Key messages

- Every newborn baby in Britain is subjected to several painful procedures
- Little is done to minimise the discomfort of these procedures
- Placing 2 ml of a 25% or 50% sucrose solution on the tongue before heel prick significantly reduces crying time
- There is a dose-response effect in the reduction of crying with increasing concentrations of sucrose
- Sucrose on the tongue may be a useful and safe form of analgesia in newborn infants

lifted its paw off a hotplate.[6] This effect was completely reversed by naltrexone. Blass and Hoffmeyer subsequently showed that 2 ml of 12% intraoral sucrose significantly reduced the duration of cry in newborn babies subjected to heel prick or circumcision.[7] Our group repeated that study with 7·5% sucrose and found no difference in the duration of crying.[8] However, we remained intrigued by the reports of Blass *et al* and undertook this study with different sucrose concentrations. We conclude that in our first study we used a sucrose solution too weak to induce a measurable analgesic effect.

Non-sucrose sweet substances such as saccharin also seem to increase pain latency in animals.[9] Other substances such as milk and in particular milk fat seem to have a similar effect through the endogenous opiate pathways.[10] We do not know whether simply cuddling an infant after heel prick is as effective in reducing crying as 50% sucrose. We are undertaking further clinical studies to evaluate the effect of sucrose and other substances in pain prevention in immature babies and older children.

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Occurrence of different cancers in patients with Parkinson's disease

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Parkinson's disease is a chronic, progressive neurological disorder with well defined clinical and pathological features. Smokers are less likely to develop Parkinson's disease.[1] The disease is associated with a reduced risk of cancer overall,[2] but the risk of malignant melanoma may be increased.[3] The objective of this study was to assess the occurrence of cancer in a large cohort of patients with Parkinson's disease.

Patients, methods, and results

The study was based on three computerised registers in Denmark. From the Danish hospital discharge register we extracted all records of admissions of patients with a primary diagnosis of Parkinson's disease during 1977-89 and identified a cohort of 7046 people with the disease (3470 men and 3576 women). Information on cancer incidence and death among cohort members from their first recorded admission for Parkinson's disease till the end of 1990 was obtained from the Danish cancer registry and from the Danish register of deaths. The expected numbers of cases of cancer were calculated from the person years at risk among cohort members and the incidences of cancer in the Danish population, with due account being taken of age and calendar period. Relative risks were calculated as the ratios of the observed to the expected numbers of cases of cancer and are presented with their 95% confidence intervals. The average duration of follow up was 4·6 years.

The overall incidence of cancer was lower than expected (table; relative risk 0·88). Relative risks were significantly reduced for lung cancer (0·29) and bladder cancer (0·42). Significantly increased relative risks were seen for skin melanoma (1·96) and for malignancies of unknown origin (1·76). Brain tumours occurred more frequently than expected (relative risk 1·61). The excess was, however, confined to the first three years after Parkinson's disease had been diag-

Relative risks of cancer in 7046 people with a primary diagnosis of Parkinson's disease in Denmark, 1977-89

Cancer	Observed No	Expected No	Relative risk (95% confidence interval)
All cancers	554	629·42	0·88 (0·8 to 1·0)
Mouth and pharynx	6	10·94	0·55 (0·2 to 1·2)
Oesophagus	7	5·76	1·22 (0·5 to 2·5)
Stomach	24	26·35	0·91 (0·6 to 1·4)
Colon	59	61·78	0·96 (0·7 to 1·2)
Rectum	32	32·76	0·98 (0·7 to 1·4)
Liver:			
Primary	6	6·80	0·88 (0·3 to 1·9)
Unspecified	5	5·60	0·89 (0·3 to 2·1)
Gall bladder	5	7·84	0·64 (0·2 to 1·5)
Pancreas	19	22·02	0·86 (0·5 to 1·3)
Lung	23	80·32	0·29 (0·2 to 0·4)*
Breast	60	49·88	1·20 (0·9 to 1·5)
Cervix uteri	6	6·96	0·86 (0·3 to 1·9)
Corpus uteri	11	12·40	0·89 (0·4 to 1·6)
Ovary	9	11·63	0·77 (0·4 to 1·5)
Prostate	40	50·68	0·79 (0·6 to 1·1)
Kidney	13	17·65	0·74 (0·4 to 1·3)
Urinary bladder	17	40·95	0·42 (0·2 to 0·7)*
Melanoma of skin	16	8·17	1·96 (1·1 to 3·2)*
Other skin cancer	104	83·92	1·24 (1·0 to 1·5)
Brain	15	9·33	1·61 (0·9 to 2·7)
Non-Hodgkin's lymphoma	9	11·91	0·76 (0·3 to 1·4)
Multiple myeloma	4	7·12	0·56 (0·2 to 1·4)
Leukaemia	13	15·82	0·82 (0·4 to 1·4)
Other specified sites	19	24·68	0·77 (0·5 to 1·2)
Metastases and unspecified	32	18·15	1·76 (1·2 to 2·5)*
Cancers associated with tobacco smoking†	91	184·60	0·49 (0·4 to 0·6)*
All other specified cancers	431	426·67	1·01 (0·9 to 1·1)

*95% Confidence interval excludes 1·0.
†Includes cancers of mouth and pharynx, oesophagus, pancreas, lung, cervix, kidney, and bladder.

nosed (11 cases; relative risk 2·42 (95% confidence interval 1·2 to 4·3)). The combined relative risk of cancers that are known to be associated with tobacco smoking was reduced (0·49), but the combined relative risk of cancers of specified sites other than those associated with smoking was close to that expected (1·01).

