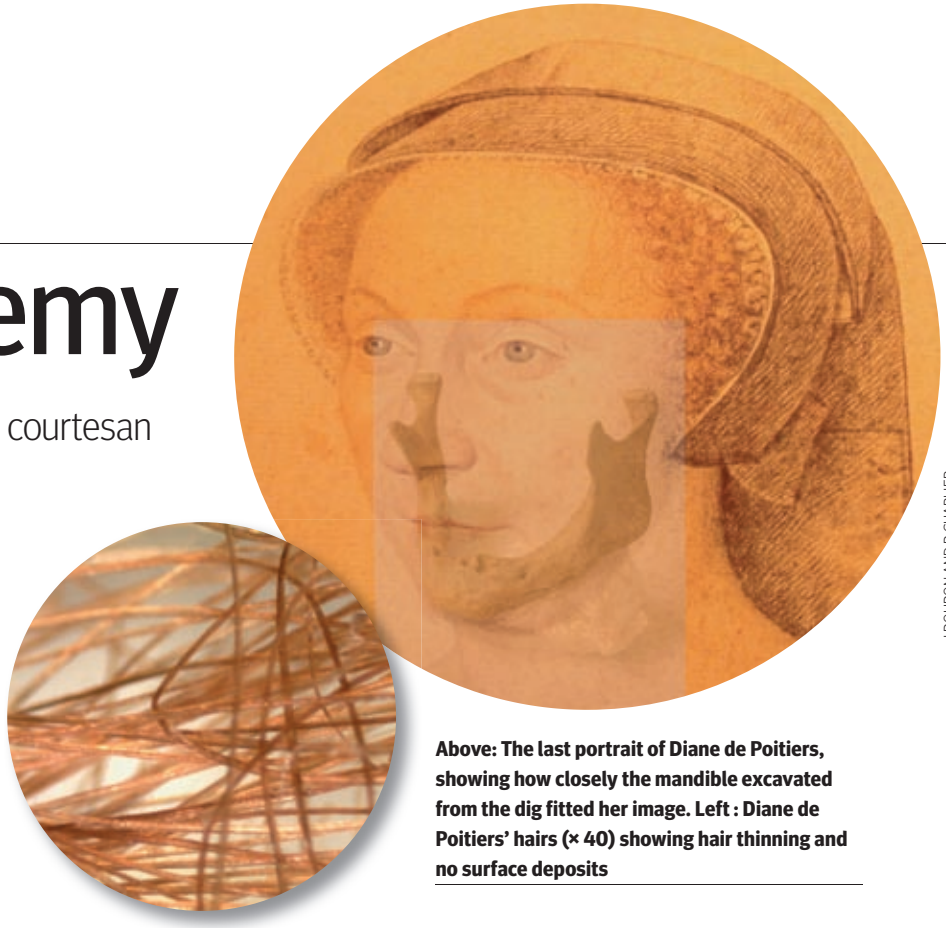
Fatal alchemy

Did gold kill a 16th century French courtesan and favourite of Henri II, ask

Philippe Charlier and colleagues



J POUPON AND P CHARLIER

Above: The last portrait of Diane de Poitiers, showing how closely the mandible excavated from the dig fitted her image. Left : Diane de Poitiers' hairs (× 40) showing hair thinning and no surface deposits

Gold's supposed powers of regeneration go back to antiquity. Pliny the Elder (AD 23-79)[1] describes the preparation of two remedies using gold and their therapeutic properties. In the 13th century, alchemists like Michael Scot, Roger Bacon, and Arnaud de Villeneuve wrote about "Aurum potabile"—drinkable gold—and how to obtain it.

Drinkable gold

Aurum potabile included many gold preparations, from almost pure water to real gold solutions prepared using nitrohydrochloric acid. Some types of drinkable gold were made by distilling alcohol solutions with sulphuric acid. During the process diethyl ether was made and this dissolved gold chloride, which formed a yellow coloured supernatant phase above a colourless aqueous phase.[2] This was considered by some to be true drinkable gold.[3]

Drinkable gold was well known in the 16th century French Court, and Alexandre de la Tourette dedicated his book on the subject to King Henri III.[4] In the 17th century, many doctors and chemists like Jean Beguin and Christophe Glaser published gold recipes, including drinkable gold, in their chemistry manuals.[5 6]

Chronic poisoning in the 16th century

In 2008, during an archaeological dig in the cemetery of Anet in France, skeletons were excavated near a monument to Diane de Poitiers. She was a favourite of King Henri II despite being 20 years his senior.[7] Diane was a particularly athletic woman, who swam, hunted, and rode horses every day. She died in 1566 when she was 66 years old, but the exact circumstances of her death are unknown. It is thought that the mass grave that was found during the excavations was where Diane's mummified remains were thrown after revolutionists opened her tomb in 1795.[8]

Identifying the remains of Diane de Poitiers

Diane de Poitiers' remains were identified from the other desecrated skeletons by some physical particularities: the preserved fragments of the pelvis were those of a woman; severe arthritic lesions and important *ante mortem* tooth loss[7] showed that she was old; and consolidated tibia and fibula fractures corresponded to those Diane sustained in a riding accident in 1565, and for which Ambroise Paré treated her. The skull showed a perfectly concordant superposition of the mandible and left jawbone when compared with the last portrait of Diane by François Clouet.[9]

When fragments of bone still covered by deposits of putrefaction fluid[10] were carbon dated,[11] they gave aberrant results (two sigma calibrated results: AD 900 to 920 and AD 950 to 1040). These results indicated that the remains had been aged by the bitumen during embalming. This was confirmed by a molecular analysis of putrefaction fluid deposits by gas chromatography mass spectrometry after an extraction with cyclohexane. The analysis showed the presence of linear alkanes and alkenes that were directly related to the fragmentation of the bitumen.

Analysing the hair

When the graves had been desecrated during the French revolution, some of Diane's hair had been preserved at the castle in Anet.[8] Analysis of this hair from the castle and the hair from the remains using inductively coupled plasma mass spectrometry showed a great concentration of gold in the putrefaction fluid deposits (111 ng/g), and demonstrated the homogeneity of the two sets of samples. Elemental analyses of this hair showed a gold concentration (about 10 000 ng/g) about 500 times the actual reference values (median 20 ng/g; range: 1 to 50 ng/g [12]). Hair thinning is a symptom of chronic gold intoxification and Diane's hair diameter was around 65µm (normal diameter 80-90µm) (see figure).[13 14] Diane is known to have undergone a long course of gold treatment hoping it was an elixir of youth. Brantôme in *Vies des Dames illustres, francaises et etrangers* wrote of her, "I saw her at seventy years of age beautiful of face, also fresh and also pleasant as she had been at thirty years of age...and especially she had a very large whiteness without any make-up. But it is said well that, every morning, she used some drinks made up of drinkable gold and other drugs which I do not know given by good doctors and subtle apothecaries."[15]

Evidence from chrysotherapy

When used to treat rheumatoid arthritis the half life of gold is 20 days,[16] which may lead to gold accumulating in tissues, including hair. Gottlieb and colleagues[17] found a concentration of 5000 ng/g in the hair of one patient treated with aurothioglucose.[17] In some patients receiving gold sodium thiomalate, levels in hair were more than 1500 ng/g.[18] Recently, we reported a case

Watch a reconstruction of Diane de Poitiers's life and the investigation of her death at bmj.com/video

of an acute intoxication after less than a month of treatment with sodium aurothiopropanolsulphonate.[19] When the treatment was stopped, gold levels were 34 278 ng/g dry tissue in liver and 158 ng/g in the hair. We might expect chronic intoxication in Diane's case, which would explain the high levels of gold in the hair compared with gold residues in other tissues.

Other explanations

Two other hypotheses may explain the relatively low levels of gold measured in the tissue residues. Firstly, she may have stopped taking gold in the few days or weeks before death, and secondly her skeleton had been buried for two centuries.

Mercury was used by alchemists to purify gold and prepare some gold remedies, and analysis of Diane's remains showed concentrations of mercury in the hair at twice the upper limits of normal. External contamination of the remains of the body by gold jewellery does not seem plausible. Not being a queen, Diane de Poitiers would not have worn a crown, and it is hard to see how other jewellery could have contaminated the hair and tissues. Indeed, after her death, Diane was embalmed so her body dried without putrefying. When the coffin was opened in 1795 the body appeared intact.[8 20] Gold is not included in the list of substances used during the embalming process.[21]

Under microscopic examination, the hairs were clean and no superficial deposits were seen. Any deposits, especially containing lead, may have occurred as a result of the reaction between the body fluids and the lead of the sarcophagus. Such lead deposits are well documented in the case of Agnès Sorel.[22] After the desecration of her grave, only her body, without any clothes or jewellery, was buried in the cemetery[8] so no contamination could have occurred since then. Moreover, hair we analysed was taken just before the burial and would have not been in contact with soil or pollutant.

Forever young?

We have identified the remains of Diane de Poitiers to a high degree of confidence. We believe that she drank gold, which is compatible with Brantôme's report.[15] The high concentrations of gold in her hair indicate that she could have died of chronic intoxication with gold.

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Right: The lock of Diane's hair preserved at Anet Castle. Below: A still from the video accompanying this article

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Competing interests: None declared.
Provenance and peer review: Not commissioned; externally peer reviewed.

