World Conference On Research Integrity

"TO PUBLISH OR NOT TO PUBLISH: COMMUNICATING SCIENCE IN A NEW GLOBAL AND FINANCIAL ENVIRONMENT"

J Lobo Antunes MD PhD FACS

Lisbon, 16-19 September, 2007

Henry Oldenburg (1617-1677)
founder of Royal Society

- "Philosophical Transactions: giving some Accompt of the Present Undertakings, Studies and Labours of the Ingenious in Many Considerable Parts of the World" March 6, 1665
- *"... That a proper person might be found out to discover plagiarys and to assert inventions to their proper authors"*

Newton

(1643-1727)

- Between 1665 and 1666 Isaac Newton on retreat at his country estate invented calculus which he called the method of fluxions and fluents, but did not feel the need to publish it.

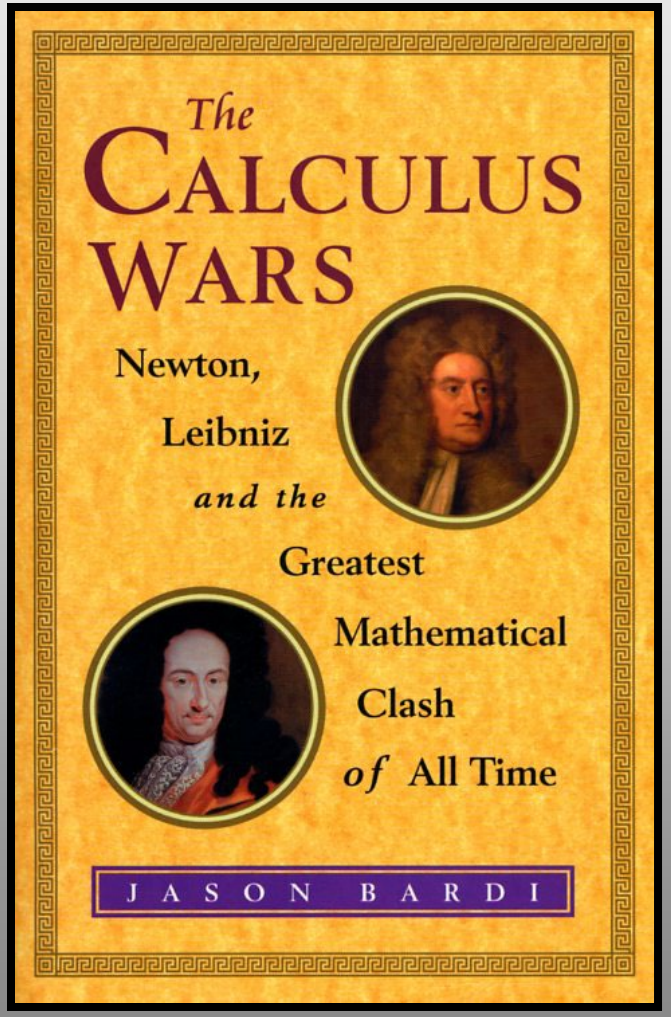
  He rather preferred to write his "New theory about light and colors" published in the Philosophical Transactions on Feb. 19, 1672

Leibniz

(1646-1716)

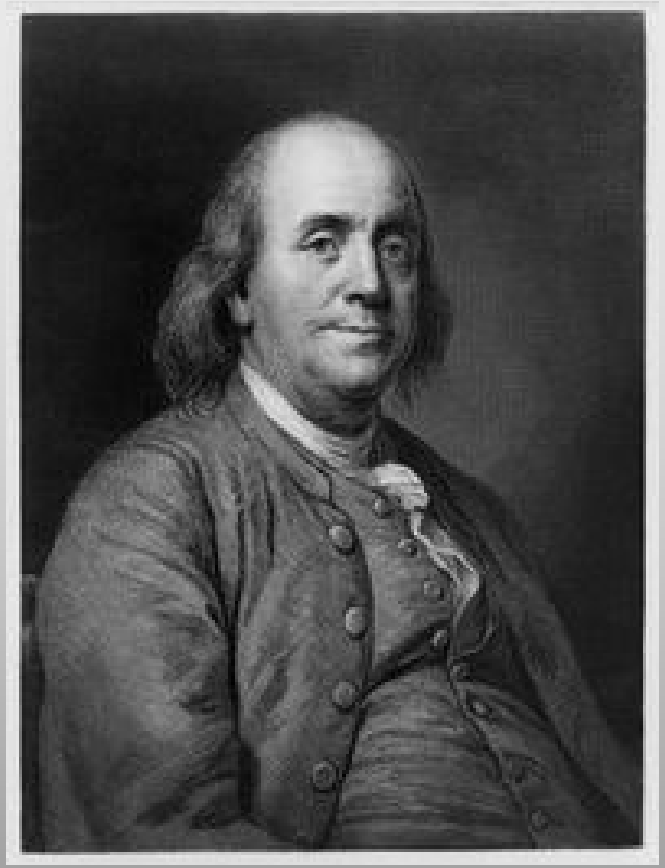
- In 1675, while in Paris, Gottfried Wilhelm Leibniz independently invented calculus and the notations still used today. We waited ten years to publish it.

