into the microalbuminuria range before it induces a rise in blood pressure.

Insulin dependent diabetic patients who developed persistent or intermittent microalbuminuria were significantly more likely to have retinal lesions at baseline than those who remained normoalbuminuric. This difference was maintained at follow up and has also been shown by other workers.²⁴

In conclusion our study shows that raised albumin excretion rate and blood pressure are concomitant phenomena in insulin dependent diabetic patients progressing to microalbuminuria. A background of poor blood glucose control compounded with a rise in blood pressure and, to a lesser extent, a history of smoking are crucial determinants of this process.

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Variable mercaptopurine metabolism in children with leukaemia: a problem of non-compliance?

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acute lymphoblastic leukaemia always take their mercaptopurine tablets.

Patients, methods, and results

We recruited 35 consecutive children with acute lymphoblastic leukaemia who were treated in Sheffield or Nottingham, were in their first remission, and had been receiving similar maintenance chemotherapy that included continuous treatment with mercaptopurine at a standard daily dose of 75 mg/m² for at least nine months. The children were seen at least fortnightly, and their drug doses were reduced if they developed neutropenia or thrombocytopenia. On the basis of whether they had ever taken the standard dose of mercaptopurine for four or more weeks continuously without developing cytopenias, we designated 22 of the children as tolerant of the treatment and 13 as non-tolerant.

After the tolerant children had completed at least four weeks of treatment with the standard dose of mercaptopurine (when the concentration of 6-thioguanine nucleotides in red cells should have been reaching a steady value) we took blood samples to measure the concentration of these metabolites. The blood was taken at the time of routine venepuncture, and the methods of measuring the metabolites have been described elsewhere.⁵ We also assessed the compliance of all 35 children with their treatment by means of a structured interview.

The table shows the highest and lowest concentrations of 6-thioguanine nucleotides recorded for each child who was tolerant of mercaptopurine and the ratios of these concentrations. The ratios for six children were 1.9 or more, indicating wide fluctuations in the metabolite concentrations. At the time of their lowest recorded concentration they had been taking a full dose of mercaptopurine for between five and 43 weeks.

Highest and lowest concentrations of 6-thioguanine nucleotides in red cells of 22 children with acute lymphoblastic leukaemia who had been taking mercaptopurine 75 mg/m² for at least four weeks

Case No	Concentration (pmol/8×10 ⁸ red cells)		
	Highest	Lowest	Highest:Lowest
1	443	413	1.07
2	275	246	1.12
3	491	425	1.16
4	305	234	1.30
5	246	186	1.32
6	622	461	1.35
7	269	198	1.36
8	377	263	1.43
9	251	174	1.44
10	287	198	1.45
11	246	168	1.46
12	497	323	1.54
13	443	281	1.58
14	425	269	1.58
15	485	305	1.59
16	605	353	1.71
17	264	138	1.91
18	690	354	1.95
19	330	144	2.29
20	228	90	2.53
21	294	108	2.72
22	282	96	2.94
Median value	318	240	
(range)	(228-690)	(90-461)	

Two children (cases 21 and 22) admitted failing to take their tablets. Both were adolescent girls in charge of their own treatment. Six others gave equivocal histories of compliance. They were all tolerant of mercaptopurine, and three had ratios of highest to lowest metabolite concentrations of 1.9 or more.

Comment

Of the 22 children supposedly taking a constant dose of mercaptopurine over a long period, six showed wide fluctuations in the concentrations of the drug's metabolites. Two of these children admitted to not taking their medication, and partial non-compliance was probable in at least three others. None of the children had no detectable metabolites, indicating that none had completely abstained from treatment. We have, however, recently received samples that had no detectable metabolites. These came from four patients from other British centres as part of a nationwide study.

Our results suggest that some one in five children with acute lymphoblastic leukaemia fail to comply fully with oral chemotherapy. If this is correct it may explain unexpected late relapses in patients with an otherwise good outlook. Recognising non-compliance is not the same as solving it. Simply escalating the dose of mercaptopurine for apparently tolerant patients who are not taking the drug is potentially dangerous if they start to comply. Serial assay of metabolites can be used to monitor suspected offenders, but continual vigilance and education in the clinic are also needed.

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MEMORABLE PATIENTS

Hearing the angels' wings

During the second world war practice in London was stressful. I recall being telephoned about eleven o'clock one night by a patient who I remembered was a naval captain. Speaking with obvious authority he asked me to see a patient. "When?" I asked. "Now," he said, "and send the bill to room 121 at the Admiralty." It was a quiet night with no air raids and soon an olive green Hillman appeared from which emerged a tall, upstanding figure in combat dress with no insignia or shoulder flashes of any sort. I dealt with his acute toothache by simple tooth pulp decompression so within half an hour he was back in the car and vanished into the mist. I ruefully compared my tensed up weariness with his air of calm and ease, and this continued to bother me even after I read of a naval raid in Norway with prisoners taken and installations blown up. The ships had got away safely.

Three years later I spotted the captain at a party. I asked him, "Do you remember that chap you sent me in the middle of the night?" When he nodded affirmatively I realised that I had known all along the answer to the question I then foolishly asked. "He didn't come back, did he?" "No," he replied, "They waited for him as long as they could."

Thirty years later the exact spot of the landing was pointed out to me. It was now a neat and tidy little place with small houses glinting in the sun. By then I was oldish

myself and I realised that at the end of life we prefer to be at home. Probably that nice young man felt the same.

I also recall a patient who visited me regularly until for reasons of health she asked for a domiciliary visit. These became more frequent, ending up in little more than inspections and conversation. With further decline in health she moved into a ground floor flat overlooking a pleasant Chelsea square with a nurse discreetly in the background. After one visit she took my hand and turned her cheek up to be kissed, which I did as gracefully as I could. It was a sunny bright March day with blue sky and scudding clouds. The trees in the square were still black without sign of leaf and I knew at that moment that she would never see them any other way. She died soon afterwards.

Doctors see patients who are ill, sometimes terminally ill. Dentists see patients who by and large are well, but in the rush and tumble of daily affairs we take these incidents as part of the day's work. It is only in retrospect we realise that if we had thought about it at the time we could have been hearing the beating of the angels' wings.—ROBERT CUTLER is a retired general dental practitioner in Surbiton, Surrey

We welcome contributions to fillers: *A patient who changed my practice; A paper that changed my practice; A memorable patient; The message I would most like to leave behind*, or similar topics.