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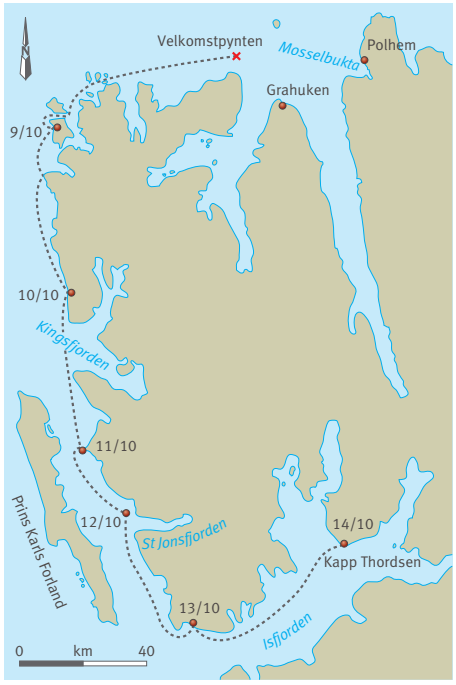
Cite this as: *BMJ* 2009;339:b5311

Lead poisoning at the Swedish House

Was scurvy really the cause of death of 17 stranded sealers in winter 1872? **Ulf Aasebø** and **Kjell G Kjær** consider a different diagnosis

In September 1872 six sealing vessels from Tromsø were north of Spitsbergen at the Grey Hook (Grahuken). A northern gale closed the bay with ice, trapping the six ships and 59 sealers with the prospect of "overwintering" with few provisions. At the same time, Adolf Nordenskiöld, the Swedish explorer,[1] was setting up his winter quarters, "Polhem," at Mossell Bay (Mosselbukta) (figure). His ships were also trapped, leaving him with a critically low food reserve.

Seven of the stranded sealers crossed the ice, some 50 km, to ask Nordenskiöld for help. He was able to help some but advised the others to spend the winter in the Swedish house at Kapp Thordsen in Isfjorden. The house had been set up in the previous summer by a mining company that aborted their project because of poor harbour conditions and was well stocked with tinned food.[2,3] Axel Envall, Nordenskiöld's physician, advised the sealers on how to avoid scurvy.[4] The 17 men then rowed some 350 km and reached the house in seven days, on 14 October. Meanwhile, the ice broke up, and the remaining trapped sealers escaped in two ships. Two chose to stay with the remaining ships and died from scurvy in April 1873.[4]



Map of the north western part of Spitsbergen, showing the rowing route

The men at Kapp Thordsen hunted polar bear and reindeer until the arctic night descended and then relied on the stored food. Through a diary they recorded all food consumed, weather conditions, sickness, and death but gave no details regarding symptoms of disease.[5]

On 2 December, two men were reported as sick; by Christmas, they were all sick. On 19 January, two men died after "hard sickness." Two more died in February, five more in March,[5] and the last one probably just before they were found on 16 June by members of a hunting expedition from the mainland who wanted to visit them.[6,7] The first two men who died were buried. The next five men to die were left outside under a tarpaulin,[6,7] six were found in an adjoining room, and the remaining in the living quarters. The rescue team buried them in a common grave.[6,7] Their deaths were attributed to scurvy due to laziness and bad leadership in allowing scurvy to occur despite an ample food supply and the means to prevent it, and the men were left little honour.[7]

In 1845, Admiral John Franklin set out with 129 men and two ships to find the northwest passage.[8] They took large amounts of tinned food. The expedition was equipped for four years but was never heard from again. Final evidence of the disaster came in 1859, when a written account of their ordeal was found in a crumble of stones.[9] The ships had been wrecked by ice, and the men eventually started to walk south, dying as they walked. In the 1980s a team from Alberta University exhumed three sailors buried in permafrost at the expedition's winter quarters and found high concentrations of lead in hair samples.[8] Bones from crew members, found scattered along the track, showed high concentrations of lead, while Inuit bones did not.[10] The conclusion was that the sailors had lead poisoning, possibly leading to their death.[10]

Open graves

Having pieced together the events in the Swedish house in 1872-3, in light of the Franklin disaster, we saw the similarities. In 2007 we discovered a previously unregistered two man grave, 540 metres from the house. Through a damaged corner, cervical vertebrae were visible and accessible for lead analysis. Several hundred empty tin cans were scattered behind the house. The inside solder was evident, and many cans had "icicles" of solder on the sides. The discovery of the tin cans with lead/tin solder supported our hypothesis that lead poisoning might have contributed to the deaths.

We applied for permission to open the two graves to take specimens for lead analysis and inspection of bones for signs of scurvy. In August 2008, we revisited the site and sampled a 1×1 cm piece of solder. We dug a shaft 50×50 cm in the upper part of the common grave and encountered wooden planks 60 cm down. Underneath we met an ice block. The bodies were in permafrost, and further exploration was abandoned.

Let us bring the story of the death of the sealers at the Swedish House to life. Listen at bmj.com/audio

Watch Ulf Aasebø and his team as they travel through the frozen tundra of Svalbard at bmj.com/video

Through the opening in the two man grave, we extracted one humerus, one clavicle, two cervical vertebrae, and a scapula; all from one skeleton. All bones had smooth surfaces with no signs of subperiosteal bleeding (scaling). We took bone and soil samples, which were analysed in Oslo.

We found no macroscopic evidence of scurvy. All bone surfaces were smooth with no scaling or enhanced ridges. The samples contained 65 µg/g of lead in dry bone, equivalent to a concentration of 102.05 µg/g.[11] The lead content of the solder was 40%. Culture for *Clostridium botulinum* was unsuccessful because of overgrowth of other bacteria.

Lead poisoning

Though the deaths of the sealers in Kapp Thordsen have been attributed to scurvy, our research indicates that lead poisoning was a more likely cause. Scurvy, caused by lack of vitamin C, was a plague of seafarers until its prevention was discovered in 1753, and intake of lime juice was implemented in the British navy in 1795.[12] The disease causes disintegration of connective tissue and can be visualised macroscopically in skeletons of people who have died from scurvy. The subperiosteal bleeding leads to diagnostic scaling of the bone surfaces and enhanced ridges of the muscle attachments.[13] The prevention of scurvy had been documented as early as 1816 in arctic Norway, where sealers and fishermen used "scurvy grass" (*Cochlearia officinalis*).[14]

The sealers at Kapp Thordsen had received instructions on how to avoid scurvy, so we think it an unlikely cause of their deaths, particularly we found no signs of previous subperiosteal bleeding. As it has been postulated that botulism might have caused the deaths of those in the Franklin expedition[15] we tested for this but did not succeed in culturing the bacteria.

Lead is a poisonous heavy metal that has acute and chronic effects on the body. According to the inventory list, the men at Kapp Thordsen consumed large amounts of tinned food. They probably reheated the tins on the stove, exposing the lead alloy to acid and dissolving the lead in the food.[16]

Lead poisoning typically leads to stomach pains and cramps, anorexia, weight loss, a blue line of the gingival margin, neuropathy particularly affecting the extensor muscles, joint pain, and a curious condition called "debility"—inertia and complete loss of incentive and interest.[17]

The content of lead in our samples was 102.05 µg/g. Samples of soil from outside the burial grounds showed 16 µg/g of lead. The lead content in the bones from the Franklin expedition ranged from 97.6 to 188.6 µg/g, accumulated over about three years.[10] In our case, the lead accumulated over a few weeks. The first men were sick by 2 December. As the accumulation of lead in bone occurs slowly, at a rate of 1 mg a year if the blood concentration is 1.8 µmol/l in cases of chronic lead poisoning,[18] our victim must have had high blood concentrations of lead. To our knowledge, there are no cases in the literature examining simultaneous blood and bone concentrations of lead. The blood concentrations must therefore be extrapolated.

In the Franklin expedition, if half the bone lead content had been accumulated during the expedition, the cumulative blood lead concentration over this time must have been 29.0-75.5 µmol/l, giving a mean concentration of 29.0-24.2 µmol/l.[10] This is three to 10 times higher the recommended upper concentrations of lead in the blood to prevent neurological damage.[18] When our "patient" had accumulated 102.6 µg/g in 13-14 weeks, he must have been suffering from acute as well as subacute lead poisoning.

The evidence gives strong indications that our "patient" died of lead poisoning. The other man in the grave also probably suffered the same fate. Possibly, lead poisoning, because of its "debilitating" effect and anorexia, worked with other factors, contributing to their death.

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We thank Tora Hultgreen of Svalbard Museum, Einar Johansen of the Polar Institute, Yngvar Thomassen of the National Institute of Environmental Health, and the National Veterinary Institute for their contributions towards this expedition. A more extensive version of this paper is in press with *Polar Record.*

Contributors: See bmj.com.

Competing interests: None declared.

Ethical approval: The study was approved by the National Ethics Committee for Medical Research and the Governor of Cultural Heritage.

Data sharing: No additional data available.

