

ecent Years have seen a Catalogue of Plagues and sundry other Contagions. Hard on

the scaly Heels of Avian Flu follows Global Warming, Swine Flu, Obesity, and now the Economic Plague. This Litany of Woes has affect'd me deeply, as these few Entries from my Diary this past Year shew

5th April

Rose early to enjoy reading the latest Bill of Mortality of Estate Agents in the Parish of St. Giles's, which show'd again a monthly Increase. The Bankers, too, have this past Year been struck low, and it transpires that their Understanding of the term "Bank" has left much to be desired; they have been sinking our Shillings in miscellaneous crackpot Schemes in the Colonies that few understand, and fewer profit from: to wit, Hedge-Funds, Subprime Mortgages, Ponzi schemes, Plans to build golden Stairways to the Moon, and God knows how many other feeble minded Schemes.

Fearful of my own Savings, I visited my Bank in the Strand this Morning, only to find to my Dismay the Building lock'd up with a large "X" marked roughly upon the Door. I rapped loudly, and Mr Madoff put his Head out the Window. When I demanded to withdraw my Savings he tossed me a Florin, saying insolently, "This is what is left, Defoe, use it wisely. Remember, past Performance is no Guarantee of future Results—as I told you when

you invested, the Value of your Savings can plummet, as well as fall briskly," and with that he slamm'd the Window with a hollow Laugh. On close Examination I discovered the Coin to be but a poor Fake, bearing the Head not of our beloved Monarch but of one *Fred the Shred*, who some claim help'd land us up to our Necks in the financial Privy in the first Place.

12th May

Walked deep in Thought to the Tavern. Much Talk there of the Change in the Climate and the dire Consequences for the Publik Health. However the Country's best Brains are at Work to identify Remedies, and I am heartened to read in a Broad-sheet that the Fashion World has come up with a Solution: viz, new "flood length trousers" which keep the wearer's Hems out of the rising Waters. We need no longer live in fear of Flooding when the Fashion Industry is working so assiduously on our Behalf.

(Mem: To Payment to Tailor for Reduction of Trousers to knee Length: 5 shillings)

JOURNAL

Plague Lear:

BEING

Observations or Memorials,

Of the most Remarkable

OCCURRENCES,

As well

PUBLICK as PRIVATE,

Which happened in

LONDON

During the last

GREAT VISITATION
In 2009.

Written by a CITIZEN who continued all the while in London. Never made publick before

LONDON:

Printed by Precision Colour Printing Limited in Halesfield

6th June

Up betimes and stroll'd down the Strand, only to be assail'd by the dismal Sight of formerly prosperous Bankers and Estate Agents begging for Alms. At Aldgate I was approach'd by one in Rags outside the Coffee House, who seiz'd me by the Elbow and hoarsely ask'd for the Price of a skinny venturi decaff soya latte with cream, an extra shot, and coffee on the side. Not to drink, mind, but simply and intransitively "To go." It would be a harder Heart than mine that could turn down such a low Wretch and I toss'd him a Florin, which he bit to test its Soundness. Would that the Bankers had always been so careful.

7th June

Read in a Broad-sheet that a Banker has choked to Death on a counterfeit Florin in St. Giles's. ²

3rd July

Remembering that a previous Plague—to wit, the Foot & Mouth—was combat'd by burning all our Cattle, and that we had to wipe our Feet when visiting our Country Estates, I am seiz'd with a Plan: viz, that all avian and porcine Visitors to the Country should wipe their Feet upon entering and that all those already here should be incinerated forthwith. In this latter Endeavour I intend to enlist the help of Britain's many Fried Pullet and Braised Offal emporia. Three

tallow Candles did I exhaust, as many Quills, and a night's Sleep dismiss, in the fever'd Exposition of my proposal. I dispatched my Opus—extending to ten Quires of copperplate Manuscript—upon the Tea Clipper Sea Difficile bound for the English Colonies in America, for Consideration by their most highly esteem'd New England Medical Intelligencer. My Fortunes assured, I retired in high Spirits to my local Tavern, the Winter Swallow, to partake of a majestic Supper, before which I was entreated by the Victualler, "Goeth ye large?" Tis but a

Ha'penny more."

The Inn's recent Refurbishment with sturdy oak Furniture, reinforced against Obesity, will be viewed by future Generations as prescient and of much Comfort and Benefit to our expanding Populace. Doctors of Physik today are wont to say that Corpulence, like Plagues before it, is borne of an "obesogenic miasma." Such an Observation is self evident, and any Man may test its Veracity. I, myself, found recently that after partaking of frequent long Walks in the Highgate Countryside I had need to entreat my Tailor to take in the Waistband of my Breeches. The only rational

Explanation must be that the fresh and vital Air of Hampstead Heath is unpolluted by the "portly Odours" of the City.

1st September

Scarcely had the Difficile docked in New England than her sister Ship, C Shanty, return'd to London bearing Missives from the Referees of the Intelligencer. These discharged upon my Paper such Bile that I was sorely tempted to dispatch a quicke Response on the first Schooner at Dawn. The Referees' Comments moreover were accompanied by an insolent Memorandum to the Effect that they receive many Epistles such as mine, and that unfortunately they can print only a sparse 10 per cent of them, etcetera. I replied by Return, saying that their Gross Inefficiency is not my Concern, and further drew their Attention to the Fact that I receive many such rejection Letters, but unfortunately I, too, can only accept 10 per cent of them.

2nd September, post meridian

With renewed Spirit, I consider'd the Views of my New World Critics and set down to draft again my Manuscript. Deftly, I filleted the Piece to one twelfth its original Length while introducing a fanciful Conclusion—to wit, that the Swine Flu might be attenuated through Variolation of the Sort that has been used to curb the Small Pox in Asia since the first Millennium. My Revision includes many clear Messages for Policymakers, Practitioners, Quacksalvers, Mountebanks, Poultry-keepers, Pill Merchants, and sundry other Busybodies, as required. To avoid any Delay by His Majesty's Royal Mail—I admit, a most unlikely Eventuality—I dispatch my Footman, Lance, to Camden Lock, where a prestigious Journal—yet one of somewhat less Standing than the Intelligencer—has its Offices.

