numbers of moles and to formation of high risk melanocytes or might indicate that prior exposure to an environmental agent—for example, perhaps the sun—caused independently both large numbers of moles and malignancy. The third potential mechanism—that the melanocytes in naevi are particularly prone to melanoma—is supported at least partially by the finding in pathological studies that in 20% or more of melanomas malignant melanocytes can be identified histologically in contiguity with benign naevus cells.¹⁵ In clinical studies a large proportion of patients with melanoma give a history of an antecedent pigmented lesion at the site of their melanoma,¹⁵ but these studies give weak evidence because there is great potential for misunderstanding (as patients may mistake the early stages of superficial spreading melanoma or lentigo maligna melanoma for a mole) and for bias.

The histology and the site, which in our study and another were most highly associated with naevi,⁸ were also those for which in other publications the greatest proportion of melanomas have been identified histologically in contiguity with benign naevus cells—namely, superficial spreading melanoma¹⁶⁻¹⁸ and trunk melanomas.¹⁶⁻¹⁷ These were also the histological type and site for which the greatest proportion of patients in the present study gave a history of an antecedent “mole” at the site of their melanoma, although, as noted above, these histories give weak evidence. The findings by histological type are in a direction compatible with the hypothesis that naevi are precursors of superficial spreading melanoma and nodular melanoma but not lentigo maligna melanoma¹⁹; this hypothesis is supported by ultrastructural evidence,²⁰ but the epidemiological evidence is also compatible with other hypotheses.

In conclusion, we suggest that people with large numbers of benign melanocytic naevi, and those with clinically atypical but not necessarily histologically dysplastic naevi, are at greatly increased risk of melanoma. Such people should be warned about recognising early melanoma and avoiding risk factors and notably advised about exposure to ultraviolet radiation. The aetiology of benign melanocytic naevi needs investigation and may elucidate the aetiology of melanoma.

We thank the Greater Glasgow Health Board Research Support Group

and Eli Lilly and Company for financial support, colleagues who allowed us to approach their patients, and the Scottish Melanoma Group for permission to refer to unpublished material.

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(Accepted 1 April 1986)

SHORT REPORTS

Self poisoning with oral cadmium chloride

Stress related to examinations is a frequent cause of self poisoning in teenagers and young adults. The agents used and amounts consumed are not usually dangerous, however, and thus the overall mortality and morbidity are low.

Deliberate self poisoning with cadmium is extremely rare, but we describe a case illustrating the severe metabolic sequelae and destruction of tissue that follow oral ingestion of cadmium chloride.

Case report

A 17 year old girl was admitted to hospital with facial swelling and vomiting. She had been fit and well earlier at school but on arrival at the accident and emergency department was too ill to provide any history. She had increasing facial, pharyngeal, and neck oedema and was hypotensive. A presumptive diagnosis of angioneurotic oedema was made, but she did not respond to steroids given intravenously and a histamine H₁ receptor antagonist.

One hour after admission a bottle of cadmium chloride crystals, which had been removed from the school laboratory reagent store, was found in her handbag. Subsequent gastric washout (roughly three hours after ingestion) produced white crystalline material, later confirmed to be cadmium chloride.

Her condition deteriorated rapidly. She suffered a respiratory arrest, requiring endotracheal intubation and mechanical ventilation. Despite treatment with edetic acid and colloid and crystalloid infusions, she continued to deteriorate, becoming hypothermic (temperature 30°C on a low reading thermometer), haemoconcentrated (haemoglobin 222 g/l, packed cell volume 0.52), glucose intolerant (glucose 55.8 mmol/l (1004.4 g/100 ml)), and acidotic (pH 6.9) without

ketones. Results of coagulation studies were severely deranged (prothrombin time 60 seconds, control 13 seconds; partial thromboplastin time 180 seconds, control 39 seconds).

Over 24 hours she developed pulmonary and generalised oedema and oliguria. Full supportive measures, chelation treatment, charcoal haemoperfusion, and positive end expiratory pressure ventilation were unsuccessful, and she died 30 hours after admission.