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Cite this as: *BMJ* 2009;339:b5038

Rusting tin cans behind the house

Smooth surfaced bones argue against scurvy

Stigma and prejudice in Tintin

Juan Medrano, **Pablo Malo**, **José J Uriarte**, and **Ana-Pía López** look for evidence of prejudice against mental illness

The Adventures of Tintin *Cigars of the Pharaoh*

In 2007, a New York library found *Tintin in the Congo* racially offensive and moved it to a secure back room. The UK Commission for Racial Equality asked for it to be removed from sale because of "hideous racial prejudice," and a Congolese student in Belgium started a complaint against the book. For Tintin's creator Hergé, the pen name for Belgian Georges Prosper Rémi (1907-83), *Congo* was a naive work, influenced by stereotypes and misconceptions common in Europe when it was first published (1930).[1]

Despite the older Hergé's efforts to offer a progressive view of himself,[1 2] the Tintin books have been accused of several forms of prejudice. The depiction of Africans in *Congo* and in *The Red Sea Sharks* suggested racism. *The Shooting Star*, published while the holocaust was taking place, was accused of anti-Semitism because a first version featured greedy Jews and a villain has an unintended Jewish surname. Misogyny was suspected because rotund Bianca Castafiore is the only remarkable feminine character. And animal rights activists deplore wildlife carnage in *Congo*.

In this article, we analyse appearances of, or allusions to, mental disease in the Tintin series to see how mentally ill people are portrayed.

Review method

We reviewed 22 books in the Spanish Tintin collection, published by Editorial Juventud (17th ed, 2005). *The Lake of the Sharks*, which was based on an animated film by Michel Regnier, was excluded. The early Spanish versions from *Congo* through to *The Crab with the Golden Claws*, published by Casterman, were also reviewed. Spanish translations were compared with those in French, English, or Basque where available. We classified our findings into four categories (table):

- Alcohol intoxication or behavioral disorders related to alcohol
- Mental disorders not caused by alcohol or head trauma
- Psychiatric disorders secondary to head trauma
- Psychiatrists and treatment.

What we found

Eighteen books had verbal references to behaviours, intentions, or ways of thinking related to mental illness. In all cases, behaviours were unwise or overtly impulsive, reflecting loss of control. In *The Red Sea Sharks* Haddock, whose rich, idiosyncratic repertoire of insults (ectoplasm, bashi-bazouk among others) was compiled in a dictionary,[3] yells "paranoid" and "schizophrenic" to a slave dealer. The English edition published by Mammoth substituted "psychopath" for schizophrenic.

Ten of the 22 books featured intoxication or behavioural disturbances related to alcohol (category one). A dangerous alcoholic in *The Crab with the Golden Claws*, Haddock later becomes a self controlled drinker, except in *Explorers on the Moon*. In *Tintin and the Picaros* alcohol is ubiquitous, with Alcazar's troops dangerously intoxicated on whisky airdropped by General Tapioca, and Haddock surreptitiously treated by Calculus with an alcohol aversive that will eventually turn the Picaros into teetotallers.

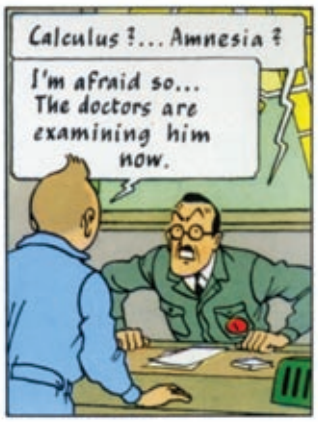
In *The Cigars of the Pharaoh*, the villains inject their enemies with rajaijah juice, which—especially in large doses—induces a psychotic disorder with childish, irrational, and dangerous features (category two). In *The Blue Lotus*, Didi, who has been injected with rajaijah juice, displays catatonic symptoms before attempting to behead Tintin. After being given fake venom, Tintin childishly pretends to be mad to fool Mitsuhirato. In *The Shooting Star*, Philippulus tries to plant a bomb before being taken to the hospital he had absconded from. In *The Seven Crystal Balls*, deaf and somewhat paranoid Calculus is kidnapped, and Haddock develops a reactive depression. Engineer Wolff's death in *Explorers of the Moon* is a paradigm of Durkheim's altruistic suicide.

With regard to category three, Calculus's amnesia in *Destination Moon* was described in a 1983 congress as, "one of the most beautiful observations of transient post-traumatic amnesia."[4] Other cases of mental disorder induced by head trauma include irrational behaviour and derailed, clinically incoherent, thought content.

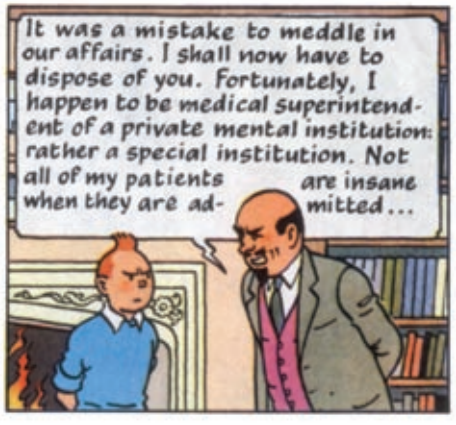
As for category four, *The Cigars of the Pharaoh*

Synopsis of psychiatric findings in Tintin

Category	Characters or feature	Depiction or intention
(1) Alcohol related disorders	Haddock, Tintin, Snowy, Pícaros, sheriff, San Theodorian militia, Bordurian policemen, drowned sailor	Childish, irrational, aggressive, funny
(2) Disorder not caused by alcohol or head trauma:		
Functional psychosis	Patients in asylum, Philippulus, Sophocles Sarcophagus, Zloty, Didi (Mr Wang's son)	Childish, irrational, aggressive, funny
Malingered psychosis	Tintin	Childish, irrational, funny
Depression, suicide	Haddock, Wolff	Dramatic
Paranoid reaction	Calculus	Funny
(3) Head trauma	Calculus, Haddock, Syldavian spy, O'Connors	Funny, childish, irrational, dramatic
(4) Psychiatrists and treatment	Nameless asylum director, Dr Müller, Dr Krollspell	Lacking empathy, repressive, evil, greedy
	Asylum, straitjacket, psychiatric assistants	Repressive, paternalistic



The Adventures of Tintin *Destination Moon*



The Adventures of Tintin *The Black Isle*

depicts an asylum with odd "non-dangerous" patients and a nameless psychiatrist who, misled by the villains, puts Tintin in seclusion and says goodbye to the true patients as they leave the place. Interestingly, for this 1934 psychiatrist the hero's complaints at his detention mean a lack of insight and, therefore, a proof of illness. Some frames later, the psychiatrist, wielding a truncheon while leading a pack of angry looking psychiatric assistants, chases after an escaping Tintin, who will finally be detained and put in a straitjacket. In *The Black Isle*, Dr Müller runs an asylum where his enemies are detained and literally driven mad. In *Flight 714*, truth serum inventor Dr Krollspell will only dessert the villain Rastapopoulos after learning that he plans to kill him. We could not agree on whether Professor Fan Shi-Ying in *The Blue Lotus* is a psychiatrist or a researcher. Were he a mental healthcare provider, this old silent Chinese man would be the only psychiatrist in the ranks of the goodies in Tintin.

Calculus's amnesia in *Destination Moon* was described in a 1983 congress as, "one of the most beautiful observations of transient post-traumatic amnesia."

Commentary

Although Tintin books have been analysed to look for a deep, dynamic, and implicit psychological significance,[5-7] to our knowledge this is the first attempt to explore psychiatric stigma. Although we reviewed Spanish translations only, a random review of books in three other languages found just one minor difference.

Even though the Tintin books depict mental disorders unfavourably, with stereotypes such as irrationality and dangerous behaviour commonly found, we cannot assume that Georges Rémi was unsympathetic towards mental illness. He had several depressive episodes himself and even consulted with Jung's pupil Dr Rickling during a period of personal turmoil. Some biographers suggest that he drank excessively,[8] and his mother was treated with electroconvulsive therapy for involutional depression.[4]

Psychiatrists are the only doctors with prominent roles in Tintin, so their unfavourable portrayal is important. Instead of sharing common stereotypes such as oddity with their patients—which could point to stigma by association—the psychiatrists lack empathy and are repressive, greedy, or plainly evil. Interestingly, such a negative view did not arise from Hergé's bitter disappointment at his mother's treatment, because all psychiatrists except for greedy Krollspell were created years before she became ill.

Given the worldwide appeal of Tintin, and the influence of children's media on negative views of mental illness,[9-11] these books may have passed on negative stereotypes to young readers. However, artistic work must be analysed as a whole. Stereotyping is commonplace in Tintin—the baddies are extremely evil, the goodies (except for Pablo in *The Broken Ear* and *Pícaros*) are almost perfect, and Scottish policemen in *The Black Isle* are prototypically British. Furthermore, the depiction of mental illness and mentally ill people in Tintin reflect the shared prototypical social views of the time. In the five decades between *Soviets* and *Pícaros*, mental illness was viewed negatively, with no awareness of the stigma faced by affected people. In the 1970s (in the last years of Hergé's career), Spain's criminal law still equated mentally ill people with dangerous animals—relatives of patients and owners of beasts were subject to the same penalties in case of abandonment. Twentieth century literature and cinema offer a plethora of examples of good artistic work that stigmatises mentally ill people. Hergé was no more disrespectful than other creators who made fun of mentally ill people. Modern comic series such as the Spaniard Francisco Ibáñez's *Mort and Phil* are far more stigmatising than Tintin. Finally, the psychiatric insult is still common in the political arena.

Although Hergé has been sternly criticised for racism, anti-Semitism, male chauvinism, and cruelty towards animals, nobody seems to have noticed his unfavourable depiction of mentally ill people. But instead of accusing Hergé of psychiatric prejudice, we would like to stress that the series merely reflects the stigma faced for decades by mentally ill people. The media, politicians, and society should carefully scrutinise words used in everyday language and recognise that some shared images or ideas are simply negative stereotypes.