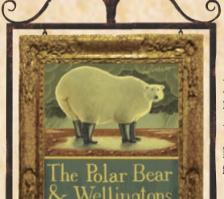
3rd September, ante meridian

I find this morning that my latest modest proposal too has been rejected by the onion-eyed Hedge Pigs4 who run this Penny Dreadful, and I repair to The Polar Bear & Wellingtons to mull over the sundry global Catastrophes which befall us and, more pressingly, to consider whether they afford me any Opportunity for Publication. I dash off a short Missive of Appeal for Consideration of my Paper.

20th December

Christmas draws nigh, and since my last Intervention, nothing but Silence from the Sots at the Journal, who no doubt are in their festive Cups

> instead of inking the Printing Presses. I repair to The Pig and Tamiflu for a small Cordial and to consider my few remaining Options.



21st December, ante meridian

A great Anxiousness afflicts me after a Night of diabolical Fever and I fear that I am finally succumbing to that most dreaded Distemper, the swine Pestilence, or, as it is now widely known, "The Pink Death." From my Sick



Bed I draft my Obituary, in which, with sincerest Modesty, I detail my glorious Achievements, Laudations and major Contributions to the World. I enclose a small woodcut Likeness of my Visage, seal the whole with Wax, and dispatch it to a local but respectable Journal—though a modest one of considerable less Impackt, again—the Provincial Medical and Surgical Journal.

21st December, post meridian

Feeling much the better. Perchance the increasingly unseasonal meteorological Conditions, in which the Temperature of London has reached 80 degrees Fahrenheit in the Shade, accounted for my Feverishness; for it seems I am to be spared. While taking Afternoon Tea, a Messenger from the Provincial Medical and Surgical Journal is shewn into my Study, bearing a dainty folded vellum Notelet. Its Message can barely be deciphered having, it appears, been impressed by a very worn India rubber Stamp and not written out, proper. "Thank you for taking the Time to consider our Journal for your Obituary," its single Sentence begins, "But we feel there would be insufficient Interest among our Readers for your Artickle."

23rd December

I console myself by spending my last 12 shillings in The Sty in Quarantine; and thankfully after downing the first two Pints of Port, much of the Rest of the Evening, and indeed this sorry Year, remains a Blur. (I have a discomfiting Memory of a semi-naked Man lying in Russell Square Fountain holding a half empty Port Bottle, and singing "Deck the halls" or a Version thereof).

24th December

Mem: To purchase of Tincture of Willow Bark: 2 shillings; Laundry of sundry Items of wet and soil'd Clothing: 6 shillings; To postage of numerous Letters of Apology to Residents of Russell Sq: £0-12-6. Mark Petticrew chair in public health evaluation, London School of Hygiene and

Tropical Medicine, London WC1E 7HT

David Morrison director, West of Scotland Cancer Surveillance Unit, Section of Public Health and Health Policy, University of Glasgow, Glasgow G12 8RZ References are in the version on bmj.com

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Will it all go wrong? Sod's law applied to medicine

Modern medicine has failed to take account of one of history's most fundamental rules and the lessons of a neglected 16th century philosopher, write **Tony Hope** and **Dominic Wilkinson**

Iudico potere essere vero che la fortuna sia arbitra della metà delle azioni nostre, ma che etiam lei ne lasci governare l'altra metà, o presso, a noi. [I believe that it is probably the case that fortune controls half of what we do, but she allows the other half to be controlled by ourselves.] Niccolò Machiavelli, 1513 (published 1532)

Modern medicine attempts to exert control over outcomes. It is the intellectual descendant of Machiavelli. But are such attempts to manipulate and minimise chance futile, do they risk making the worst outcome more likely? Such questions were anticipated and debated five centuries ago by a contemporary of Machiavelli, now largely forgotten, the Italian philosopher Girolamo Di Sod.

Girolamo Di Sod

Di Sod was born in Florence to a poor aristocratic family, towards the end of the 15th century. He was almost certainly in correspondence with Machiavelli before the age of 20.2 With Machiavelli's support, he was invited to take part in the literary gatherings at the Oricellari Gardens, where he engaged with some of the finest political thinkers of the age.

Although none of Di Sod's works has survived, descriptions by other members of Orti Oricellari suggest that he was both brilliant and eccentric. He studied with the Franciscan Luca Pacioli who



DI Sod, not playing dice

had, a decade earlier, written the first printed work to discuss probability.³ However, Di Sod quickly transcended his teacher in his efforts to quantify and control the element of chance. One of Di Sod's most distinctive views related to the conservation of personal fortune—episodes of fortune must be balanced by episodes of misfortune. He developed a pathological fear of gambling, convinced that good luck in such games might hasten his death. This fear, commented on by his contemporaries, gave rise to a common aphorism in the 16th century (later misquoted by Einstein), "Di Sod does not play dice."

Di Sod's behaviour became progressively more extreme, including the imposition of severe dietary restrictions (he ate only plain bread) and insistence on wearing weatherproof clothing in the height of summer.⁴ In his last years he wore a metal helmet while riding his horse in case of falls. The circumstances of his early death in his late 20s are unclear, but one report suggests that he may have been the victim of a lightning strike.⁵ If so, his customary head covering may have contributed to his demise—a striking confirmation of his famous law.

What is Di Sod's law?

None of Di Sod's writings survives. The sad irony is that Di Sod, determined that his writings should survive beyond his death, stored them in a fireproof box

in a locked safe at the centre of his house. However, it seems that the manuscripts were lost during the siege of Florence in 1529, two years after his death. The keys to Di Sod's strong box (which he had stored in several hidden locations in the house) could not be found in time to save the work before the house was demolished. 4

Di Sod's major work "In un'istanza di sventura" (On the instantiation of misfortune) has been lost. What we know of his famous law comes from secondary sources. What we find are references to examples of its operation, and we must infer its content from these examples. Modern statements of the law do not do justice to the depth of Di Sod's thinking. None deals with the important issues with which Di Sod and his contemporaries were struggling: the epistemological status of the law; the underlying causal mechanisms of the law; and, crucially, the limits of human agency in the events of history.

Di Sod and Machiavelli

Any analysis of the law must start from an understanding of Di Sod as a critic and intellectual combatant of Niccolò Machiavelli. Machiavelli had seen his beloved Florence decline from a powerful and independent city state to become a second rate power under domination from Spain and later France. He sought to understand the role of human agency in such changes: specifically how



Expecting the worst, and not disappointed

the behaviour of rulers can affect outcomes for good or for bad.

