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Imported occupational lead poisoning: report of four cases

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Summary
Background: *In most industrialized countries, occupational lead poisoning has become increasingly rare, however this metal remains a serious health hazard in the rest of the world.* **Report of cases:** *We observed four male patients (aged 35 ÷ 54 years) who had suffered recurrent abdominal pain due to recent lead exposure (for 7 to 13 months) in two Chinese battery recycling plants. On their return to Italy, three of them presented normocytic, normochromic anaemia. The diagnosis was confirmed by high lead levels in the blood and urine, decreased erythrocyte δ-aminolevulinic acid dehydratase (ALA-D), raised erythrocyte zinc protoporphyrin (ZP), and elevated urinary excretion of δ-aminolevulinic acid (ALA-U) and porphyrins. Chelation with EDTA resulted in increased urinary lead excretion, improvement of the clinical picture, decreased ZP, and progressive normalization of the other lead biomarkers (Pb-B, ALA-D, ALA-U, urinary porphyrins).* **Conclusions:** *Temporary work in developing countries may result in imported lead poisoning. Differential diagnosis of this unusual condition requires careful medical history collection and specific toxicological analysis. Preventive measures for workers going abroad are needed.*

Riassunto
«Saturnismo d'importazione: descrizione di quattro casi». **Introduzione:** *Nei paesi maggiormente industrializzati, l'intossicazione professionale da piombo è ormai di rara osservazione. Questo metallo rimane tuttavia un serio rischio per la salute nel resto del mondo.* **Descrizione dei casi:** *Quattro pazienti maschi (età: 35 ÷ 54 anni) sono giunti all'osservazione dopo avere sofferto di dolore addominale ricorrente causato da recente esposizione al piombo (durata: 7 ÷ 13 mesi) in due impianti cinesi di riciclaggio batterie. Al rientro in Italia, tre di loro presentavano anemia normocitica normocromica. La diagnosi è stata confermata dal riscontro di: livelli elevati di piombo nel sangue e nelle urine, diminuzione dell'acido δ-aminolevulinico deidratasi (ALA-D) eritrocitaria, aumento della zinco protoporfirina (ZP) eritrocitaria, elevata escrezione urinaria di acido δ-aminolevulinico (ALA-U) e di porfirine. La chelazione con EDTA ha portato ad aumentata escrezione urinaria di piombo, miglioramento del quadro clinico, diminuzione della ZP e normalizzazione degli altri indicatori biologici (Pb-B, ALA-D, ALA-U, porfirine urinarie).* **Conclusioni:** *Periodi temporanei di lavoro in paesi in via di sviluppo possono essere causa di saturnismo d'importazione. La diagnosi differenziale di questa rara condizione richiede accurata anamnesi e analisi tossicologiche mirate. Sono necessarie adeguate misure preventive per i lavoratori che si recano all'estero.*

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Introduction

Since ancient times, lead has been extensively mined, produced, and used worldwide in a variety of occupational settings, such as metallurgy, construction, production of plastics, ceramics, paints and pigments (6, 7, 9). Lead and its compounds are systemic toxicants, and a wide range of adverse health effects (including haematological, gastrointestinal, neuropsychiatric, cardiovascular, renal, endocrine, and reproductive disorders) has been described in exposed workers (3, 7, 9). The general population (particularly children) may also be exposed to toxic lead levels due to air, soil, food, water and medication contamination (7, 9, 12). In Italy and other industrialized nations, thanks to the improvement of workplace hygienic conditions, lead poisoning (plumbism, saturnism) has become increasingly rare (3, 9). However, this heavy metal is still a serious occupational hazard in the rest of the world. For this reason, temporary workers in developing countries may be exposed to unusually high lead levels (for western standards).

Report of cases

Four male patients were referred to our Institute after temporary work in southern China (table 1), where they had suffered general malaise, dyspepsia, and recurrent episodes of abdominal pain. In addition, case 1 suffered nausea, vomiting, and abdominal colic, requiring symptomatic treatment in a local hospital.

On their return to Italy, they were examined by the authors on different days, over two months. Case 1 still complained of occasional, moderate disturbances (asthenia, abdominal pain), while the others were asymptomatic. Physical examinations were unremarkable. With the exception of case 2, blood tests showed normocytic, normochromic anaemia, with reticulocytosis (table 1). The morphology of erythrocytes was normal, without basophilic stippling. The parameters of hepatic and renal function were normal.