Comment

We found a low incidence of cancers associated with tobacco smoking, mainly lung and bladder cancer, among patients with Parkinson's disease. In addition, smokers are less likely to develop Parkinson's disease.[1] The most simple explanation of these findings is that tobacco smoking in some way exerts a protective effect against the development of Parkinson's disease, possibly through the effect of nicotine on dopamine concentrations in the brain,[5] and that patients with Parkinson's disease therefore tend to have smoked less during their lives than the population at large.

The close temporal association between diagnosis of Parkinson's disease and incidence of brain tumours suggests that brain tumours may on rare occasions be erroneously diagnosed as Parkinson's disease. We found an excess of six cases of brain tumours among 7046 patients with Parkinson's disease. This implies that no more than one in 1000 diagnoses of Parkinson's disease is an unrecognised brain tumour.

The increased incidence of malignant melanoma lends support to the idea that treatment with levodopa may increase the incidence of malignant melanoma.[3] Malignant melanoma cells possess a unique biochemical pathway for the conversion of levodopa to melamine, and they selectively incorporate levodopa.[4] Levodopa treatment may therefore accelerate the growth of a preclinical melanoma. We emphasise, however, that the observed effect is rather weak: around one excess case per 3500 patients with Parkinson's disease per year.

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Effect of physical activity on femoral bone density in men

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Although most patients with osteoporosis are women, up to one third of hip fractures occur in men. There is little information about which factors influence bone density in men.[1] Vigorous activity may lead to bone gain, while immobilisation causes bone loss. A sedentary lifestyle could, therefore, increase the risk of fractures.[2] We therefore examined the relation between physical activity and bone density in normal men.

Subjects, methods, and results

One hundred and thirty seven healthy white men, comprising husbands of women attending our osteoporosis clinic, laboratory staff, and hospital workers who were enrolled in a normal bone study, listed their regular physical and sporting activities. Subjects taking drugs or with diseases likely to affect calcium metabolism were excluded. Forty eight were smokers (mean 15 cigarettes/day), and 120 drank alcohol (mean 8·6 g of alcohol/day). The time per week spent on each activity was multiplied by the energy expenditure for that activity and expressed in METs per week (a MET is an arbitrary unit of metabolic activity equivalent to average sitting oxygen consumption); 56 METs per week were subtracted for sleeping time.[3]

Bone density was measured in the forearm by single photon absorptiometry (Molsgaard Bone Mineral Analyser) and in the spine (L2-L4), femoral neck, Ward's triangle, and trochanter by dual energy x ray absorptiometry (Lunar DPX-L). Results were analysed by Student's t test and linear regression; age correction was done by multiple linear regression with age expressed as a quadratic function. Since bone loss accelerates in men over 50,[1] measurements were evaluated separately in men aged 50 and over and in those aged under 50. A P value $<0·05$ was considered significant.

The subjects' mean age was 47 (range 20-83), weight 77 kg (range 60-98), height 177 cm (range 157-200), and body mass index 24·7 kg/m^2 (range 18·8-32·1). Forearm bone density was lower in those aged 50 and over than in those aged under 50 (472 (SD 77·6) *v* 522 (56·5) 95% confidence interval for difference: 25·6 to 74·4; $P<0·001$), but energy expenditure was similar in the two groups (129 (14·7) METs per week in the former and 131 (17·1) in the latter), equivalent to about 2·5 hours' jogging or 5·5 hours' walking. In the whole set activity was related to age-corrected bone density in the femoral neck ($r=0·26$, $P<0·01$) but not in the forearm or spine ($r=-0·056$ and 0·140 respectively). Activity and bone density were not related in men aged 50 and over. In those aged under 50 they were significantly related in the spine, femoral neck, Ward's triangle, and trochanter. These relations were unaffected by adjustment for age (table). Femoral neck bone densities in all subjects who jogged (22), walked regularly (53), or were sedentary (21) were 1·098 (0·121), 0·984 (0·152), and 0·962 (0·120) g/cm^2 respectively; the difference between the joggers and sedentary men was significant (0·136; 95% confidence interval: 0·097 to 0·225; $P<0·01$).

Partial coefficients of correlation (age corrected) of bone density variables and activity score

	Age <50 (n=71)		Age ≥50 (n=66)	
Site	r	P value	r	P value
Forearm	0·028	0·796	−0·148	0·304
Lumbar	0·245	0·039	0·031	0·929
Femoral neck	0·394	0·001	0·106	0·552
Ward's triangle	0·305	0·010	0·221	0·142
Trochanter	0·257	0·031	0·126	0·378

Comment

The major new finding in this study is of a continuous positive relation between physical activity and bone density in normal white men. This relation may reflect selection bias, inherent in a cross sectional