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Competing interests: None declared.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Cite this as: *BMJ* 2009;339:b5308

Animated ophthalmology

Daniel Ezra and colleagues warn that eye problems in cartoon characters often go undiagnosed

Ophthalmology has had a long tradition of studying the differences in presentation and natural course of disease in national and ethnic groups. The globe and orbit vary considerably in different groups, and this can predispose to different diseases.[1] Large population based studies have been carried out in diverse groups such as Mongolian,[2] Latino,[3] and Inuit[4] patients as well as patients from different geographical locations from Scandinavia to Ouagadougou.[5 6] However, one group that remains overlooked is cartoon characters, whose health problems have been marginalised for decades.

Moorfields Eye Hospital is the largest specialised eye hospital in the world with over 250 000 patient episodes a year. The unique volume and mix of clinical material seen at our institution, coupled with the academic resources provided by partnership with the Institute of Ophthalmology at University College London, has allowed us present the first case series of eye disorders in cartoon characters.

The aim of this case series is to highlight the varied and serious ophthalmic diseases that afflict cartoon characters and to show that many of these blinding conditions are treatable. Informed consent was taken from each patient, and the study was conducted in accordance with the declarations of Helsinki and Narnia.

Case 1 Sleepy — Levator disinsertion

An achondroplasic white man in his late 50s presented to a primary care ophthalmology clinic. His presenting complaint was drooping eyelids, which had begun to interfere with his work. The ptosis was also affecting his confidence, and he was now being called Sleepy at work. He had a complex social history; he was of central European origin and had been doing heavy manual work and mining for many years. On direct questioning, he admitted snoring heavily at night with notable daytime hypersomnolence and was found to have an Epworth somnolence score of 20.[7] He had no symptoms related to bulbar palsy, and indeed sings in a miners' close harmony male choir.

On examination he had bilateral symmetrical ptosis and high upper lid skin crease measurements but normal levator function. Marked frontalis overaction was observed. The results of cranial nerve examination were normal, and no diplopia was detected. There was no limb weakness or muscle wasting, although syndactyly of second and third digits was noted on both hands.

Diagnoses of myasthenia gravis, dystrophia myotonica, chronic progressive external ophthalmoplegia, and senile levator disinsertion were considered. Myasthenia gravis was thought unlikely as he had symmetric ptosis and was orthophoric (no strabismus) in the primary position. He had no limb weakness or myotonia, which makes dystrophia myotonica unlikely (although there is some frontal balding). The powerful frontalis overaction excludes a serious facial myopathy, which is common in chronic progressive external ophthalmoplegia and universal in dystrophia myotonica. Levator disinsertion was diagnosed on clinical grounds.

The patient had bilateral anterior approach levator repairs. He was referred on for sleep studies and was found to have obstructive sleep apnoea. He now uses continuous positive airway pressure support and reports being much more alert during the day. He is being investigated for pulmonary silicosis, and an occupational injury claim to his mining company is ongoing.

Case 2 Homer Simpson — Orbital varices

Mr Simpson, a white man in his mid-40s, presented to the emergency department with a painful and sudden anterior luxation of his left globe after having been strangled by a Scottish school caretaker. He reported

THE SIMPSONS © CREATED BY MATT GROENING WITH JIM BROOKS & SAM SIMON/FOX BROADCASTING

no other preceding ophthalmic symptoms. He works as a nuclear safety inspector and is a father of three. On examination he was grossly overweight and systemically jaundiced. A full neurological examination showed no abnormality, but syndactyly of the second and third fingers was again noted. An ophthalmic examination found no signs of optic neuropathy with no errors on reading Ishihara plates and no relative afferent pupillary defect. Funduscopy showed no abnormal retinal vessels or retinal haemorrhage. He was treated with gentle manipulation to reduce the globe behind the orbital septum. The eye settled well with no corneal exposure or optic nerve compromise. Mr Simpson was later to perform a Valsalva manoeuvre while lowering his head below his knees. This elicited a proptosis of the globe. No bruit was noted on auscultation of the orbit.

A differential diagnosis of floppy eyelid syndrome[8] (common in obese men of this age) and thyroid eye disease was considered, but the history of proptosis while being garrotted and during a Valsalva manoeuvre was highly suggestive of orbital varices. The cause of the jaundice was unknown but had been present since birth with a strong family history.

Mr Simpson's occupational exposure to radiation was such that computed tomography was considered unwise. Magnetic resonance imaging of the orbits and brain confirmed the diagnosis of orbital varices. Haematological investigations confirmed an unconjugated hyperbilirubinaemia with no macrocytosis and no evidence of haemolysis or hepatitis.

Case 3 Mr Magoo — High myopia

Mr Magoo, a man in his 70s, was referred from the geriatricians for ophthalmic review. He had been admitted to hospital after a fall. His family said that he had been constantly bumping into things for many years with unexpected and sometimes amusing consequences. He refused to admit that he had any problem with his vision but was noted to be unable to read the top letter of the Snellen chart, even at a distance of 1 metre.

On assessment, he denied any subjective visual problems, but his visual acuity was recorded as hand movements only. He was noted to be peering through closed lids, a common technique used to increase acuity by people with large refractive error. An assessment by the local optometrist indicated a refractive error of about −20.0 dioptres in both eyes. He had no evidence of cataract, and glaucoma and age related macular degeneration (for which high myopia is a risk factor) were excluded by visual field testing, scanning laser ophthalmoscopy, optical coherence tomography, and fluorescein retinal angiography. High myopia was diagnosed and several treatment options were considered.

Mr Magoo discounted wearing spectacles because of the spherical aberration at high levels of refractive error. Rigid gas permeable contact lenses were not practical as his dexterity was limited by syndactyly of the second and third digits, making cleaning the lenses impossible.

He preferred a permanent solution, but laser treatment was not appropriate for such high myopia. Finally, he was encouraged to have his lenses replaced with prosthetic intraocular lenses.

One month after intraocular surgery his visual acuities were measured at 6/6 unaided in both eyes. He reported that his life had become much more uneventful since his vision had improved, and he was discharged from the clinic.

Case 4 Kenny — Pauciarticular juvenile chronic arthritis

Kenny McCormick, a 9 year old boy, was referred by his general practitioner. The doctor was concerned that he may have conjunctivitis but was unable to examine him as he refused to remove his hood). A full history was limited as his speech was incomprehensible and muffled by his hood. He had a difficult social background, coming from a poor household presided over by his violent, alcoholic, and unemployed parents.

An examination under anaesthesia was required. Under aseptic technique, the hood was carefully removed by releasing the medial and lateral check ligaments. A flap was then raised and reflected by carefully dissecting in the appropriate plane. Once the face was exposed, a refraction and funduscopy were performed. The ocular media were found to be hazy bilaterally and a portable slit-lamp examination found severe bilateral anterior uveitis. Photophobia caused by uveitis was thought to be the reason for wearing the hood.

Investigations included chest radiography, serum calcium, HLA-B27, syphillis serology, full blood count, erythrocyte sedimentation rate, and C reactive protein. A high erythrocyte sedimentation rate, high antinuclear antibody titre, and low serum albumin concentration were noted. Tuberculosis, sarcoidosis, and HLA-B27 related uveitis were excluded and pauciarticular juvenile chronic arthritis was diagnosed.

The joint manifestations were mild, with significant uveitis and photophobia being the predominant symptoms. He was started on a course of intensive topical steroids and regular mydriatics as well as oral non-steroidal anti-inflammatory drugs. He improved dramatically, and after several weeks he remained asymptomatic and controlled with methotrexate with no further photophobia. Sadly, in his first venture out of the house without his hood up he was killed after being dragged on to train tracks by his go-cart and trampled by a herd of cattle. His body was eaten by rats.

SOUTH PARK © CREATED BY TREY PARKER & MATT STONE/COMEDY CENTRAL/MTV

Discussion

These cases show the wide spectrum of ophthalmic and orbital disease in cartoon characters, and the life changing effects of appropriate management. Equality and access to health care have been made a central plank of the NHS next stage review,[9] but cartoon characters clearly are at the thin end of the wedge. Tragically, many of the conditions we have encountered are treatable causes of blindness that are often missed. We hope that this case series will alert the medical profession to be more aware of this vulnerable and overlooked group.

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Contributorship: DGE and GP conceived this study. The article was drafted by DGE and all authors appraised and reviewed the final manuscript. GP told DGE that he watches too much television, but AC and GR were too busy operating to comment. GP is the guarantor.

Competing interests: None declared.
Provenance and peer review: Not commissioned; externally peer reviewed.

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Cite this as: *BMJ* 2009;339:b4948

Lying obliquely—a clinical sign of cognitive impairment: cross sectional observational study

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Cite this as: *BMJ* 2009;339:b5273
doi: 10.1136/bmj.b5273

Abstract

Objective To determine if failure to spontaneously orient the body along the longitudinal axis of a hospital bed when asked to lie down is associated with cognitive impairment in older patients.

Design Cross sectional observational study.

Setting Neurology department of a university hospital in Germany.

Participants Convenience sample of 110 older)· 60 years) inpatients with neurological conditions and 23 staff neurologists.

