antibiotics. Her most recent

infection had been treated with erythromycin and oxytetracycline. Despite this she had developed fever (37.8°C), shortness of breath, and left pleuritic pain.

On examination she was distressed and dyspnoeic with a blood pressure of 140/80 mm Hg and a pulse rate of 98 beats/min. Further examination showed signs of pneumonia of the left lower lobe but no other abnormality. Haemoglobin concentration was 10.5 g/dl and white cell count $13.8 \times 10^9/l$ with 1% neutrophils and 99% lymphocytes, of which 10% were hairy cells. Platelet count was $31 \times 10^9/l$, and biochemical investigations gave normal results. A chest radiograph showed shadowing at the left base with loss of diaphragmatic and cardiac borders. Cultures of sputum, urine, and blood yielded negative results. Empirical treatment with ceftazidime 2 g eight hourly and vancomycin 500 mg eight hourly with infusions of granulocytes produced little clinical response. Bronchoscopy performed 10 days after admission showed copious secretions in the bronchial tree. Films of bronchial lavage fluid from the left lower lobe, treated by Grocott's silver method, showed septate branching hyphae. Examination of these preparations showed phialides and conidia resembling a *Paecilomyces* species. Definitive diagnosis was achieved after five days' incubation at 37°C when granular yellow brown or khaki colonies appeared. Cultures stained by lactophenol cotton blue showed chains of unicellular conidia arising from basally swollen phialides characteristic of *Paecilomyces* species. Amphotericin B 60 mg daily by infusion for six hours was added to the treatment. Within three days she had improved considerably; her fever settled and over six weeks radiographs of her chest cleared. She was discharged and remained well.

Comment

Many different opportunistic infections have been reported in patients with hairy cell leukaemia. Mycotic infections show a correlation with treatment with steroids but may occur due to defective function of T cells and monocytopenia,¹ as in our patient, who had not had any specific treatment for four years. Patients with hairy cell leukaemia often present with fever and abnormal chest radiographs, and routine bacteriological examination fails to detect a causative organism. As infection in these patients may be rapidly fatal appropriate diagnostic procedures must be performed early. Bronchoscopy is of special value in diagnosing mycotic infections.³

Paecilomyces species were first reported as pathogenic in man in 1950. Impaired host defences or the presence of foreign bodies predisposes to infection with such fungi.⁴ Although *P. varioti* has not been reported as a causative agent of pneumonia, a related fungus, *Penicillium lilacinum*, has been isolated from a pleural effusion in an otherwise healthy man.⁵ Our patient, having a low neutrophil count and no monocytes, was particularly susceptible to infection with an unusual fungus. Although bacterial pneumonia with secondary fungal infection was a possibility, the response to amphotericin B and failure to respond to broad spectrum antibiotics makes *P. varioti* the likely causative organism.

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Amoxycillin induced pancytopenia

We describe an elderly man who developed pancytopenia after treatment with amoxycillin and co-trimoxazole. Results of bone marrow culture studies incriminated amoxycillin.

Case report

A 79 year old man was admitted after collapsing at home with a three week history of unresolving chest infection despite oral antibiotics. He had suffered two nosebleeds the previous week. He also had a long history of maturity onset diabetes mellitus, well controlled by chlorpropamide and metformin; chronic bronchitis and emphysema with several acute exacerbations; and left ventricular failure controlled by digoxin, frusemide, and oral potassium supplements. For the chest infection he had been treated at home with oral amoxycillin 250 mg thrice daily for 10 days followed by sulphamethoxazole 800 mg with trimethoprim 160 mg twice daily for 11 days.

On examination he was found to be pale, weak, feverish, clinically dehydrated, and dyspnoeic at rest with signs of infection at his left base. Haemoglobin concentration was 9.2 g/dl, white cell count $1.7 \times 10^9/l$, platelet count $10 \times 10^9/l$, and plasma urea concentration 18.5 mmol/l (111 mg/100 ml). Oral hypoglycaemic agents were stopped and he began cimetidine 200 mg thrice daily and oral phytomenadione 10 mg twice daily empirically and was transfused with 2 units of whole blood.

On the second day the full blood picture was: haemoglobin concentration 12.0 g/dl, white cell count $1.3 \times 10^9/l$ (neutrophils 13%, lymphocytes 84%, monocytes 3%), platelet count $14 \times 10^9/l$, and reticulocyte count $16 \times 10^9/l$. One further unit of blood was transfused, rehydration continued, and oral antifungal agents and erythromycin 250 mg four times a day instituted. No further blood products were required. His chest infection resolved slowly and his general condition improved. Few haemorrhagic problems were

encountered. Plasma urea concentration fell to 8.9 mmol/l (54 mg/100 ml) by day 11 after admission.

On day 11 bone marrow trephine biopsy and aspiration with marrow culture was carried out. This showed a normocellular marrow with active myelopoiesis and normal numbers of megakaryocytes with a left sided shift in maturity. Erythropoiesis was poorly active with few early forms. Platelets increased from a nadir of $8 \times 10^9/l$ on day 3 to $663 \times 10^9/l$ on day 16, neutrophils from a nadir of $0.17 \times 10^9/l$ on day 8 to $10.6 \times 10^9/l$ on day 11, and reticulocytes from $16 \times 10^9/l$ on day 2 to $87 \times 10^9/l$ on day 23. Unfortunately, despite his marrow recovery the patient died shortly afterwards of an acute myocardial infarction.

Culture studies—Bone marrow culture for formation of colony forming units-granulocyte macrophage (CFU-GM) was carried out as described.¹ Stock solutions of preservative free sulphamethoxazole, trimethoprim (both Sigma UK Ltd), and amoxycillin (Amoxil; Bencard, England) were prepared by dilution in HEPES buffered TC-199 (Gibco-Europe Ltd).

Effect of amoxycillin on CFU-GM formation. Shaded area represents extreme limits of mean and SD of replicate cultures for four separate normal bone marrow samples: ●—● Mean and SD of replicate cultures for patient's bone marrow studied on day 11.

Each antibiotic was incorporated in both layers of the culture system at concentrations up to five times their expected peak in plasma. The peak plasma concentrations assumed were: sulphamethoxazole 20 mg/l, trimethoprim 1 mg/l, amoxycillin 5 mg/l. Four separate normal bone marrows were cultured similarly as a control. There was no significant difference between patient and normal bone marrow colony growth in the presence of sulphamethoxazole or trimethoprim. The figure shows the effect of amoxycillin on CFU-GM formation. In each normal marrow and that from the patient the colony count in the absence of any drug was taken as 100%. The patient's cells were more sensitive than normal cells to amoxycillin at concentrations to which he would have been exposed in vivo.

Comment

Co-trimoxazole is often blamed for neutropenia or pancytopenia after even relatively short periods of administration, whereas there are comparatively few reports of this occurring with amoxycillin.²⁻⁴ Our culture studies make it likely that in our patient co-trimoxazole was not implicated in the neutropenia and that he had an idiosyncratic reaction to penicillin.

With increasing attention being paid to the unwanted effects of drugs, this technique offers the prospect of identifying the likely causative agent in cases of multidrug administration and exonerating "innocent bystanders." The only other report of amoxycillin associated neutropenia suggested an immune mediated pathogenesis for the phenomenon,⁵ whereas our observations suggest that amoxycillin was directly toxic to our patient's CFU-GM.

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