Subclinical lead exposure: a possible cause of gout

Joint pains have long been recognised as a symptom of lead poisoning. They occur in 25% of patients with chronic lead poisoning in the UK and are often associated with hyperuricaemia. Serum urate values may be higher in lead nephropathy than in comparable degrees of renal failure from other causes, and an increase in nuclear-protein turnover may contribute to this. A history of frank lead poisoning is uncommon in patients presenting with gout in the UK, a study of the effects of chronic low-grade lead exposure from drinking water showed hyperuricaemia to be significantly associated with raised blood lead concentrations in a symptom-free population. We have studied the blood lead concentrations in patients with gout who gave no history of overt lead exposure.

Patients, methods, and results

We studied 32 patients suffering from gout. Their ages ranged from 18 to 70 years, and all were men. All had clearly documented gouty arthritis, having been found to have hyperuricaemia and urate crystals in articular aspirate. Most of the patients had normal serum urea (5.5 ± 1.8(SE of mean) 0.2 mmol/l (35-2 ± 1.2 mg/100 ml)) and creatinine (108 ± 30 mmol/l (0.9-2.5 mg/100 ml)) concentrations, but serum urea was raised in five patients and serum creatinine in three. We also studied 32 age- and sex-matched controls. None had a history of joint pain or hypertension or raised serum urea or urate concentrations. A history of known lead exposure was a ground for exclusion in both groups. Serum urate was estimated by a standard automated technique and the blood lead concentration by atomic absorption spectrophotometry using a Perkin-Elmer 306 flameless atomic absorption spectrophotometer with HGA 72 graphite-cell power source.

As a group the patients with gout had higher blood lead values than the controls (see table). For example, none of the gouty subjects had a blood lead concentration of under 0.4 µmol/l (8-3 µg/100 ml), and whereas only four controls had blood lead concentrations of over 1-5 µmol/l (31 µg/100 ml) 16 of the patients exceeded this concentration. In only three of the 32 pairs did the control have a blood lead concentration in a higher range than the patient. Reference to the binomial distribution yielded a highly significant result (P<0.001).

<table>
<thead>
<tr>
<th>Blood lead (µmol/l)</th>
<th>&lt;0.4</th>
<th>0.4-8 0</th>
<th>1.2-16</th>
<th>1-20</th>
<th>20-25</th>
<th>&gt;25</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>0</td>
<td>2</td>
<td>13</td>
<td>6</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>No of controls</td>
<td>5</td>
<td>2</td>
<td>12</td>
<td>6</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>
| Conversion: SI to traditional units: Lead: 1 µmol/l=1.207 µg/100 ml.

Discussion

These findings leave no doubt that raised blood lead values and gout are associated, though they do not prove that lead helped to cause the gout in these patients. Gout nephropathy may have caused diminished renal lead excretion with a resulting increase in blood lead concentrations, but this group of patients mostly had normal renal function. Moreover, even severe renal failure may not depress renal lead excretion. Some unknown factor may reduce the excretion of both lead and urate. This, however, seems unlikely since urate is excreted by the renal tubules, whereas lead seems to be excreted mainly by glomerular filtration.

Thus our findings, taken with the association between lead and symptomless hyperuricaemia found previously, suggest that lead is sometimes a causal factor in gout. Gout may be another manifestation of subclinical lead poisoning.

1 Campbell, B C, and Baird, A W, British Journal of Industrial Medicine, 1977, 34, 296.
2 Emmerson, B T, Australasian Annals of Medicine, 1963, 12, 310.
3 Ludwig, G D, Archives of Internal Medicine, 1957, 100, 802.
4 Campbell, B C, et al, British Medical Journal, 1977, 1, 482.
Anaphylaxis after oral penicillin

Allergic reactions to penicillin are not uncommon, but anaphylaxis is rare. Anaphylaxis after oral ingestion is rarer still, and many doctors are unaware of its existence. We describe here two patients who suffered near-fatal anaphylaxis after taking oral penicillin who were admitted within ten days of each other to the Leicester Royal Infirmary.

Case 1

A 29-year-old woman was prescribed penicillin V for a sore throat. Within three minutes after taking the first tablet she developed generalised pruritis and flushing, followed by abdominal cramps, nausea, and one episode of vomiting. When first seen 30 minutes after ingestion, she was responding only to commands and had severe peripheral cyanosis, a tachycardia of 120 beats/min, and blood pressure of 70/50 mm Hg. She was initially treated with 0.5 ml 1/1000 adrenaline subcutaneously, 200 mg hydrocortisone intravenously, and 10 mg chlorpheniramine intravenously, and subsequently with an infusion of hydrocortisone for 12 hours. She regained full consciousness over the next 30 minutes and her blood pressure returned to normal after three hours. On subsequent questioning she admitted having taken penicillin on several previous occasions.

Case 2

A 47-year-old man was prescribed talampicillin for a cough of one week's duration. Thirty minutes after taking the first tablet he developed facial oedema, pruritis, and nausea and then lost consciousness. When first seen at home he was severely cyanosed and was responding only to painful stimuli. He was given 10 mg chlorpheniramine intravenously together with 200 mg hydrocortisone, and a 19-G needle was inserted into his trachea. After transfer to hospital and further treatment with antihistamines and steroids his conscious level and respiration improved but he remained hypotensive for several hours before recovering fully. Subsequently he said that he had taken penicillin preparations on several other occasions with no adverse effects, the last time being three months previously.

Comment

These two patients suffered severe anaphylactic shock after oral ingestion of penicillin and both had been treated with penicillin preparations previously with no symptoms suggestive of allergy. The incidence of anaphylactic shock in all patients treated with penicillin is between 0.015 and 0.04%, with death occurring in 0.002% of cases.\(^1\)

Anaphylaxis after oral ingestion is, however, even less common than after parenteral administration, and Batson\(^2\) could find only 28 cases in a survey of published reports up to 1960. There have been four reports of fatal anaphylaxis due to oral penicillin preparations.\(^3\) Patients who develop anaphylactic reactions have usually been treated with penicillin before—for example, 25 of the 28 patients in Batson's series and three out of four patients quoted by Spark\(^4\) had received previous treatment.

The main antigenic stimulus in penicillin allergy is now thought to come from the breakdown products of the penicillin molecule: the penicilloyl group, with the "minor antigenic determinants," such as Na-benzylpenilloate and Na-benzylpenicilloate, being particularly relevant in the development of anaphylactic reactions. Since all semi-synthetic forms of penicillin are built around the same molecular nucleus, this accounts for cross-allergy to different preparations, and activation of allergy in already sensitised individuals often requires only minimal amounts of penicillin, particularly with regard to anaphylactic reactions. This was well illustrated by our patients. We want to draw attention to this point and also to the fact that oral penicillin preparations can cause as rapid and as severe an allergic reaction as parenteral preparations.


(Received 15 September 1978)

Department of Neurology, Hammersmith Hospital and Royal Postgraduate Medical School, Du Cane Road, London W12 0HS

N. J. L. WIG, MB, MRCP, consultant and senior lecturer.


(Received 12 September 1978)