Main outcome measures The main outcome measure was the association between the angle of the body axis and the results of three cognitive screening tests (mini-mental state examination, DemTect, and clock drawing test). Staff doctors were shown photographs of a model taken at a natural viewing angle to determine their subjective perspective of what constitutes "oblique."

Results 110 neurological inpatients (mean age 70.9 (SD 6.8) years) were included after exclusions. Evidence of cognitive impairment was found in 34, with scores indicating dementia in eight, according to the mini-mental state examination, and in 11 according to the DemTect. Across all patients, the mean angular deviation of the body axis from the longitudinal axis of the bed (range 0-23°) correlated linearly with the mini-mental state examination ($r=-0.480$), DemTect ($r=-0.527$), and the clock drawing test ($r=-0.552$) scores ($P<0.001$ for all), even after removing age as a covariate. Overall, 90% of staff doctors considered a minimal body angle of 7° to be oblique. Angular deviation of at least 7° predicted cognitive impairment according to the three different tests, with specificities between 89% and 96% and sensitivities between 27% and 50%.

Conclusion Clinicians might suspect cognitive impairment in mobile older inpatients with neurological disorders who spontaneously position themselves obliquely when asked to lie on a bed.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Clinical signs detected during physical examination may provide important clues to cognitive abilities that are not confounded by the patient's reaction to an explicit testing situation

The ability to predict cognitive impairment from positioning behaviour has not been studied in clinical settings

WHAT THIS STUDY ADDS

Failure to orient the body axis in bed is an easily recognisable clinical sign

This sign in older mobile neurological inpatients was associated with poor performance on several cognitive screening tests

This sign may be useful to alert clinicians to the possibility of cognitive impairment and to prompt further investigations

This article is an abridged version of a paper that was published on bmj.com. Cite this article as: *BMJ* 2009;339:b5273

Introduction

More than 30% of older (≥60 years) inpatients in general medical units have major cognitive impairment[1-3] but this often remains unrecognised.[1 2] We determined whether failure to spontaneously orient the body axis to the longitudinal axis of the bed when lying down is associated with cognitive impairment.

Methods

From March 2007 to April 2008 and from June to July 2009 we obtained convenience samples of inpatients aged 60 or more and being treated for neurological disorders at the University of Wuerzburg.

To determine the orientation of the body axis we asked the patients to lie down from a sitting position on the side of a bed and took a digital photograph using a camera mounted above the patient (fig 1). The procedure was repeated from the other side of the bed for 88 patients.

The patients were not specifically asked to remove their footwear. We defined the body axis angle as the angle between the patient's body axis and the longitudinal axis of the bed (see bmj.com). The angle was assessed by an examiner blinded to the results of the cognitive tests.

Cognitive testing

Cognitive testing was carried out on the same day as the assessment of body axis using the mini-mental state examination,[4] the DemTect,[5] and the clock drawing test.[6 7] Among them, the mini-mental state examination is the best evaluated test for cognitive screening.[8] The DemTect has high sensitivity for detecting and grading mild cognitive impairment,[5 9] independent of age and education.[5] The clock drawing test is a simple tool, can be applied quickly, and is sensitive for visuospatial deficits and executive functions.[10-12] The tests were presented in random sequence during one session. We operationally defined dementia as a mini-mental state examination score of less than 24[4] or a DemTect score of less than 9.[5] Mild cognitive impairment[13] was operationally defined by a mini-mental state examination score of between 24 and 26[5 14] and a DemTect score of between 9 and 12.[5] Results of the clock drawing test[15] were considered abnormal when the score was less than 5 (scale 1-6).[11]

Subjective estimate of obliqueness

To obtain an estimate of which body axis angles would be perceived as oblique, we showed 23 staff neurologists photographs of a man lying at different body axis angles. They were asked to classify the orientation of the body axis as "reasonably straight" or "oblique" (see bmj.com). The photographs were taken from the foot of the bed. The actual body axis angle was determined from overhead photographs, which were not shown to the neurologists.

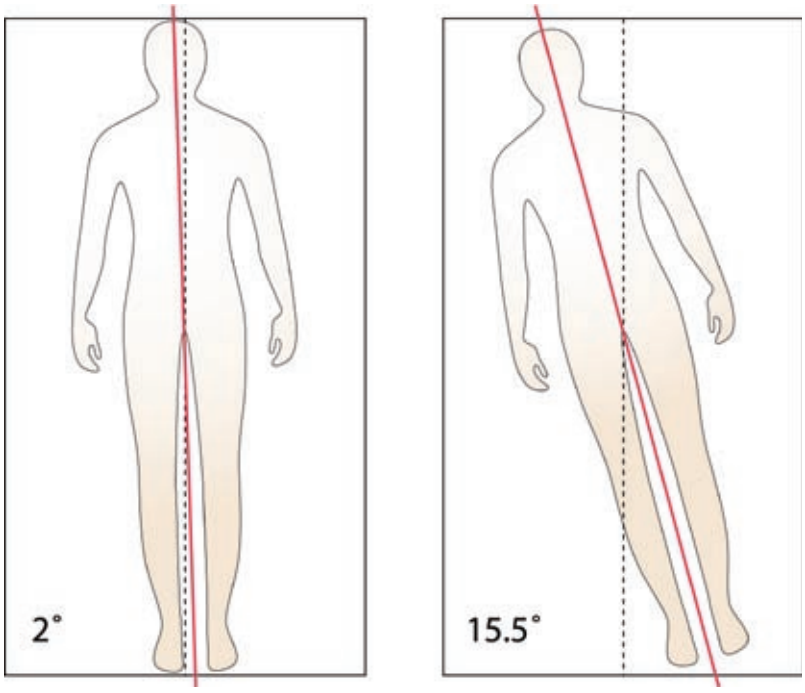

Fig 1 | Measurement of body axis angle. Left: intact. Right: Failed

The smallest angle, which was perceived as oblique by at least 90% of the neurologists, was considered the angle for obliqueness.

Statistical analysis

We carried out a correlational analysis (Pearson product moment correlation) on angular deviation using the mini-mental state examination, the DemTect, and the clock drawing test, respectively. Partial correlations were computed to control for age as a confounding factor. To compare the correlations between the tests and angular deviation, we computed *t* statistics for the differences between correlation coefficients.[16]

Receiver operating characteristics[17] were generated by calculating the sensitivity and specificity for each value of body axis angle and plotting 1 minus specificity against sensitivity for each of the three cognitive screening tests. Data are presented as means with standard deviations. We considered results to be significant at P<0.05.

Results

Overall, all but one of 110 included patients (see bmj.com) completed the tests and complied with instructions. All patients whose body axis orientation was found to be skewed by the examiner were able to achieve a straight orientation on verbal directions. For patients who laid down from both sides of the bed, body axis angles measured on the one side were linearly correlated with those on the other side (Pearson's correlation coefficient r=0.631; P<0.001). The angles were not statistically different (P=0.317; paired two tailed *t* test). For these patients the mean angle of both sides was considered in the analysis. The absolute value of the angle of the body axis orientation ranged from 0° to 23° with a median of 3°.

Scores for the mini-mental state examination suggested cognitive impairment in 24 patients, with scores below the dementia cut-off value in eight. For DemTect, cognitive impairment was suggested in 34 patients, with 11 of them having scores for dementia. For the clock drawing test, cognitive impairment was suggested in 33 patients.

Larger angles were associated with greater severity on cognitive test scores. Fig 2 shows the relation between body axis angles and cognitive tests scores in the patients.

Linear regression analysis using Pearson product moment correlation showed that angular deviation correlated significantly (P<0.001 for all tests) with the mini-mental state examination (r=−0.480), DemTect (r=−0.527), and clock drawing test (r=−0.552). Correlations remained significant (P<0.001 for all) even when age was removed as a covariate: mini-mental state examination, r=−0.407; DemTect, r=−0.444; clock drawing test, r=−0.467. The correlations between each cognitive screening test and body axis angle were similar (all *t*<1, all P>0.05).

Patients were stratified into three categories of cognitive status ("normal," "mild cognitive impairment," and "dementia") as determined by the results of the mini-mental state examination and DemTect. Analysis of variants showed significant effects of "cognitive status" on body

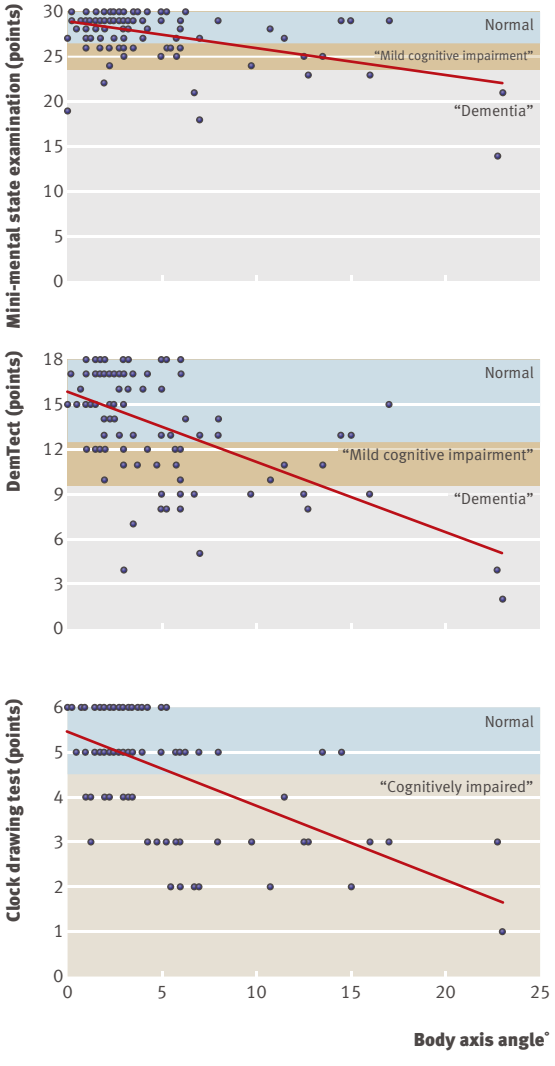

Fig 2 | Relation between body axis angle and scores for cognitive screening tests

axis angle (see bmj.com). The body axis angles of patients reaching dementia scores were significantly larger than those with normal scores (see bmj.com). For the clock drawing test, angles of patients with normal test scores differed from those of patients with less than normal test scores. The association of oblique body axis and poor results in cognitive screening tests remained if the data were reanalysed after exclusion of four patients wearing shoes when lying down from a subgroup of patients (n=78) with footwear status that could be determined from the photographs.