Di Sod's reading of history profoundly opposed that of Machiavelli. Where Machiavelli saw failure of proper leadership, Di Sod saw the unrolling of events outside human control. Where Machiavelli saw examples of successful leadership, Di Sod saw only temporary success followed by disaster. Di Sod came to two central conclusions: the powerlessness of human agency and a general pessimism about the effects of events on human aspirations. All historians since Di Sod, whether they agree with him or oppose him, have had to take a view on both these matters.

How should Di Sod's law be understood?

So where does this leave us with regard to an understanding of Di Sod's law? There have been, broadly, four interpretations.

Empirical prediction

"Each individual misfortune, to be sure, seems an exceptional occurrence; but misfortune in general is the rule."

A common example of Sod's law is that toast will usually fall butter side down. This is a testable empirical prediction. The generalised form of this interpretation is that if there are two or more possible outcomes the most likely is the one that is judged to be the worst.

What humans notice

According to this interpretation, Sod's law tells us more about ourselves than about the external world. We notice when the toast falls butter side down in a way that we do not notice when it falls butter side up: we are more aware of bad outcomes than of good ones.⁸

Human judgment

According to this view we tend to judge whatever happens in a negative way. If toast usually falls butter side down then we judge this to be the worse side for it to fall. We could have considered it better for toast to fall butter side down because, if it does, we notice the accumulated detritus (dog hairs, grit, nail parings) and throw it away, thereby avoiding any risks to health. According to this interpretation, the toast falling butter side up would be the worse outcome because we would probably make some ineffectual attempt to brush the toast and then eat it, thereby exposing ourselves to the risk of disease.

As an exhortation to prepare for the worst

According to this interpretation, Di Sod's law is an elliptical way of stating how we should think or behave. If we prepare for the worst, the worst will be less likely to happen, and if it does, we will be less psychologically affected by it. This is the interpretation of the Italian guild of umbrella

makers (Fratellanza dei costruttori di ombrelli), who, in the 18th century, marketed their leather umbrellas to farmers citing Di Sod and claiming that the purchase and use of an umbrella would ensure long periods of sunshine.

Implications of Di Sod's law for medicine

As will be clear there are two profoundly opposed conclusions to be drawn from these interpretations—that bad outcomes can be reduced by appropriate preparation (the last interpretation above) or that we can do nothing to reduce bad outcomes (the other three interpretations). The first conclusion, favoured by Leibniz, implies that a systematic scientific approach to medicine may enable us to create the best possible world10: assiduous attention to the latest evidence averts misfortune for our patients. The second conclusion, favoured by Schopenhauer, 11 is that misfortune is inevitable. This implies that seeking the best evidence to guide medical treatments is at best useless and at worst may increase the chances that we will get it wrong. For example, antihypertensives may produce clear benefits in trials, but in clinical practice they may lead to worse outcomes-for example, causing patients to fall and fracture their hips.

Conclusion

Attention to his pessimistic outlook gives credibility to the view that the correct interpretation of Di Sod's law is that misfortune is inevitable. If this view is correct it has profound implications for epistemology. It implies that if we view knowledge as providing us with tools to change outcomes, then no true knowledge exists. Evidence based medicine is an illusion that has no valuable effect on the care of patients. In other words, in the end we know Di Sod all.

As a footnote we would like to emphasise the irony that Di Sod has virtually been written out of history. It is only in Britain, Australasia, and a few other places that his famous law is known by his name. Even in his native Italy it is named after the American engineer, Murphy, who lived four hundred years later. Modern uses of Murphy's law lack completely the profundity of Di Sod's law and are little more than cocktail party banter.

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Competing interests: None declared.

Provenance and peer review: Not commissioned; externally peer reviewed. This paper arose from speculation over a theinated beverage about the origin and meaning of Sod's law. Neither of the authors is a medieval scholar or Italian speaker, and it is possible that they may have misunderstood or just made up some of the details about Di Sod's life. Contemporary references are more reliable. Tony Hope is the guarantor, and guarantees that it will rain if he forgets his umbrella.

References are in the version on bmj.com

Cite this as: BMJ 2009;339:b5299

Patent medicines and secret remedies

As arguments between doctors and advocates of alternative medicine continue, **Jeff Aronson** describes how the secret ingredients of patent medicines were uncovered a century ago

atent means open (box 1), but patent medicines have traditionally contained secret ingredients.

The Oxford English Dictionary defines a patent medicine as "a proprietary medicine manufactured under patent and available without prescription." However, the term and its current definition are historically misleading. From the start, the hallmarks of patent medicines were that they were advertised direct to the pub-

lic and sold over the counter. They were rarely patented because it was advantageous to be secretive about ingredients that were often ineffective and even hazardous. If a product had a patent it was generally because the remedy was effective—Epsom salts, marketed by Nehemiah Grew in the late 17th century, contained magnesium sulphate as a purgative.

Patent medicines could be purveyed by physicians and apothecaries or by unqualified quacks, mountebanks, and charlatans (boxes 1 and 2). Historian Roy Porter suggested that between 1600 and 1850 there were more similarities than differences between quacks ("less cheats than zealots") and regular practitioners, ² an assertion that is borne out by the history of patent medicines.

Sales of patent medicines burgeoned during the 18th century. They were often named after their inventor (Swaim's Panacea, Turlington's Balsam of Life); after a famous, but often conveniently dead, practitioner (Dr Boerhaave's red pills, Dr Radcliffe's drops), or after the place of origin (Epsom salts, California vinegar bitters). The name might include the source of the



medicine (Clark Stanley's snake oil liniment) or its supposed indication (Dr D Jayne's expectorant, Mayr's wonderful stomach remedy). Exoticism could be an advantage (Indian panacea, Green Mountain magic pain remover).

Advertisements for such products, promoting (?) their value in wide ranges of conditions, indeed often for all conditions, might be accompanied by recommendations from patrons—Dr Scott's bilious

pills had benefited "the Dukes of Devonshire, Northumberland and Wellington, the Marquesses of Salisbury, Angelsea, and Hastings, the Earls of Pembroke, Essex and Oxford and the Bishops of London, Exeter and Gloucester." Testimonials from grateful patients were also cited—an advertisement for Lydia Pinkham's vegetable compound for women stated, "Lydia Pinkham's private letters from ladies in all parts of the world average one hundred per day." 5

Secret remedies yesterday

Regular practitioners have always been critical of patent medicines. In 1790, for example, James Adair, a Scottish physician, published a scathing indictment.⁶ "Many persons have been destroyed by quack drugs," he wrote, "but dead men tell no tales." He and others pointed out that quack medicines contained conventional treatments (such as opium and ipecacuanha in Dover's powder), poisons (such as hemlock), or nothing of value whatsoever.