Occupational history revealed that the subjects were employed by an Italian company specialized in lead and aluminium recycling, that fulfilled the legal requirements regarding workplace hygiene, health surveillance and biological monitoring. The four workers had been healthy before being sent abroad, with normal haematologic values and blood lead levels below 3.0 μg/dL. During their stay in China, they had worked intensively for several months in two lead recycling plants, where used electric batteries were ground and melted (temperature > 1000°C). The fused lead was then refined and cast to produce ingots. The patients' tasks were teaching and training of local employees, supervision of the production lines, maintenance and repair. In both factories, they reported bad hygienic working conditions, no aspiration systems, and heavy exposure to lead fumes and vapours (and also lack of protective respiratory devices). This description was confirmed by convincing photographic documentation (figures 1 and 2). Meals were consumed at the workplace, probably contributing to lead intake. Other possible, non-occupational exposure sources were excluded. No environmental or biological monitoring data (or other information on the health status of the local workers) were available.

As shown in table 1, lead levels in both blood (Pb-B) and urine (Pb-U) were still elevated several weeks after the last exposures (except case 4). Erythrocyte δ-aminolevulinic acid dehydratase (ALA-D) was decreased (except case 4), and zinc protoporphyrin (ZP) was increased. Urinary excretion of porphyrins, and their precursor δ-aminolevulinic acid (ALA-U), was elevated.

The patients were treated with ethylene-diaminetetracetic acid (EDTA: 1 g/die i.v., on 3 non-consecutive days): chelation was well tolerated (without alteration of the hepato-renal function), and revealed a high lead body burden, as indicated by increased urinary excretion (figure 3). After the third EDTA infusion, Pb-B values were below 35 μg/dL in all patients. This was paralleled by normalization of the haematological parameters (in particular, haemoglobin, haematocrit, and reticulocytes) and biomarkers for lead effects (ALA-D, ALA-U, urinary porphyrins), except ZP (≥ 100 μg/dL).

The cases were reported to the appropriate legal authorities, as established by the Italian Penal

Table 1 - Temporal aspects of lead exposure and main results of blood and toxicological tests on admission

	Case 1	Case 2	Case 3	Case 4
Age (years)	40	35	54	35
Pb exposure (months)	7	5	13	4
Time since last exposure (weeks)	6	9	5	11
Erythrocytes (10^6/μL) (normal: 4.5 ÷ 6.3)	3.8	4.9	4.2	4.3
Haemoglobin (g/dL) (normal: 14 ÷ 18)	12.7	15.2	13.3	13.8
Haematocrit (%) (normal: 38 ÷ 52)	37.3	43.9	38.3	40.4
Mean corpuscular volume (fL) (normal: 77 ÷ 91)	90.5	89.5	89.3	89.9
Reticulocytes (%) (normal: 0.5 ÷ 1.5)	1.9	1.0	1.8	1.3
Pb-B (μg/dL)*	76	60	38	16
Pb-U (μg/24 hr)**	81	74	101	25
ALA-D (U/L) (normal: > 25)	1.5	10	12	34
ALA-U (mg/dL) (normal: < 0.45)	0.76	0.77	0.16	0.20
Uroporphyrins (μg/24 hr) (normal: < 20)	37	21	15	17
Coproporphyrins (μg/24 hr) (normal: < 100)	614	117	108	80
ZP (μg/dL) (normal < 40)	275	236	163	121

*The reference range (5^{th}-95^{th} percentile) for the Italian population is 1.1 ÷ 3.0 μg/dL (24). In Italy, the legal limit value for exposed workers is 60 μg/dL (action level 40 μg/dL). The ACGIH biological exposure index (BEI) is 30 μg/dL (4).
** Reference range (5^{th}-95^{th} percentile) for the Italian population: 0.01 ÷ 2.00 μg/L (24).

Figure 1 - Loading of a rotary kiln for lead fusion

Figure 2 - Working environment pollution by lead vapours and fumes.

Code, and referred to the Italian Workers' Compensation Authority (INAIL).

Discussion

People travelling abroad, for tourism or occupational reasons, can be exposed to various noxious agents absent in the country of origin. As a consequence, they may return home with "imported diseases", such as malaria (17), other transmissible illnesses (19), or food poisoning (e.g., ciguatera) (8). We describe here four unusual cases of imported occupational lead poisoning, presenting with two classical clinical features: abdominal pain (with saturnine colic in case 1) and anaemia (3, 11).

This condition is observed only exceptionally in developed countries, where Pb-B in exposed