The obliqueness angle determined by 23 neurologists was 7° (see web extra on bmj.com). Using different outcome measures, the test characteristics of this obliqueness angle were determined by the receiver operating characteristics analysis. Angles equal to or greater than the obliqueness angle detected cognitive impairment, with sensitivities between 27% and 50% and specificities between 89% and 96% (see bmj.com).

Discussion

Deviation of the spontaneous body axis angle from the longitudinal axis of a bed was highly predictive of impaired performance in three cognitive screening tests. As each of the tests has been validated for cognitive impairment,[18] lying obliquely probably indicates cognitive impairment. A body axis angle of 7° was classified as oblique by 90% of neurologists. At this angle, specificity of more than 80% predicting impaired cognition was obtained in all tests, with sensitivities between 27% and 50%. Therefore lying down obliquely may be regarded as a simple clinical sign for cognitive impairment.

Conclusions were derived from a population of older (≥60 years) inpatients with neurological disorders that was skewed against vascular dementia and dementia associated with hypokinetic movement disorders. Those patients who kept their shoes on may have felt awkward about getting on to the bed, which could have affected the way they lay down. However, the association between oblique body axis and cognitive impairment remained after exclusion of patients who wore their shoes.

Performance in the clock drawing test alone explained some 29% of variance in the data. As clock drawing has been shown to mainly tap into visuospatial and executive abilities,[10 12] disturbance in either of these cognitive domains may be an important component of the mechanism underlying failure to orient the body axis. Disorders of orientation discrimination—the inability to detect the orientation of an object in relation to others[19]—have been associated with Alzheimer's disease[20] and postural disorders.[21-24] For example, pusher syndrome, a behaviour in which patients with stroke in an upright position actively push away from the non-hemiparetic side and tilt the body towards the hemiparetic side, has been linked with the inability of patients to determine when their own body is oriented in a vertical position in the frontal plane.[21 22] Similarly, it has been proposed that disrupted perception of verticality in the sagittal plane leads to backward tilt in the upright position in older people,[23] and may be related to falls.[24]

Obliqueness was clearly present in patients with cognitive impairment but who had not reached dementia scores in either the mini-mental state examination or the DemTect. This finding is consistent with the notion that impairment below the level of dementia may involve deficits in cognitive domains other than memory.[13]

We thank Klaus V Toyka (Department of Neurology, University of Wuerzburg) and Reinhard Gentner (Human Cortical Physiology Laboratory, Department of Neurology, University of Wuerzburg) for helpful comments, and staff doctors for participating.

Contributors: See bmj.com.

Funding: This study was part of OG's MD thesis. The study was supported by research funds from the State of Bavaria. The sponsor did not have any active role in the study. The researchers were independent of the funders.

Competing interests: None declared.

Ethical approval: This study was approved by the ethics committee of the University of Wuerzburg.

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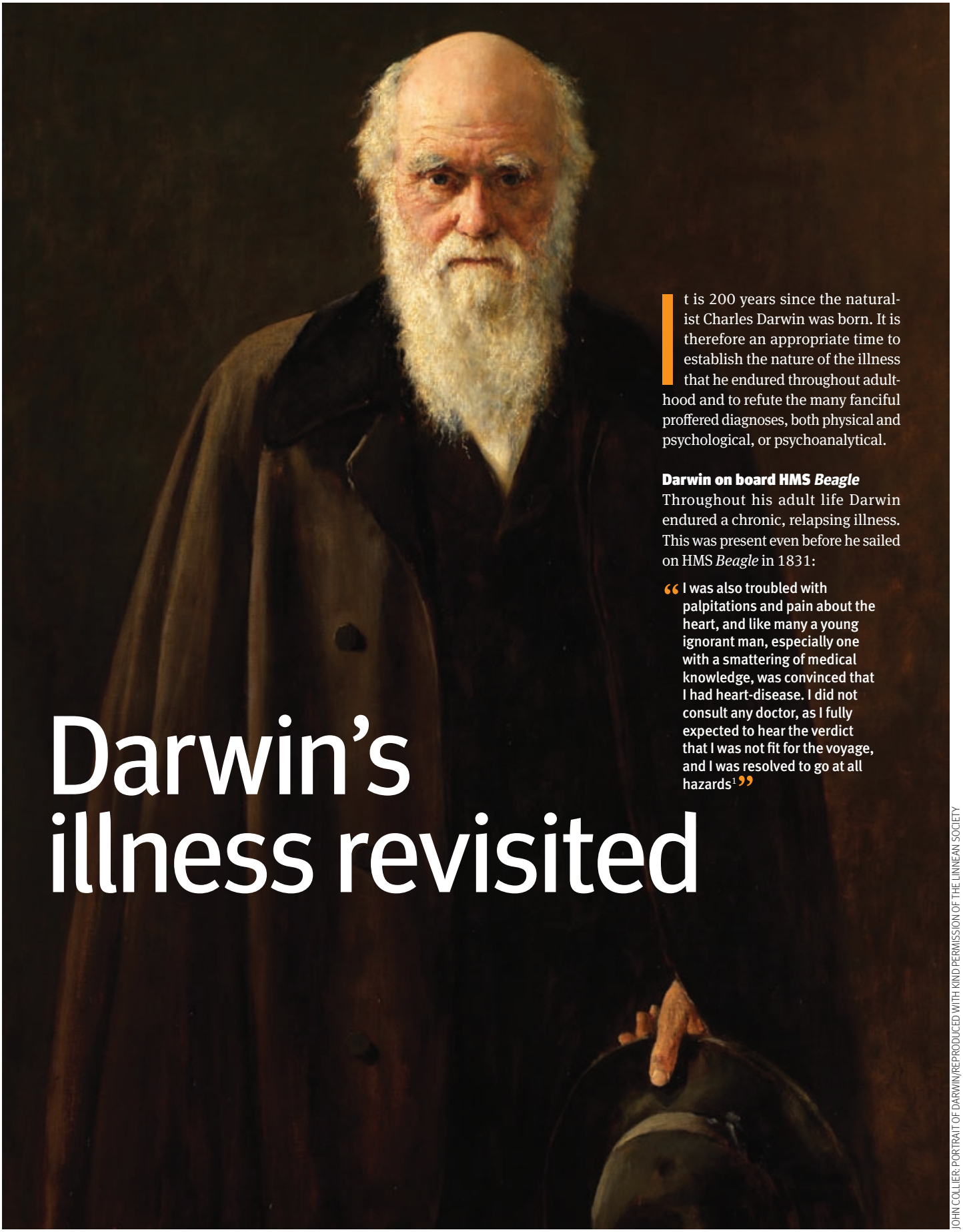
Accepted: 17 November 2009



Darwin's illness revisited

It is 200 years since the naturalist Charles Darwin was born. It is therefore an appropriate time to establish the nature of the illness that he endured throughout adulthood and to refute the many fanciful proffered diagnoses, both physical and psychological, or psychoanalytical.

Darwin on board HMS *Beagle*

Throughout his adult life Darwin endured a chronic, relapsing illness. This was present even before he sailed on HMS *Beagle* in 1831:

> "I was also troubled with palpitations and pain about the heart, and like many a young ignorant man, especially one with a smattering of medical knowledge, was convinced that I had heart-disease. I did not consult any doctor, as I fully expected to hear the verdict that I was not fit for the voyage, and I was resolved to go at all hazards[1]"

JOHN COLLIER: PORTRAIT OF DARWIN/REPRODUCED WITH KIND PERMISSION OF THE LINNEAN SOCIETY

We discuss Darwin's illness in a BMJ podcast, and find out what prompted John Hayman to investigate, at bmj.com/audio

Sea sickness was a major problem for Darwin, to the extent that he was incapacitated for days at a time. On 30 December 1831 and again in January, he recorded his feelings in a diary (box).