Necropsy showed pulmonary oedema, pleural effusions, and ascites. There was haemorrhagic necrosis of the stomach, duodenum, and jejunum, focal hepatic necrosis, and slight pancreatic haemorrhage. The kidneys appeared normal. Tissue, blood, and urinary cadmium concentrations were measured by atomic absorption spectrophotometry (Varian 475 spectrophotometer) and found to be considerably raised (blood cadmium 208 µmol/l (23 g/l), normal range <89 nmol/l (10 µg/l); urinary cadmium 153 µmol/l (17 g/l); liver cadmium 3.6 nmol/kg (0.4 µg/kg) wet tissue; lung cadmium 1.7 nmol/kg (0.2 µg/kg) wet tissue).

Comment

In the United Kingdom we are not aware of any reported cases of cadmium used for self poisoning. Cadmium is strongly bound to a carrier protein metallothionein, has a long biological half life, and is widely distributed in the body,¹ particularly the kidney, which contains one third of total body cadmium.

Smelters or welders accidentally exposed to high concentrations of cadmium develop the syndrome of “fume fever,” characterised by cough, dyspnoea, and myalgia. After 24-48 hours pulmonary oedema develops, which may be fatal. Chronic exposure to low concentrations of cadmium usually results in renal tubular dysfunction, proteinuria, a fall in creatinine clearance, and a rise in urinary β microglobulin.² Other manifestations include osteomalacia, emphysema, and hypochromic anaemia.³

Cadmium, like other heavy metals, is highly toxic, binding rapidly to extracellular and intracellular protein, and thus disrupting membrane and cell function. Immediate gastric washout and rapid chelation treatment are the most effective methods of treatment. In studies of animals chelation treatment has been shown to be effective only if given soon after ingestion of cadmium.⁴ Charcoal haemoperfusion is ineffective because of the high protein binding of cadmium.

Our patient had ingested a massive dose of 150 g of cadmium chloride, and, although the initial diagnosis was delayed, it seems unlikely that any treatment would have prevented the membrane dysfunction and destruction of tissue. The case, however, illustrates the catastrophic effects of ingested cadmium on organ function.

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(Accepted 11 March 1986)

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Assessment of thyroid function: complications after treatment with fenopropfen

The assessment of thyroid function has become increasingly complex as more drugs have been shown to have either in vivo or in vitro effects. Amiodarone, for example, has been shown to induce antithyroid antibodies¹ whereas fenclufenac interferes by displacing thyroxine from binding sites, resulting in an apparent decrease in the total thyroxine concentration.² We describe the previously unreported effects of fenopropfen on some biochemical variables used in the assessment of thyroid function.

Patients, methods, and results

During routine testing of thyroid function a 63 year old woman was found to have a raised free triiodothyronine concentration with normal thyroid stimulating hormone activity and slightly decreased free thyroxine concentration (free triiodothyronine concentration=30 pmol/l (19.5 pg/ml), normal range=2.9-8.6 pmol/l (1.9-5.6 pg/ml); thyroid stimulating hormone activity=4.8 mU/l, normal range 0.4-5.6 mU/l; free thyroxine concentration=8.8 pmol/l (6.9 pg/ml), normal range 9.4-25 pmol/l (7.3-19.5 pg/ml)). As she was not clinically thyrotoxic drug interference was suspected. When treatment with fenopropfen was withdrawn her free triiodothyronine concentration fell to 5 pmol/l (3.3 pg/ml), free thyroxine concentration rose to 11.8 pmol/l (9.2 pg/ml), and thyroid stimulating hormone activity remained within normal limits.

