the patients had been delivered, but 11 out of a possible 16 of the gentian-violet series and 34 out of 47 of the nystatin series did attend, and the relapse rates are shown in Table IV. Three of the women who had been treated with nystatin were seen by colleagues at about the appropriate time and were free from obvious infection.

TABLE IV.—*Relapse Rate in Patients Seen Four Weeks After Cessation of Treatment*

	Gentian Violet			Nystatin		
	No. of Patients	Candida Present	Relapse Rate	No. of Patients	Candida Present	Relapse Rate
Pregnant ..	2	2	100%	14	4	29%
Non-pregnant ..	9	3	33%	20	3	15%
Total ..	11	5	46%	34	7	21%

Discussion

Although the patients treated with nystatin had only a short course of treatment the results have proved to be most promising and distinctly better than those in the patients treated with gentian violet in a comparable scheme. Moreover, treatment with the nystatin pessaries is much simpler and does not have the disadvantage of staining linen, etc., as does gentian violet. The insertion of the pessaries could be easily done by the patient, thus saving much time for the patient and for the nursing and medical staffs. Also, as nystatin acts mainly on fungi and yeasts and has very little effect on bacteria, it means that there is much less interference with the normal flora than is the case with gentian-violet treatment.

Relapses, which are probably reinfections, are less frequent after nystatin than after gentian violet. It has been shown that oral nystatin greatly reduces the yeast population of the intestinal tract (Sternberg *et al.*, 1953), and it may be that combined oral and local treatment may clear the more persistent or recurrent infections. Sarewitz (1955) reported five cases of genito-urinary infection with candida which were improved or cured by oral therapy. We have treated one patient with oral tablets alone (500,000 units thrice daily for one week) with an excellent result, there being no symptoms and the culture being negative after six weeks. However, as there is no good evidence that high blood levels can be obtained by oral therapy it is unlikely that better results would accrue from this method alone. In fact, Childs (1956) has noted that systemic treatment had little or no effect on the numbers of candida organisms in the sputum and throat. Stewart (1956) and Childs (1956) reported nausea as a side-effect of oral nystatin, and our patients also complained of nausea with some abdominal pain.

Summary

Of 53 women with monilial vaginitis treated with a new vaginal pessary containing 100,000 units of nystatin, 47 (88%) were free from infection one week after treatment, whereas of 36 treated with gentian violet, only 17 (47%) were cured.

Out of a group of 18 who had not responded to gentian violet, 16 were cleared with nystatin.

In the patients seen four weeks after treatment the relapse rate was 46% in those treated with gentian violet and 21% in those treated with nystatin.

No side-effects or local discomfort has occurred with nystatin, whereas six of the women treated with gentian violet had a reaction which made it necessary to stop treatment.

One patient was treated with oral nystatin only, with an apparent cure.

We thank the obstetric and gynaecological staff of St. Mary's Hospitals for permission to treat their patients, and in particular Dr. E. A. Gerrard and Professor W. I. C. Morris for help in the planning of the investigation. Mr. Peter Stenton carried out

a large proportion of the bacteriological investigations, and Messrs. Squibb and Son supplied the nystatin preparations.

REFERENCES

- Brown, R., Hazen, E. L., and Mason, A. (1953). *Science*, **117**, 609.
 Childs, A. J. (1956). *British Medical Journal*, **1**, 660.
 Drouhet, E. (1955a). *Ann. Inst. Pasteur*, **88**, 298.
 — (1955b). *Presse méd.*, **63**, 620.
 Hazen, E. L., and Brown, R. (1950). *Science*, **112**, 423.
 Robinson, R. C. V. (1955). *J. invest. Derm.*, **24**, 375.
 Sarewitz, A. B. (1955). *Ann. intern. Med.*, **42**, 1187.
 Sloane, M. B. (1955). *J. invest. Derm.*, **24**, 569.
 Sternberg, T. H., Tarbet, J. E., Newcomer, V. D., Muddleson, H. G., Weir, R. H., Wright, E. T., and Egeberg, R. O. (1953). *Antibiotics Annual, 1953-54*, p. 199. Medical Encyclopaedia Inc., New York.
 Stewart, G. T. (1956). *British Medical Journal*, **1**, 658.

THE BREATH IN ACUTE LEUKAEMIA

BY

E. K. BLACKBURN, M.D., F.R.F.P.S.

Consultant Haematologist, the Royal Infirmary and Hospital, Sheffield

It is well known that a fetid breath may be found in patients with leukaemia in association with lesions of the upper alimentary and/or respiratory tracts. These lesions may be gum hypertrophy, petechiae and ecchymoses, or oozing of blood, gingivitis and mucosal ulceration, and necrosis. The smell is presumed to arise from the bleeding and from secondary infection.