However, during the second half of the 19th century, with the rise of the chemicals industry and the consequent beginnings of drug companies, such as Hoechst and Bayer in Germany and Burroughs–Wellcome in the UK,⁷ the criticism became more intense and evidence based. Pharmacology (the word dates from the start of the 18th century⁸) was becoming scientific.

In America, concern about adulterated and misbranded foods and drugs culminated in the publication of 11 articles by Samuel Hopkins Adams in Collier's Weekly in 1905, titled "The Great American Fraud," in which he exposed many of the false claims made about patent medicines. This led directly to the 1906 Pure Food and Drugs Act. Doctors, supported by the American Medical Association, then published robust criticisms of the purveyors of patent medicines. They were met by a riposte in the form of a pamphlet, published by the Proprietary Association.9 The Proprietary Association collected newspaper reports of adverse events, including deaths that had been attributed to various medicines, and claimed that patent medicines were less dangerous than other medicines. Something of the flavour of this report emerges from the data on whiskey and alcohol (84 cases, 61 deaths) and Cannabis indica (one case, no deaths).

In the UK, patent medicines had been specifically excluded from the Pharmacy Act of 1868 and the Sale of Food and Drugs Act of 1875, and their contents could therefore be kept secret. ¹⁰ ¹¹ Many of them, such as Battley's



Box 1 | Etymologies

Patent comes from the hypothetical Indo-European root PET, to spread or open out. Petals spread out; patellas, spatulas, and spades look like open dishes; space is an open area; and paella is cooked in an open pan. According to the Oxford English Dictionary, letters patent (Latin litterae patentes) were originally open letters from a monarch or government, intended "to record a contract, authorize or command an action, or confer a privilege, right, office, title, or property"; the term then came to mean documents that grant "for a set period the sole right to make, use, or sell some process, invention, or commodity." It was subsequently shortened to patent.

Quacks, originally quacksalvers, supposedly quacked or boasted about their salves; a mountebank was a man who would mount a soapbox (Italian: montare in banco) to shout his wares at a fair; charlatans were wont to prattle (Italian: ciarlare) about their medicines¹

SOUTHING SYRUP

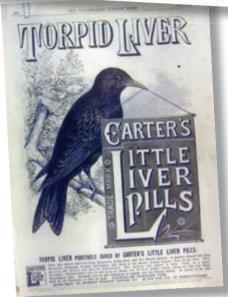
sedative solution, Daffy's elixir, and Godfrey's cordial, contained opium, and their sales increased. In the 1880s, therefore, doctors, supported by Ernest Hart, editor of the *British Medical Journal*, started to campaign against this abuse.

A Patent Medicine Bill in 1884, which would have controlled these products, failed because of pressure from the Society of Chemists and Druggists. Undaunted, the campaigners used as a test case Dr Collis Browne's chlorodyne, which contained chloroform, morphia, tincture of Indian hemp, and prussic acid and was responsible for a large number of cases of poisoning. The chairman of the parliamentary bills committee of the British Medical Association sent a memorandum to the Pharmaceutical Society, the Society of Apothecaries, and the General Medical Council, attacking patent medicines in general and chlorodyne in particular. Questions were asked in the House of Commons in 1891, to no avail. However, the parliamentary bills committee then persuaded the Treasury's solicitor to prosecute the manufacturers of chlorodyne. The magistrate defined a patent medicine as one that was issued with a government patent. Chlorodyne, having no such patent, therefore came under the 1868 Pharmacy Act. What had once been secret became open. The manufacturers were fined for marketing a scheduled poison. Other similar patent medicines were thus brought under the act

Box 2 | History of apothecaries

Apothecaries were originally members of the grocers' livery company. However, during the late 16th and early 17th centuries, under the leadership of Francis Bacon and the Huguenot refugees Gideon de Laune and Théodore Turquet de Mayerne, they sought to secede. Eventually, the Worshipful Society of Apothecaries of London was incorporated by royal charter of James I on 6 December 1617, although it continued to be allied to the Society of Grocers. The grocers stocked perishable goods, the apothecaries non-perishable ones, including spices, sweetmeats, preserves, and medicines.

Apothecaries purveyed and compounded drugs, dispensed physicians' prescriptions, and charged for medicines. Physicians employed apothecaries or used them as required and charged for consultation and advice. The decision of the House of Lords in 1704 in the case that the College of Physicians brought against an apothecary called William Rose, accusing him of administering medicines without licence from the college, without the direction of any physician, and without taking or demanding any fee for his advice, established that apothecaries could independently prescribe and dispense medicines. The college's monopoly was broken.3 In 1711, the Worshipful Society of Apothecaries was established as a separate livery company.



The hallmarks of patent medicines were that they were advertised direct to the public and sold over the counter. They were rarely patented because it was advantageous to be secretive about ingredients that were often ineffective and even hazardous







VELLCOME IMAGES

and controlled. Some manufacturers removed opioids from their products. Sales fell.

However, patent medicines continued to be sold, and the campaign continued. In the 1900s, the BMI published a series of articles under the general title "The Composition of Certain Secret Remedies," dealing with drugs used to treat epilepsy, 12 headache, 13 kidney diseases, 14 and other conditions. In 1906 it started to reprint similar articles from the Deutsche Medizinische Wochenschrift.15

In 1909, the BMA gathered the articles into a single volume, Secret Remedies, 16 Public interest was enormous, fuelled perhaps by H G Wells's 1909 novel Tono-Bungay ("slightly injurious rubbish at one-and-three half-pence a bottle"). Secret Remedies sold 62 000 copies by June 1910.12 A second collection was published in 1912.17 The entries listed the ingredients in each product, details of the "claims and exuberant boasts" made by their manufacturers, and the prices charged. Comparisons with the actual costs showed how large the manufacturers' profits were. The table summarises some of the entries, whimsically chosen from the two volumes

Although the ingredients of UK patent medicines are now stated on packets. the information will mean little to most consumers, and important information may in any case not be available

Although a select parliamentary committee was subsequently appointed to investigate patent medicines, it published its report on 4 August 1914, when public attention was focused not on Dr Boschee's German Syrup, but on Germany itself; its recommendations were not pursued.18

Secret remedies today

Two Latin tags summarise the success of patent medicines, even today. The first, omne ignotum pro magnifico (ignorance makes everything look superb), was quoted in the preface to the first volume of Secret Remedies. The second, populus vult decipi (the public wants to be deceived), appeared as the legend to an early 17th century engraving by the Dutch artist Jan van de Velde, showing eager customers clustering around a quack and his wares. In 2007, American adults spent \$12bn consulting practitioners of complementary and alternative medicine and \$22bn buying their products. 19

Although the ingredients of UK patent medicines are now stated on packets, the information will mean little to most consumers, and important information may in any case not be available.