Darwin's seasickness was clearly more severe than that normally experienced and lasted throughout the voyage. He was sick for days, even under relatively mild conditions. To his sister Susan he wrote:

> "For the last four months I have not slept more than one night in the Beagle; today took all my things on board meaning to stay–But I am writing this on shore; and what do you think is the reason? . . . Sea sickness[3]"

Darwin's continuing illness

Darwin's sickness continued after the voyage. His illness was characterised by episodes of nausea, vomiting, intermittent abdominal pain, weakness, and lethargy and often associated with headache, dizziness ("swimming of the head"), visual disturbances, and palpitations. At times he complained of "inordinate flatulence" and diarrhoea:

> "I am weak enough today, but think I am improving. My attack was very sudden: it came on with fiery spokes and & dark clouds before my eyes; then sharpish shivery & rather bad not very bad sickness. I got up yesterday about 2 & about 7. I felt rather faint & had a slight shaking fit & little vomiting then slept too heavily; so today I am languid and stomach bad, but do not think I shall have any more shivering & I care for nothing else[4]"

Extract on seasickness from Darwin's diary

- **Dec 30th** At noon Lat. 43, South of Cape Finisterre & across the famous Bay of Biscay: wretchedly out of spirits & very sick. I often said before starting, that I had no doubt I should frequently repent of the whole undertaking, little did I think with what fervour I should do so. I can scarcely conceive any more miserable state, than when such dark & gloomy thoughts are haunting the mind as have to day pursued me
- **January 1 (1832)** The new year to my jaundiced senses bore a most gloomy appearance. In the morning almost a calm, but a long swell on the sea. In the evening it blew a stiff breeze against us. This & three following days were ones of great & unceasing suffering.
- **Monday 2nd** Heavy weather. I very nearly fainted from exhaustion[2]

Darwin also had eczema and had several attacks of boils. Interestingly, when his eczema erupted his main illness remitted, and remission also occurred during attacks of "rheumatism." Emma Darwin, his wife, wrote:

> "He has had a better week with much less sickness owing to a tightness of the chest & excema. The excema alas is gone & was hardly enough to affect him much but I am glad it is still lurking about him[5]"

The episodes of sickness were at times completely disabling and Darwin was confined to his sofa in a constant nauseated state for days—even weeks—at a time. He was aware that the episodes could be initiated by excitement or stress, even by pleasurable events. In a letter to his old shipmate Philip King he wrote:

> "I grieve to say that my health is so indifferent, I cannot stand seeing at present anyone here. Twice lately I could not resist seeing old friends . . . & the excitement made me so ill afterwards that I have been advised not to do so again. I am well enough in the mornings and when I keep quiet"

Again, a month later, writing to Thomas Rivers, a nurseryman specialising in the cultivation of fruit trees, he stated:

> "I suffer severely from ill-health of a very peculiar kind, which prevents me from all mental excitement, which is always followed by spasmotic sickness, and I do not think I could stand conversation with you, which to me would be so full of enjoyment[6]"

Darwin went through many different treatments, without lasting improvement from any. The most famous of these was Dr James Gully's cold water treatment, at his clinic in Malvern, Worcestershire. Darwin may well have gained some relief from this treatment, which would explain why he persisted with it for six months. Such relief may, however, have been due as much to the boredom of the place as to the prescribed therapy.

> "I am rather weary of my present inactive life & the Water Cure has the most extraordinary effect in producing indolence & stagnation of mind; I cd not have believed it possible[7]"

Proffered diagnoses

The nature of Darwin's illness has been the subject of much and very varied speculation. Psychological diagnoses offered include hypochondria, neurasthenia, panic disorders, and agoraphobia.

Psychoanalysts have put Darwin's illness down to "repressed anger towards his father," nervousness about his relationship with his wife, and guilt over conflict with his earlier religious beliefs.[8] Darwin was no hypochondriac or neurasthenic; he fought against his illness and struggled to work even when he was severely unwell. He did have anxiety but this may well have been engendered by his illness rather than being the cause of it. In later years he became almost a recluse for the good reason that travel, social contact, and meetings could trigger an attack.

Suggested physical diagnoses include maladies such as Meniere's disease (due to middle ear damage from game shooting), arsenic poisoning (from prescribed drugs),[9] and Chagas' disease resulting from an insect bite during his sojourn in South America.[8] These diagnoses have all been disallowed for good reasons. Darwin never had deafness; nausea and vomiting rather than tinnitus were his main symptoms. Arsenic (Fowler's solution) was prescribed for a variety of complaints and Darwin may have taken it as a young man for eczema. There is, however, no evidence that he received large amounts of arsenic. Darwin's symptoms were episodic, and between episodes he could feel entirely well. Chagas' disease is rejected for several reasons; exposure was too brief and Darwin had symptoms before he sailed. His tolerance of exercise was good and despite being examined by several eminent doctors he showed no evidence of organic disease.[10]

Speculation aside, we do know much about Darwin's illness. It was chronic but intermittent (initially he had periods of sickness alternating with periods of being well). Episodes of sickness could be initiated by stress or overwork, even by pleasurable events, and they could last for days or weeks and were at times completely disabling. The illness was not fatal; it was present probably for at least 50 years and became less severe in old age

JOHN CHANCELLOR: HMS BEAGLE IN THE GALAPAGOS/© GORDON CHANCELLOR/WWW.JOHNCHANCELLOR.CO.UK

Darwin suffered symptoms before, during, and after his voyage on HMS *Beagle*

(he died at 73 with symptoms of cardiac ischaemia and heart failure). He had no internal physical abnormalities.[10] The illness did not impair his fertility; as well as being the father of modern biology he fathered 10 children, all conceived during his long period of ill health.

The diagnosis

Darwin's symptoms are those of cyclical vomiting syndrome.[11] Although this is primarily a disease of children it may persist into adulthood or may appear for the first time in adulthood.[12] The disease is related to classic migraine and abdominal migraine but is also linked to abnormalities of mitochondrial DNA,[13 14] with mutations in the MTTL1 gene.[15] This disease is neither well known nor well recognised, particularly in adults, although it was first described in the English literature in 1882.[16]

People with cyclical vomiting syndrome experience abdominal, circulatory, and cerebral symptoms, including headaches and anxiety. Symptoms overlap with those of classic and abdominal migraine, except for a lack of aura. Affected people may experience some or all of these symptoms, with each individual having similar symptoms with each episode. Over time, however, progression or change may occur in the most prominent feature, and episodes may coalesce. Many people report severe motion sickness, and this may be associated with a full episode.

Episodes of illness may be divided into three phases—prodromal, emetic, and recovery—often with definite triggering events. Symptoms in the prodromal phase include fatigue, palpitations, and sweating. The emetic phase may consist of continuous nausea, with vomiting two to 20 times an hour. In most people this is associated with severe abdominal pain. Episodes may last one or two days or up to a week.

Many people with cyclical vomiting syndrome have eczema that may be related to various food allergies. The eczema is a form of atopic dermatitis—Darwin was diagnosed posthumously as having atopic dermatitis.[17] Affected people harbour staphylococci in their skin and often have recurrent skin infections.[18] Many of the people in the reported series had transient alleviation of symptoms by taking baths or showers, although these, unlike Dr Gully's hydrotherapy, were mostly with warm water. Many patients report a link between episodes and excitement, even pleasurable excitement, as did Darwin. Being in an institution where there was dull routine may have helped Darwin recover from months of sickness as much as the cold water therapy.

Darwin's mother Susannah died with abdominal pain when he was 8. As a child she had vomiting and boils, experienced motion sickness, had excessive sickness during pregnancies, and "was never quite well."[19] Her younger brother Tom had similar symptoms, with headaches, abdominal pains, and motion sickness. A sister, Sarah, considered that Charles and his uncle Tom had the same illness.[20] Evidence of a matrilineal inheritance pattern is good, consistent with an abnormality of mitochondrial DNA.

Conclusion

Darwin's symptoms may be explained by the diagnosis of cyclical vomiting syndrome, with secondary complications such as atopic dermatitis with staphylococcal infections, dental decay, oesophageal tears, and skin pigmentation. He had a severe form of this illness with periods of coalescence of episodes. His was a well defined but not well known inborn illness; he did not primarily have hypochondriasis, neurasthenia, agoraphobia, or any of the strange psychoanalytically derived maladies that have been proposed.

Darwin was not aware of mitochondria or of genes and genetic mutations but he was very aware of random variations within species. This was the keystone for his theory of the "survival of the fittest," the driving mechanism of evolution. His personal inherited genetic variation made him substantially "less fit," but his survival prospects were greatly increased by his driving intellect; loyal colleagues; devoted wife, family, and household servants; and personal wealth.

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The Complete Work of Charles Darwin Online (John van Wyhe ed), (http://darwin-online.org.uk) and the Darwin Correspondence Project, containing 5000 of Darwin's letters online (www.darwinproject.ac.uk) are the source of abundant original material. John Bertram and Dave Souza read the original draft and made suggestions.

Funding: None.

Competing interests: None declared.

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Cite this as: *BMJ* 2009;339:b4968

House calls

Intrigued by a common assumption that neurological cases are over-represented in published case reports, **Rhys Thomas** and **Naomi Thomas** investigate whether this is true and explore possible reasons

FOX

Neurophobia—the fear of neurology[1]—is well described in medical students and is postulated as the reason for an apparent bias favouring neurology in case studies. Neurological cases represent more than a quarter of all *Lancet* case reports: 29% of 523 cases during 1996-2002[2] and 26% of 360 cases during 2003-8.[3] Coles et al attributed this to "the trepidation and interest that neurological syndromes generate among physicians."[2] They considered this stigmatisation of a core medical specialty to represent our continued inability to demystify the subject.