Over the last few years some patients have been seen in whom acute leukaemia was accompanied by a peculiar sweet odour of the breath resembling that of a freshly opened corpse, but not associated with clinical involvement of the gums, mouth, or upper respiratory or alimentary tract. As the smell of the breath was of assistance to me in the clinical diagnosis of some of these patients, the results are recorded of my findings from this aspect in 73 cases of leukaemia which presented in hospital practice. In each case the presence or absence of halitosis was confirmed by at least one other medically qualified observer.

The 73 cases comprised 51 cases of acute leukaemia (34 myeloblastic, 15 monoblastic, 2 erythro-leukaemic) and 22 cases of the chronic group (11 granulocytic, 11 lymphocytic).

Results

Of 51 cases of acute leukaemia, 12 (9 myeloblastic, 3 monoblastic) had the characteristic halitosis without obvious clinical involvement of the mouth or respiratory and alimentary tracts (see Table). In six of these (Cases 5-10)

Blood Picture in the 12 Cases of Acute Leukaemia with Characteristic Halitosis

Case No.	Sex	Age in Years	Type of Leukaemia	Hb (%)	Total W.B.C./c.mm.	Blast Cells/c.mm.
1	M	17½	Myeloblastic	82	3,000	1,230
2	F	49	"	70	4,000	1,040
3	M	71	"	58	1,000	520
4	M	2½	"	35	4,000	2,000
5	M	18	"	40	200,000	198,000
6	M	29	"	88	5,000	600
7	M	41	"	47	23,000	12,420
8	M	9	"	35	13,000	9,880
9	F	46	"	45	5,000	550
10	M	28	Monoblastic	48	24,000	2,880
11	M	68	"	63	45,000	14,950
12	F	44	"	47	80,000	12,000

there were other signs and symptoms such as splenomegaly, etc., which suggested the true diagnosis. Clinical examination of the remaining six patients (Cases 1-4, 11, and 12) helped very little, for they had no sternal tenderness, haemorrhagic lesions, hepato-splenomegaly, or lymphadenopathy, and it was only after examination of the blood and bone marrow that a firm diagnosis could be made. One patient (Case 1) had had an appendectomy followed by

treatment for suspected paratyphoid fever during the six weeks before admission to the Royal Infirmary, Sheffield, while another (Case 2) had shown features of erythema multiforme. Case 3, a medical practitioner, had been admitted on the surgical side with pain in the right hypochondrium radiating to the back, upward flatulence, distaste for fatty foods, and a positive Murphy's sign. So far as the haemopoietic system was concerned, the only physical sign was mucosal pallor. Case 4 had complained of lethargy and had shown mucosal pallor only for two months. The fifth patient of this group (Case 11) had had progressive loss of energy, dyspnoea on effort, flatulent dyspepsia, and pallor of the mucous membranes only for four months, while the sixth patient (Case 12) had had a six-weeks history of malaise and pallor only, with no other suggestive physical signs.

A further 26 of the cases of acute leukaemia (15 myeloblastic, 10 monoblastic, 1 erythro-leukaemic) had the well-known fetid breath associated with a variety of intra-oral leukaemic lesions. In addition, five of these patients had epistaxis, one haemoptysis, three melaena, and two haematemesis plus melaena.

The remaining 13 cases of acute leukaemia (10 myeloblastic, 2 monoblastic, 1 erythro-leukaemic) had no halitosis at all. Five of these patients had oral petechial haemorrhages, and, in addition, one had nasal petechiae with epistaxis.

None of the 11 cases of chronic lymphatic leukaemia had halitosis, and only one had oral lesions consisting of slightly swollen gums. Ten of the 11 cases of chronic myeloid leukaemia had neither halitosis nor upper respiratory or alimentary lesions. The other case had a fetid breath. This patient had, however, bled excessively into the gut and the abdomen following partial gastrectomy for a large chronic gastric ulcer five days previously, and had received repeated blood transfusions. His tongue was tender and enlarged, the surface being dry, cracked, and yellowish red in colour.

Discussion

In 6 out of 73 cases of leukaemia, the peculiar sweet-smelling breath was of value in reaching a tentative diagnosis of acute leukaemia after clinical examination only. So far as I am aware, this physical sign has not been described previously in its present context. This may well be due to the fact that halitosis is usually associated with obvious lesions in the upper respiratory and/or alimentary tract, and/or with abnormal physical signs elsewhere suggesting the diagnosis.