The two volumes of Secret Remedies constituted a landmark publication in the control of over the counter medicines. Their story has modern resonances. Nostrums are still available over the counter. Perhaps another edition of Secret Remedies is needed.

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This article is based on JKA's Gideon de Laune Lecture, given to the Society of Apothecaries in 2008.

Competing interests: JKA is president of the British Pharmacological Society, a member of a NICF technology appraisal committee, and a member of the formulary committees of the British National Formulary and the British National Formulary for Children. The views expressed here are not necessarily shared by those organisations.

Provenance and peer review: Commissioned; not externally peer reviewed.

References are in the version on bmi com

Cite this as: BMJ 2009;339:b5415

See EDITORIAL, p 1386

	Examples of secret remedies ¹⁶¹⁷			
Product	Claim	Stated contents	Price (cost of manufacture)*	
Blair's gout and rheumatic pills	"Immediate relief and cure of acute and chronic gout, rheumatism, suppressed gout, rheumatic gout, gouty skin diseases, bronchitis and asthma, sciatica, lumbago, and neuralgia"	Powdered <i>Colchicum</i> corm, burnt alum	1s 1½d(<1d)	
Damaroids	"A safe and sure remedy for general weakness, spinal exhaustion, neurasthenia, physical decay, and loss of nerve power"	Iron hypophosphite, quinine sulphate, sugar, talc	2s 9d(3d)	
Pink Pills for Pale People	"When the muscles and nerves are tortured by poisons in the blood, be the result rheumatism, sciatica, or lumbago anaemia, indigestion, palpitations, influenza's after-effects, eczema, sciatica, St Vitus' dance, spinal weakness, the many forms of nervous disorders dreaded by men; also the special ailments of women"	Iron sulphate, potassium carbonate, magnesia, powdered liquorice, sugar	2s 9d(11d)	
"Professor" O Phelps Brown's vervain restorative assimilant	"For the positive and speedy cure of epilepsy or fits, dyspepsia, indigestion, all derangements of the stomach and bowels, and for every form of debility"	Vervain, port wine, rectified spirit	2s 9d(5d)	
Wood's cure for tobacco habit	"Tobacco habit conquered in 3 days"	A series of formulations containing: phenolphthalein, quassia, aloin, and strychnine; asafoetida, iron, and strychnine; methylene blue; and methyl salicylate	£11s	



I should cocoa

My great grandfather was William Tibbles, the originator of Dr Tibbles' Vi-Cocoa, which became well known in the first part of the 20th century. I have no idea whether he was really medically qualified, although the BMJ carried obituaries of his sons and grandson. I have found several articles and letters by them in the BMJ's online archive, but nothing about Dr Tibbles' Vi-Cocoa, which James Joyce mentioned briefly in Ulysses.

The *Lancet* was fulsome in its praise (according to an advertisement in Newfoundland's Evening Telegraph), saying it "must be assigned to a place in the front rank of really valuable foods, since it is the embodiment of all the numerous principles contained in Malt, Hops, Kola and Cocoa. Of distinct value as a restorative and stimulant food."

Its effects were probably due to cocaine. It was certainly very

popular in the Commonwealth and was widely advertised, carrying endorsements from doctors, nurses. postmen, writers, blacksmiths, and many others. A "dainty" free sample was always on offer.

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This is an abridged entry for our competition for the most interesting use of the BMJ online archive (1840-2009).

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Winner of our competition for the most interesting use of the journal's archive

The Spanish flu through the BMJ's eyes

Can the "Spanish flu" of 1918-9 teach us anything about future pandemics? **Tom Jefferson** and **Eliana Ferroni** investigated contemporary accounts in the *BMI*

he great Spanish influenza of 1918-9 is perhaps the best known of all pandemics. A vast number of books have been written on the topic, and "Spanish flu" still represents a rich topic of discussion and research.1 Although many scientific questions posed at the time have been answered by nearly a century of subsequent discoveries, some puzzles remain-such as the reason for the high case fatality rate (>2.5% according to some estimates),2 the high incidence in young adults,3 and the role played by the first world war and its aftermath.4 At the time, the aetiology was not known and the disease's mode of transmission could only be hypothesised by careful observation. In addition the effects of preventive measures remained largely unevaluated. Most descriptions of the event seem to be based on secondary sourcesthat is, they are not direct eyewitness accounts although recently efforts to go back to primary sources have been made.4

Reliance on secondary sources is a potential source of selection bias: the reader gets a selected view of events, and some of the contemporary observations and explanations are lost. Interpretation of events and actions of a bygone era from a modern perspective is another perilous activity.

We exploited the opportunity to consult the newly digitised *BMJ* archives to carry out a review of what was published at the time. We tried to look at the pandemic through the eyes of contemporary *BMJ* contributors and readers and give them their voice back. We chose the Spanish influenza pandemic because we believed some of the observations and issues raised at the time may still be relevant to the events of today, although some have been forgotten.



Tin miners at Redruth mine, Cornwall

Methods

We carried out a search of the *BMJ* archives using the keywords "influenza," "flu," "pandemic," and "Spanish influenza" for the period 1918 to 1924. We read the content of each article, looking for unusual or forgotten observations and still unresolved questions. We excluded well known facts (such as clinical descriptions and presentation of the disease), and we did not carry out a detailed analysis of observations that are explicable with today's knowledge (such as the contemporary conclusion of the presence of "filterable virus," which was then invisible and unidentified).

We grouped the findings by broad headings covering the capricious nature of the spread of disease and its relation to climatic conditions, the possible multifactorial nature of the high case fatality rate, the unusual effects of poison

gas on munitions workers' health, and possible causality and preventive measures.