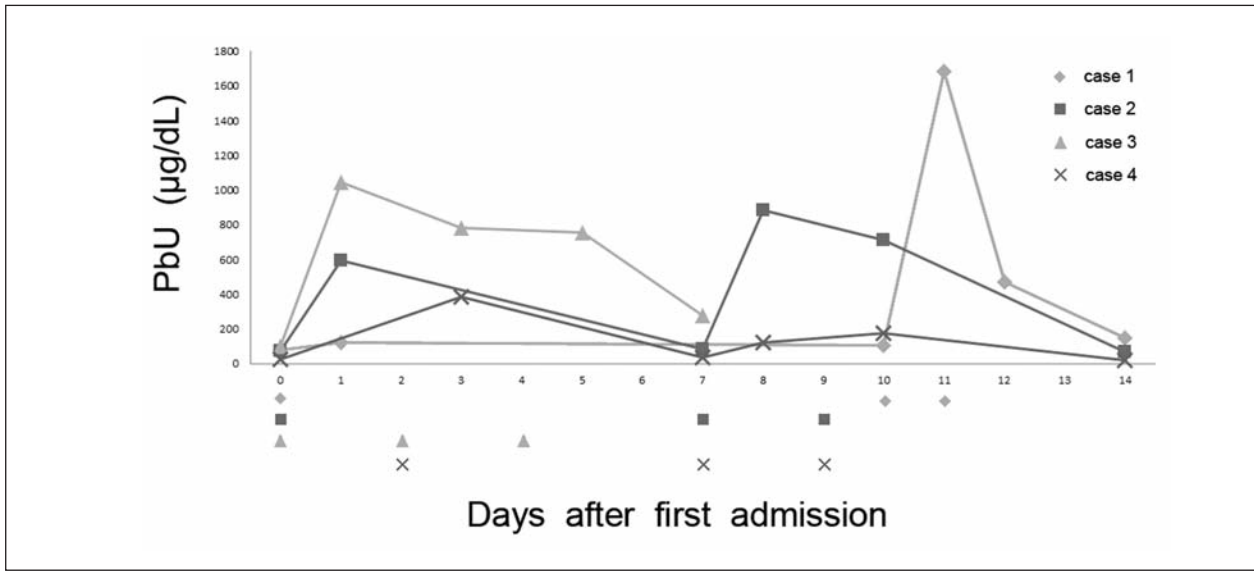

Figure 3 - Effect of chelation on urinary lead concentration (Pb-U). For each patient, single EDTA infusions are indicated by the corresponding symbol below the abscissa axis

workers (the most reliable index of internal dose) nowadays rarely exceeds 60-80 µg/dL, over which overt toxicity occurs (23). On the other hand, poisoning is not unusual in other countries, where rapid industrialisation has increased the demand for lead and its use, but with a complete lack of adequate preventive measures. Alarming occupational and environmental exposures were documented in China (13, 27-29), other Asian countries (5, 14, 15, 26), Africa (1, 18, 22), and Latin America (10, 21).

The clinical manifestations of occupational lead poisoning appear after a latency period of months to years after the beginning of exposure (3, 7). The bone marrow is the most sensible target for lead toxicity: the metal interferes with a variety of haeme biosynthetic enzymes, including ALA-D (conjugating levulinic acid to form porphobilinogen) and ferrochelatase, incorporating Fe^{2+} into protoporphyrin IX. Resulting anaemia may be microcytic or, as reported here, normochromic normocytic, with reticulocytosis. Basophilic stippling of erythrocytes (not observed in our patients) is another typical feature, due to the persistence of cytoplasmic proteins (2, 11).

The pathogenesis of other possible toxic manifestations has not been fully elucidated. It is known, however, that lead-induced accumulation of porphyrins is partly responsible for gastrointestinal disturbances (7). Lead colic (first described by Hippocrates in 370 B.C.) may mimick an acute abdomen condition (3, 25).

Saturnism should always be suspected in the presence of compatible clinical symptoms in association with an occupational or environmental history of lead exposure. Diagnosis is usually confirmed by Pb-B determination: the concentration gradually declines over 2-4 weeks after the patient has been removed from the source. On the other hand, ZP (resulting from the binding of free protoporphyrin IX with zinc) is a biomarker that remains in the blood for the lifetime of the erythrocyte, reflecting lead exposure over the prior 3-4 months. Urinary lead excretion after chelation is useful to estimate the body burden. ALA-D and ALA-U are both sensitive and specific indicators of lead exposure, though they are not utilized routinely in the clinical setting (16, 23).

ALA-D is the first biomarker to normalize after Pb exposure has ceased (23). Accordingly, ALA-D was found normal in case 4, who underwent the shortest exposure and was examined 11 weeks after its cessation, presenting normal blood lead levels and slight anaemia (table 1).

Management of lead poisoning requires, first of all, interruption of exposure. Chelating agents, which form lead complexes that are eliminated in the urine, are useful in rapidly reversing the clinical and biochemical effects of the metal: EDTA is currently considered the most reliable and safe drug, the principal risk being nephrotoxicity (20). As in the patients described, ZP is the last biomarker to normalize after exposure has ceased, and chelation carried out (16, 20, 23).

In conclusion, physicians should be aware of the possibility of lead poisoning in workers returning from developing countries. In such cases, careful anamnesis and toxicological analysis are crucial to differentiate this condition from a variety of internal and surgical diseases which may present similar symptoms (11, 12). In turn, correct diagnosis is important for prognosis, treatment, and occupationally-related legal medicine issues. Adequate preventive measures (e.g., risk assessment, health education, health surveillance) for workers going abroad must be adopted.

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