The abnormal breath at present under discussion does not appear to be related to enlargement of the liver, spleen, or lymph nodes, to the haemoglobin level, to the total leucocyte count, or to the blast-cell count (see Table). A sweet, slightly faecal odour likened to the smell of mice or to a freshly opened corpse has been described in hepatic failure (Sherlock, 1955), but in none of the present cases was there clinical evidence of such a state. Recent work has shown that, in both man and animals, the lung plays an active part in the removal (from blood and organs) and release (to blood and organs) of leucocytes and platelets under various stimuli (Bierman, 1955). The mechanisms whereby these changes are induced remain to be clarified. They may possibly play a part in the halitosis, but this is only conjecture. Finally, the odour in the above six cases may have been due to lesions in the alimentary and/or respiratory tract which were not found on ordinary clinical examination.

Summary

A physical sign is described consisting of a peculiar sweet odour of the breath found in relation to 73 cases of leukaemia (51 acute, 22 chronic). It was present in 12 of the cases of acute leukaemia without obvious clinical involvement of the gums, mouth, or upper respiratory and alimentary tracts. In six of these cases there

were signs and symptoms, such as splenomegaly, to suggest the true diagnosis, while ordinary clinical examination of the other six cases, halitosis apart, was unrewarding, and it was only after examination of the blood and bone marrow that a firm diagnosis could be made. Possible sources of the halitosis are discussed.

I am indebted to my medical and surgical colleagues in the United Sheffield Hospitals and in the Sheffield Regional Hospital Board area for referring their cases, and to the medical staffs who have confirmed the observations. I also thank Dr. H. T. Swan for reading the manuscript.

REFERENCES

- Bierman, H. R. (1955). *Amer. J. Surg.*, 89, 130.
 Sherlock, S. (1955) *British Medical Journal*, 1, 1383.

Medical Memoranda

Congenital Absence of Spleen Associated with Cardiac Abnormalities

Polhemus and Schafer (1952) described four cases of congenital absence of the spleen associated with gross cardiac abnormalities and reviewed the literature up to that time. Since then Ivemark (1955), Gasser and Willi (1952), Bush and Ainger (1955), Polhemus and Schafer (1955), and Nihoyannopoulos *et al.* (1956) have reported further cases. Bush and Ainger lay emphasis on the unusual peripheral blood picture which may be found in this condition—namely, normoblastaemia, reticulocytosis, leucocytosis, Howell-Jolly bodies, and a decreased osmotic fragility.

Details of a further case are given below. I have been unable to trace any previous report of this condition occurring in an infant born in Britain.

CASE REPORT

A male child was admitted to hospital 48 hours after birth because of an imperforate anus and possible upper intestinal obstruction. The mother's pregnancy and labour had been normal. The birth weight was 5 lb. 1 oz. (2.3 kg.). The two previous pregnancies had resulted in one miscarriage and one living healthy child.

On admission the infant's general condition was good. There was no cyanosis or dyspnoea. A precordial systolic murmur was detected at this time, but, despite repeated auscultation, was not heard again for 10 weeks. The abdomen was not distended, but there was a tight anal stenosis, probing of which produced a small amount of meconium. The anus was dilated and gave no further trouble. Straight x-ray examination of the abdomen showed gas shadows only as far as the duodenum. A laparotomy was therefore performed by Mr. A. Jolleys under general anaesthesia. An atresia of the third and fourth parts of the duodenum was found. The continuity of the lumen was restored by anastomosing the blind ends.

Progress was uneventful for the next 12 days, when the infant started passing loose green stools which became increasingly offensive. These were at first thought to be "starvation stools" because of the small feeds the child was taking, but the loose stools persisted when normal feeds were taken. The blood count at this time showed a haemoglobin of 96%. The total nucleated cell count was 19,000 per c.mm., with polymorphs 27%, lymphocytes 22%, monocytes 9%, eosinophils 2%, late normoblasts 40%. The reticulocyte count was 30%. In an attempt to account for the normoblastaemia the osmotic fragility of red cells was investigated and a slight decrease of fragility was found, 50% of cells being still present at a dilution of 0.36%, the indirect Coombs test was negative, and the urine contained no bilirubin or excess of urobilin.

When the infant was 5 weeks old, cyanosis appeared and gradually increased in intensity. In view of the absence of