However, the literature does not tell us whether neurological cases are genuinely over-represented or merely appropriately common. We set out to determine this by comparing the pattern of cases from a UK publisher (*BMJ Case Reports*) with the UK burden of disability. We also hypothesise that a more eloquent explanation for neurological case dominance is not neurophobia, but rather that the cases are simply more entertaining. Perhaps clinical neurology is not a dark mystery but a popular thriller. To test this assertion, we needed to examine cases where the motivation is to entertain rather than educate: the television medical drama *House MD*.

For those doctors who are allergic to medical drama, *House MD* stars Hugh Laurie as the maverick Gregory House. He is a diagnostician with an acerbic charm who solves mysteries loosely based on real medicine. The character resembles Sherlock Holmes—a drug using misanthrope and music loving genius. The series was reported to be the most watched television programme in 2008, with 82 million viewers worldwide.[4]

METHODS

The World Health Organization publishes "the global burden of disease" as disability adjusted life years (DALY), calculated using standard categories and methods to ensure cross-national comparability. We extracted the age standardised data for the UK in 2004 from their survey[5] and then examined the final diagnoses from *House MD* (series one to five).[6] We grouped the WHO data and the *House* diagnoses into similar categories as Coles et al,[2] but included extra categories for aetiology (such as infectious, genetic, or oncological). Using the same method, we then scrutinised the *BMJ Case Reports* archive.[7]

RESULTS

Many episodes from *House* had more than one diagnosis, some had none. The two most common categories were neurological (27.5% of cases) and infectious conditions (16%) (see table): occasionally cases represented both (such as Lyme disease). Seizures were commonly seen, both as the presenting symptom and as a result of (often inappropriate) treatment.

Proportion of case reports by system and aetiology. Values are numbers (percentages)

System and aetiology	*House MD**	*BMJ Case Reports*†	UK burden of disease‡
Neurology	55 (27.5)	172 (17.3)	600 (5.1)
Gastroenterology	11 (5.5)	83 (8.3)	347 (3)
Rheumatolåogy	3 (1.5)	40 (4)	526 (4.5)
Respiratory	5 (2.5)	48 (4.8)	1017 (8.7)
Dermatology	3 (1.5)	34 (3.4)	85 (0.7)
Cardiology	10 (5)	166 (16.7)	1694 (14.5)
Haematology	13 (6.5)	31 (3.1)	164 (1.4)
Endocrinology	8 (4)	65 (6.5)	723 (6.2)
Obstetrics and gynaecology	7 (3.5)	20 (2)	154 (1.3)
Renal	3 (1.5)	24 (2.4)	70 (0.6)
Ear, nose, and throat	0	21 (2.1)	320 (2.7)
Psychiatry	8 (4)	25 (2.5)	2601 (22.3)
Ophthalmology	0	34 (3.4)	702 (6)
Poisoning	14 (7)	19 (1.9)	14 (0.1)
Infectious	32 (16)	84 (8.4)	1007 (8.6)
Allergy	4 (2)	14 (1.4)	—
Genetic	13 (6.5)	29 (2.9)	—
Oncology	11 (5.5)	87 (8.7)	1664 (14.2)

*Series 1 to 5.[6]
†2007 to Aug 2009.[7]
‡Values from WHO,[5] as age standardised disability adjusted life years (DALYs) per 100 000 of population.

Neurological conditions were also the commonest category in *BMJ Case Reports* (17.3%), with cardiovascular second (16.7%), and oncology, infectious disease, and gastroenterology also well represented (8-9%). However, the greatest burden of disability in the UK is provided by psychiatric disease (22.3%), cardiovascular disease (14.5%), and oncological causes (14.2%).

DISCUSSION

The burden of UK disease cannot be appreciated from case reports alone: the dominance of neurology in *BMJ Case Reports* is disproportionate but is similar to that found in the *Lancet*.[2 3] This bias is mirrored in the *House* episodes, suggesting neurological cases do make a gripping yarn. Why is neurology so well suited to both case reports and the television?

Neurology is poorly understood by many, and mystery can be compelling. We suggest that neurology's myriad symptoms make it suitable for an entertaining case report. The symptoms are fascinatingly diverse: presentations include isolated loss of colour vision, an inability to name familiar objects, or fatigable drooping eyelids. With sufficient knowledge, you can have the satisfaction of predicting correctly where the lesion must be to cause these symptoms. It is no surprise therefore that the public has such an appetite for cases as in Oliver Sacks' *The Man who Mistook his Wife for a Hat*,[8] but there has never been much demand for "the man who passed frequent bloody stools."

In addition, the fear of neurodisability is deeply entrenched, and neurological symptoms can be devastating: watching House "cure" someone who was thought to have motor neurone disease (this is an example, not a plot spoiler) does have more emotional resonance than treating glue ear or piles. Furthermore, neurological disease is seen as permanent or progressive, and, therefore, any case that ends with "a twist in the tail" (that is, a remedy) is deemed worthy of report. Finally, the blurred line between organic and functional disease can lead us to question our very sense of self, and conflict is the essence of good drama.

The general enthusiasm for neurological stories should be harnessed to ensure that we lose the stereotype of neurology as the impenetrable preserve of eggheads in bowties. We can engage students in the entertaining detective work of clinical neurology—without perpetuating unnecessary neurophobia.

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We thank Adam Handel and Leone Risdale, who provided ideas for our discussion, and Phil Smith for his support.
Competing interests: None declared.
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Cite this as: *BMJ* 2009;339:b5256

George Clooney, the cauliflower, the cardiologist, and phi, the golden ratio

The challenge for scientists of all disciplines is to discern basic patterns and laws of nature that can be described mathematically—all this in a universe generated apparently from chaos and influenced by random events.

The "golden ratio" is one such phenomenon and has been known to mathematicians since ancient times. Two quantities are in the golden ratio when the ratio between their sum and the larger one is the same as the ratio between the larger one and the smaller. The Italian mathematician Leonardo Pisano, often known as Fibonacci, discovered the sequence (which was named after him) from which phi (Φ), the golden ratio, can be calculated. Stakhov et al show in a review that Φ (1.6180339887...) can be found in many aspects of nature and art.[1]

Leaf branches and the florets in a cauliflower head exhibit Φ proportions. The proportions can also be found in architecture of the past (such as the Notre Dame cathedral in Paris and even as far back as the Parthenon in Athens) and were consciously adopted by more modern architects, such as Le Corbusier. Even in the structure of DNA, Φ has its place. The DNA molecule is 3.4 nm (34 angstrom) long and 2.[1] nm (21 angstrom) wide, resulting in a length:width ratio of 1.61905.[1]

Similarly, evidence exists that Φ is also present in the design of the human body. For example, in the "perfect" body, Φ can be found by splitting certain distances (such as head to pelvis, or fingertip to wrist) into numerous segments—for example, mouth and nose are found at Φ proportions of the distance between the eyes and the chin. The American actor George Clooney exhibits the golden ratio in his face proportions).

Anecdotal reports have been published on the importance of Φ in cardiovascular physiology. A heart beat that produces a Φ relation between the T waves in an electrocardiogram has been reported to represent a state of health, peace, and harmony.[1] However, surprisingly little exploration of Φ relations has been undertaken in medical research. One problem is that very large datasets are needed to reduce the effects of random error.

We hypothesised that Φ can be found in important biological variables, such as arterial blood pressure. The Vorarlberg Health Monitoring and Promotion programme, covering a primary care based cohort of 166 377 people (mean age 42 years) in the far west of Austria, has offered routine screening periodically over two decades.[2] We evaluated the ratio between systolic and diastolic arterial blood pressure at first visit in the cohort database. Although the systolic:diastolic blood pressure ratio in the whole population was 1.6235, the mean ratio was 1.6180 in the participants who did not die during the 20 year observation period and 1.7459 in those who did. This finding suggests that blood pressure values in "well" individuals, but not in those who are at risk of dying, exhibit the golden ratio. Although this finding is not likely to be of practical relevance for individual clinicians, at a population level this may be an important phenomenon and should be investigated in other cohorts.

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Competing interests: None declared.

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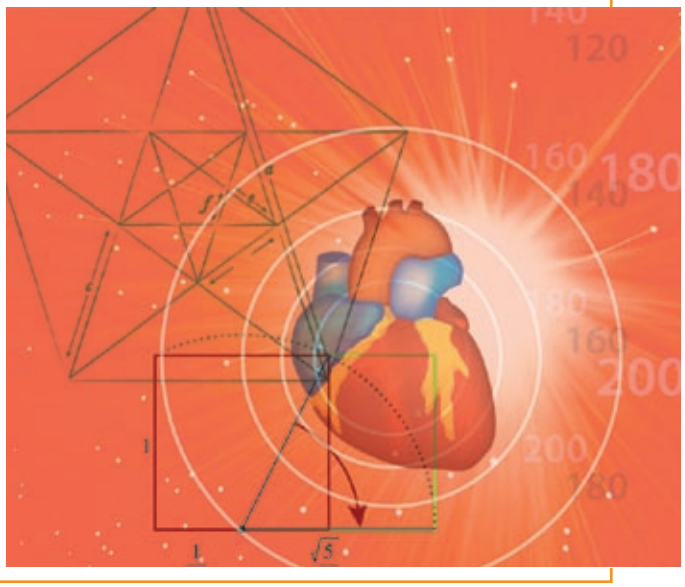
Cite this as: *BMJ* 2009;339:b4745



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