We did not carry out a systematic review but selected items that we consider still highly relevant today but largely forgotten. We make no claims as to the completeness or fairness of our selection, but we have listed our search yield and sources in the appendix on bmj.com to encourage readers to consult the original records.

Results

We found 55 articles of varying nature—including studies, reports, and letters—published between July 1918 and October 1920.

Spread of disease and its relation to climatic conditions

One of the least studied aspects of the pandemic was the appearance of synchronous cases or clusters of cases either apparently unconnected or a great distance apart. This had also been a feature of the 1789 and 1889 pandemics (and would be again in 1957 and 1968).⁵

Dr Andrew Garvie, a general practitioner in Halifax describes the conundrum: "But why the first case in the household was, on the average, more serious than the sporadic, and why the 'clumping' should occur, is difficult to understand. Casual observation might lead one to suppose that the spread was due to actual contagion from one house to another. At first I regarded it simply as due to 'neighbourliness,' but later on became convinced that this could only be a partial explanation

Table 1 | BMJ reports of associations between exposure to poison gas and other gases and influenza and other acute respiratory illness

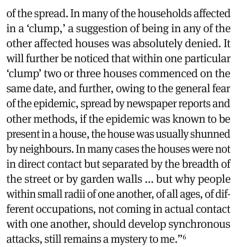
Reference	Type of tgas	Population	Observation
Ball, 1919 ¹²	SO ₂	Copper smelters	"Consumption was practically unknown"
Shufflebotham, 1919 ¹³	Sulphurated hydrogen, chloro-picrin, and chlorine	Poison gas workers	"Poison gas workers were practically immune from influenza in this district"
	Mustard gas	Gas workers	"The amount of absenteeism during the two epidemics was not increased beyond normal"
	Phosgene	Gas workers	"Workers were more prone to influenza infection than other classes of the community"
Gregor, 1919 ¹⁴	${ m NO_2}$ and ${ m SO_2}$	Workers	"Certain gases have a powerful inhibitory action on post-nasal flora, and such action is quite sufficient to render many workers in those gases immune to diseases which invades the body through the upper respiratory passages"

Table 2 | Exposure to gas and incidence of influenza (adapted from Gregor, 1919¹⁴). (Values are numbers of subjects unless stated otherwise)

Population	Cases	Total	Case incidence (%)
Navy	446	1350	30.2
Army	210	1050	20.0
Cordite workers:			
Not working in fumes	221	732	30.1
Working in fumes	15	318	4.7
Gas workers	10	148	6.7
Tin mine workers:			
Not working in fumes (one epidemic)	14	23	60.8
Working in fumes (one epidemic)	3	27	11.1

Table 3 | Effects of influenza vaccines in British troops in 1918-9 (adapted from Leishman, 1920¹⁷). (Values are numbers of subjects unless stated otherwise)

Population	Pulmonary complications	No pulmonary complications	Incidence rate per 1000
Inoculated (n=15 624)	26	15 598	1.66
Uninoculated (n=43 520)	583	42 937	13.40



Dr Major Greenwood, later first professor of epidemiology and vital statistics at the London School of Hygiene and Tropical Medicine, writing arguably the most complete description of the UK pandemic in the autumn of 1919, had the following explanation for the observation: "A mass attack, indeed, forms an invariable link in the chain of events, but scattered individual cases are antecedent. This observation removes the most formidable objection to a belief that influenza is contagious, and it is easy to understand why we discover no confirmation in historical records. In such epidemic diseases as plague the preceding sporadic cases are recorded because their high fatality leads to illusion in bills of mortality; but in consequence of the very low fatality of primary epidemic influenza early mortality records are wanting. The mass phenomenon strikes the imagination of the recorder and an illusion of suddenness and simultaneity is produced."7

In other words ascertainment bias was the most likely explanation for the observation.

Greenwood and other *BMJ* contributors (such as Dr Mercer Watson writing in 1919⁸) dedicated a lot of time to describing the prevailing atmospheric conditions in relation to the subsequent

waves of the pandemic. This may be a relic of the old miasma versus contagion debate of previous centuries.

High case fatality rate

A hallmark of the Spanish influenza pandemic was its high case fatality rate. Greenwood described its causes in the spring and summer of 1918 period as "excessive mortality being mainly due to the accident of season, aided by the special circumstances of overcrowding and fuel shortage which are due to the war. In a word, this is not essentially a war epidemic."7 The role of wartime shortages and troop concentrations and movements has always been a moot point with historians and epidemiologists. Those who refute these as factors cite the example of whole countries or isolated communities not involved in the war being virtually wiped out-that is, being fatal exceptions to the theory.9 However, a closer look at the description of conditions by BMJ contributors shows the importance of studying context in the devastation.

Surgeon Lieutenant Francis Temple Grey in charge of the Samoa relief expedition is cited by the BMJ in 1918 explaining the high native mortality compared with the white population: "The incidence among the natives was 80 per cent. Out of a population of 36,405 the deaths numbered 7,264." Grey attributes the high mortality partly to the fact that natives, although apparently of fine physique, have generally a poor chest expansion, and to their habits. "The native house has a raised floor of coral and lava pebbles, a thatched roof supported on poles, and no walls, but at the beginning of the epidemic, when a native fell ill he lay down in his hut, and his family, having pulled down the blinds, which are usually lowered only in wet weather, lay down with him in sympathy. When the fever was at its height, on the third day, the natives cast off their clothes, pulled the blinds up, and many of the men went into the sea to cool themselves. This was often followed by pneumonia,



although, except in children, few cases, even with precautions, escaped bronchopneumonia. At the height of the epidemic many lives were lost owing to want of food consequent on the cessation of its collection. On December 8th, 1918, food collecting was resumed, and the decline of the epidemic was popularly dated from that... Among the whites the incidence was put at 60 per cent, and the case mortality at 2 per cent."¹⁰

Writing in 1920, Dr A H Macklin, formerly of the Imperial Trans-Antarctic Expedition, helps us to understand some of the reasons behind the often quoted devastation in Lapland: "The Laplanders had a very thorough if unsympathetic way of dealing with their cases. The settlements were composed of wooden huts, small, but generally well made and warm. A common type consisted of but one room used by the family for all purposes. Better class Lapps had better huts, with two or three rooms. In each settlement one of the single-room huts had been set apart, and into this each case of sickness as it arose was unceremoniously pushed; and none were permitted to return to their own huts until completely recovered. Whilst there they received practically no attention, and no healthy person ever entered to attend to their wants. Occasionally a bowl of water or reindeer milk was hastily passed in at the door, or a huge chunk of reindeer meat thrown in, uncooked and uncarved... Constipation was a constant factor, and many cases had not had their bowels opened since the onset of their illness-in some cases seven to ten days. Others had voided urine and faeces just as they lay. In some huts those of the patients who had passed the worst stages of their illness assisted and looked after those more acutely ill."11

The effects of poison gas on munitions workers' health

By 1918 the use of poison gas, first introduced in 1915, was routine when bombarding enemy trenches. A great number of workers were



assigned by the Ministry of Munitions to produce shells filled with the noxious substances. Numerous *BMJ* authors remark on the apparent protection afforded by all types of gas production except phosgene (table 1).