Range of thyroid stimulating hormone activity and free triiodothyronine and free thyroxine concentrations in five healthy volunteers after taking fenopropfen

Time after ingestion of fenopropfen (minutes)	Thyroid stimulating hormone* (mU/l)	Free triiodothyronine† (pmol/l)	Free thyroxine‡ (pmol/l)
0	1.0-1.2	6.8-8.5	14.2-18.0
90	0.8-1.0	15.4-19.8	12.8-16.7
180	0.8-1.0	13.2-14.4	12.1-17.3
300	0.8-1.1	10.4-13.0	12.0-17.3
420	0.7-1.2	7.6-11.2	11.2-15.4
Methodology	Sensitive thyroid stimulating hormone assay (NETRIA)	Amerlex M (Amersham)	Amerlex M (Amersham)

*Normal range for men=0.4-3.7 mU/l, for women=0.4-4.9 mU/l, and for postmenopausal women=0.4-5.7 mU/l.

†Normal range=2.9-8.6 pmol/l.

‡Normal range=9.4-25 pmol/l.

Conversion: SI to traditional units—Free triiodothyronine: 1 pmol/l≈1.5 pg/ml. Free thyroxine: 1 pmol/l≈1.3 pg/ml.

To assess the effect that fenopropfen may have on the measured variables of thyroid function 300 mg of fenopropfen (Dista Products) was taken by five healthy volunteers working in the laboratory, who were biochemically euthyroid and not receiving any other treatment. Blood samples were taken before they ingested fenopropfen and 90, 180, 300, and 420 minutes afterwards. After the ingestion of fenopropfen all specimens showed a large increase in the free triiodothyronine concentrations, reaching a maximum, which was roughly twice the upper limit of normal, at 90 minutes and remaining raised for over seven hours (table). The thyroid stimulating hormone activity remained normal whereas the free thyroxine concentration decreased slightly by roughly 7% at 90 minutes and remained so for seven hours.

Comment

As the peak absorption of fenopropfen occurs between 60 and 120 minutes (Dista Products, personal communication) and the free thyroxine concentrations did not show a concomitant rise our results suggest a cross reaction or some interference with the free triiodothyronine assay.

Neither the manufacturer nor the Data Bank at Surrey University have received any reports indicating the possible interference of fenopropfen with thyroid function or the assay of thyroid hormones. We therefore suggest that free triiodothyronine concentrations measured in patients taking fenopropfen should be interpreted with caution and that other analytical methods should be checked for comparable interference. We have extended these studies to other phenylpropionic derivatives of the arylalkanoic acids and have found that flurbiprofen interferes in the same way as fenopropfen but ibuprofen (as Nurofen) does not interfere.

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(Accepted 11 March 1986)

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Lyme disease in a Hampshire child—medical curiosity or beginning of an epidemic?

In 1975 in the town of Old Lyme, Connecticut, a group of children was investigated for recurrent attacks of arthritis, mainly affecting larger joints.¹ Over a quarter of the affected children had had an antecedent tick bite that developed into an expanding erythematous lesion typical of erythema chronica migrans. Follow up studies of "Lyme disease" showed it to be a complex multisystem disorder, the manifestations of which include erythema chronica migrans; flitting arthralgia; arthritis (mainly affecting large joints and possibly erosive); varying degrees of atrioventricular block, myocarditis, pericarditis; meningitis, encephalitis, cranial neuropathy (commonly VII nerve palsy), peripheral radiculoneuropathy; and lethargy, fatigue, non-productive cough, and muscular aches.

The causal agent has been identified as the spirochaete *Borrelia burgdorferi*, which is sensitive to penicillin and tetracycline. The vector is the ixodid species of tick, and the reservoir is usually a deer. Since Lyme disease was first recognised the number of reported cases has reached epidemic proportions in many American states and isolated reports have emerged from Europe and Australia.^{2,4} In the United Kingdom a 15 year old boy was reported to have erythema chronica migrans but no other manifestations of Lyme disease.⁵ We report on a 9 year old boy with classic features and serological evidence of Lyme disease, probably acquired in Hampshire.

Case report

A previously healthy 9 year old boy was admitted to hospital in August 1985 with an eight day history of fatigue, headache, neck stiffness, and photophobia. Three weeks earlier he had been bitten by a tick on his back during a visit to a local country park. At the site of the bite he developed an expanding erythematous lesion, which spread to 30 cm in diameter. This rash subsided over the next five days. He had no other symptoms.