Dr Gregor, writing in 1919, informs us that it was apparently "custom to take children suffering from whooping cough to the nearest gasworks and expose them to the fumes emanating from the oxide of the iron purifiers during the process of cleansing, and the parents of these children firmly believe that by doing so the attack is much mitigated." He goes on to report a comparative cohort analysis of the incidence of influenza in populations with different exposure levels to gases (table 2). Assuming that uniformed personnel were the fittest population, the difference in incidence is striking.

Causality and prevention

By 1919 Dr Benjafield of the British Expeditionary Force in Egypt thought that "In this case it is more than possible that the primary etiological agent is ultramicroscopic and is a filterable virus, which renders the individuals infected hypersensitive to organisms which formerly only possessed a low degree of pathogenicity." ¹⁵ This

Women working in the huge cordite explosives factory in Gretna, Scotland

was also the conclusion of Rose Bradford et al of the British armies in France. ¹⁶

If this hypothesis were true, experimental vaccines against a collection of bacteria would be expected to achieve at least partial effectiveness. This is exactly what Sir William Leishman experimented with, using it on troops during the closing stages of the war. The vaccine contained a mixture of *Bacillus influenzae* (*Haemophilus influenzae* type b), streptococci, and pneumococci. Leishman's *BMJ* paper does not report details of methods, but his observation of effectiveness against influenza, pulmonary complications, and deaths is upheld by our reanalyses. For example, the odds ratio for pulmonary complications was 0.12 (95% confidence interval 0.08 to 0.18) (table 3).

The views on the effectiveness of other interventions such as masks and distancing were varied.

Discussion

We found several articles reporting unusual observations. Even today many of these have no explanation. We feel that the observations should first be corroborated and perhaps explored further. The idea that exposure to gaseous fumes (even potentially toxic) prevented or ameliorated respiratory disease seemed established at the time. Today, however, that is flatly contradicted by unreferenced statements in publicly available documents.¹⁸

The causes of the high case fatality rate are still unclear, but modern research suggests that the pandemic was a lot more than just a "one germone disease" affair. ¹⁹ This view is supported by the apparent success of antibacterial vaccines against influenza and its complications (with all the probable methodological shortcomings of Leishman's study).

Agents other than the influenza virus probably played a part. Above all, the environmental explanations of the high Samoan and Lapp mortality rates indicate the peril of generalising across contexts and simplifying causation models. The

origin and spread of the pandemic are also far from clear, but the repeated reporting of multiple synchronous foci should be investigated in today's pandemic. This may give us an indication of the means of seeding, trigger, and possible spread of respiratory viruses.

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We acknowledge the keen interest and accurate reporting of our predecessors, who kept their nerve in the midst of an ugly pandemic and the carnage of war.

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BMJ archive: the videos

Late last year the journal's full archive was uploaded on to bmj.com, enabling readers to trawl 169 years of articles, letters, and research papers direct from the website. Suddenly, luminaries such as John Snow, David Livingstone, Arthur Conan Doyle, and Florence Nightingale can be found through a simple search.

But we wanted to do more to bring such figures and their contributions to life. Given the success of a

short video we commissioned last Christmas to accompany a paper on Oliver Twist's workhouse diet, we approached the science producer Martin Freeth.

He enlisted the neurobiologist Colin Blakemore, former head of the UK's Medical Research Council, to present two films, *The Evidence*, and *The Stories*, which provide an overview of the archive and its historic significance. After these we commissioned seven further films, each one devoted to a separate study or series of clinical studies.

One of the films we commissioned gained poignancy last month with the death of the respiratory specialist John Crofton, at the age of 97. A few months earlier Professor Blakemore had interviewed Crofton about using streptomycin to treat tuberculosis. The two talked about the importance of randomisation

and blinding and how this has helped to make medicine more evidence based.

You can watch all nine films at http://bmj.com/video. Did we choose the right lives to feature? Would you have included any others? Tell us by responding to this article at bmj.com.

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Ingested foreign bodies and societal wealth: three year observational study of swallowed coins

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Abstract

Objective To examine the relation between coins ingested by children and the Dow Jones Industrial Average. **Design** Observational study.

Main outcome measures Total value of coins ingested and number of incidents of coins versus other objects swallowed, measured before and after the stock market crash of October 2008.

Results Eighteen objects, including 11 coins, were ingested (NASDAQ (numismatic and sundry detritus acquired) composite of 18). The total value of the 11 coins swallowed was \$1.03 (FTSE 100 (fraction of the US\$ or 100 cents) index of 103). The pecuniary extraction ratio (PE ratio) was 0.57 (9/16). Comparing values for a period before and after October 2008, the mean monthly NASDAQ composite (0.41 (SD 0.67) v 0.5 (0.85), P=0.75), FTSE 100 index in cents (2.3 (6.8) v 3.1 (7.8), P=0.77), and PE ratio (0.54 (0.52) v 0.66 (0.29), P=0.50) did not change. The mean end-of-month closing value of the Dow Jones, however, decreased significantly (12 537 (841.4) v 8388 (699.8), Px0.001)

Conclusion There was no detectable difference in the total value of coins ingested, or ratio of coins to other objects swallowed, before or after a massive stock market crash.

Introduction

Aspiration and ingestion of foreign objects are well recognised problems in young children.¹ One festive Australian toddler aspirated a plastic Christmas tree,2 while around Guy Fawkes Day British children prefer fireworks.³ The culinarily more sophisticated Italians reported an aspirated lobster antenna,4 while an adventurous American 2 year old staying at a roadside motel aspirated an unfortunate cockroach, which remained undetected for three days.5 Coins are a common foreign object swallowed by small children. 6 Historically, the frank, mark, guilder, lira, drachma, and other currencies went down best in Europe, but the introduction of the euro saw a wave of new paediatric euroaspirants.⁷⁻⁹ As the offending objects therefore reflect the environment, we hypothesised that the trickle down effect from the stock market, good or bad, would be reflected in what trickles down the paediatric oesophagus.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Small children often swallow coins

The stock market valuations have been extremely volatile in recent years

WHAT THIS STUDY ADDS

Children decrease the supply of coins in circulation It is difficult to detect the plausible association between the value of the stock market and the value of coins children ingest

We therefore examined the relation of coins ingested to the Dow Jones Industrial Average.

Methods

After ensuring that our institutional review board had a well developed sense of humour, we compiled data on all numismatic and sundry detritus acquired (NASDAQ composite index) from children's gastrointestinal tracts by the paediatric gastroenterology service at our hospital between August 2006 and July 2009. We identified these from the computerised records of the endoscopy suite. No patients were excluded. We calculated the financial total swallowed and extracted as a fraction of the US\$ or 100 cents (FTSE 100 index), and the ratio of patients with coins versus all those with foreign objects removed (pecuniary extraction ratio, PE ratio). We calculated the mean end-of-month closing value of the Dow Jones Industrial Average. 10 We examined whether there was a change in the monthly mean NASDAQ, FTSE, and PE ratio before and after the collapse of the Dow Jones Industrial Average of October 2008. We used a two sample t test, assuming unequal variances.

Results

The patients were aged 1 to 15 years. The NASDAQ composite index was 18. Eleven coins were retrieved from nine patients: three pennies (or cents), five nickels (1 nickel=5 cents), no dimes (1 dime=10 cents), and three quarters (1 quarter=25 cents), giving a total return on ingestment for the period, or FTSE 100 index, of \$1.03. Seven other objects in seven children included an unsafe safety pin (open), a battery, a marble, a ballbearing, a magnet, a dentist's guard, and a rubber doorstopper. The PE ratio was therefore 0.57 (9/16). The table shows data before and after the stock market collapse.

Discussion

We examined the value of coins ingested by children during a time of profound changes in the stock market valuation. We found no change in the FTSE 100 index (2.3 ν 3.1, P=0.77) or PE ratio (0.54 ν 0.66, P=0.5) during a period of dramatic alterations in Dow Jones (12 537 ν 8388, P<0.0001), despite the NASDAQ composite index remaining stable (0.4 ν 0.5, P=0.75). In other words, despite a massive swing in the stock market there was no concomitant absolute or relative change in paediatric wealth intake against an unaltered background rate of foreign body ingestion.

Strengths and limitations

We used a sensitive and well recognised marker of environmental conditions: the objects ingested by children. $^{1-5}$ $^{7-9}$ Indeed, the validity of this model is illustrated by the fact that our 27% penny aspiration rate (n=3/11) was lower than the 36% penny pinching rate reported in 1982.

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Fig 1 | X ray pictures can easily detect an ingested coin. Position of coin on lateral view (left), relative to anterior (right) or posterior picture affects size of image on film (Madoff effect)





Fig 2 | Coin denominations extracted



This is exactly as one would predict, given inflation rates over time. Our inability to detect a change in coin ingestion might, however, be credited to a unique confounder expected to influence both the risk factor (changes in stock market value) and the societal wealth marker (paediatric coin ingestion): the supply of credit. A reduction in credit supply will mean that, to meet household obligations, the use of relatively difficult to ingest credit cards will be swapped for more palatable hard cash denomination. This credit denomination swap obligation could result in a paradoxical increase in the rate of paediatric wealth consumption, while lack of credit simultaneously restricts economic growth and depresses the stock market. This potential confounder might influence the risk factor and the societal wealth marker in opposite directions, hence masking a relation between them.

Other studies

Despite the thousands of articles about aerodigestive foreign bodies, there is surprising little gastropecuniary literature. This might be because of non-standardisation of numisluminal terminology and measurement. East of the Atlantic, the diphthong is widely used (oesophagus, aetiology, paediatric, for example), while on the western fringes (edema, anesthesia, humor, by illustration), its employment is typically limited to Miami Beach. The introduction

Objects ingested before and after collapse of stock market. Values are means (SD) unless stated otherwise

Value	Before October 2008	After October 2008	Pvalue
Dow Jones Industrial Average	12 537 (841.4)	8388 (699.8)	<0.001
NASDAQ composite index	13	5	_
Monthly mean	0.41 (0.67)	0.5 (0.85)	0.75
FTSE 100 index (US\$)	0.72	0.31	_
Monthly mean (cents)	2.3 (6.8)	3.1 (7.8)	0.77
PE ratio	0.54 (0.52)	0.66 (0.29)	0.50

 $NASDAQ = numismatic \ and \ sundry \ detritus \ acquired \ from \ gastrointestinal \ tract;$ FTSE 100=full total swallowed and extracted, as fraction of US\$ or 100 cents.

of the euro brought a welcome standardisation of units of ingestion, at least in the eurozone. $^{7.9}$

Clinical practice

The fate of an aspirated coin can be followed on x ray film to see what develops. The asymptomatic child can be re-examined later to see if there is any change, but symptomatic coins or those lodged in the oesophagus need to be removed. The positioning of the x ray plate affects the image, 11 such that, for example, an anterior-posterior view can produce an apparent increase in the size, and hence value, of deposits in the anterior abdomen (the Madoff effect) (fig 1). A small overestimation of the diameter of a penny can lead to the misassumption that it is a nickel (5c), or similarly that a nickel is a quarter (25c), a Madoff effect of 400% (fig 2). While this insider information might be marginally more reliable than a parliamentarian's expense account, this insight can be turned to good use when wagering on the value of the coin to be extracted. Parenthetically, before placing one's retirement funds on gastroesophaegal futures or derivatives, attention should be directed to the more proximal gastrointestinal tract to ensure the tongue is firmly in the cheek.

Further details on how our findings could affect an economy's money supply can be found on bmj.com.

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Competing interests: The desires of the authors to earn Wall Street salaries conflict with their jobs in academic medicine.

Ethical approval: A member of the institutional review board of the Massachusetts General Hospital thoroughly approved of this study. Data sharing: No additional data available.

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