- In mean time Newton wrote very kindly of Leibniz: (his method) “is certainly extremely elegant and would sufficiently display the writer’s genius even if he should write nothing else”.
- However, he concealed some of his own data, “Because I cannot proceed with the explanation now. I have prefered to conceal it thus: 6 accdoe 13 eff 7i 319 n 404 qrr 4s8t 12ux”. (He translated this 20 years later!)



In 1711 the CALCULUS WAR exploded

- Newton – “Commercium Epistolicum”
- Leibniz – “Charta Volans”

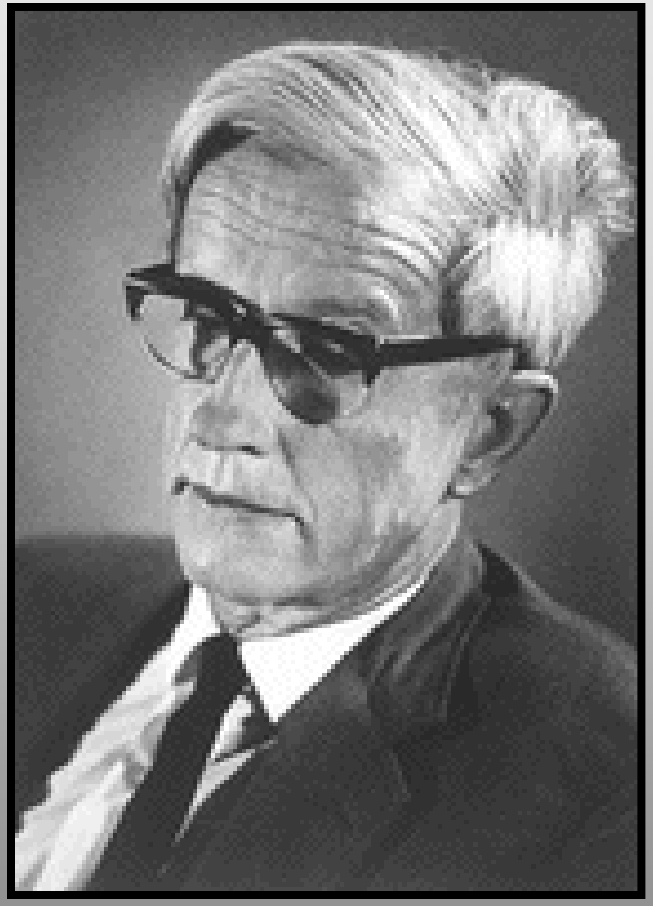


“TO STUDY, TO FINISH, TO PUBLISH”

Benjamim Franklin

Science does not exist until it is published.

Drummond Rennie. Lancet 1998;352:SII18



Max Delbrück

(1906-1981)

Nobel speech, 1969

- “The artist’s communication is linked forever with its original form, that of the scientist is modified, amplified, fused with the ideas and results of others, and melts into the stream of knowledge.”

“The Audit Society”

Publications are fundamental units of information exchange, proof of productivity and creativity, and bases for future research and development

Academic promotion
- Productivity (quantity)
- Independence (first or senior authorship)
- Significance (impact factors)

World's twenty most prolific researchers

	Name/Field/Nation	No. papers* 1981-90	Ave. days per paper	Ave. citations per paper
1	Yury Struchkov/Chemistry/USSR	948	3.9	3.0
2	Stephen Bloom/Gastroenterology/UK	773	4.7	21.4
3	Mikhail Voronkov/Chemistry/USSR	711	5.1	2.0
4	Aleksandr Prokhorov/Physics/USSR	589	6.2	3.1
5	Ferdinand Bohlmann/Chemistry/Germany	572	6.4	6.2
6	Thomas Starzl/Surgery/USA	503	7.3	16.8
7	Frank Cotton/Chemistry/USA	451	8.1	11.4
8	Julia Polak/Histochemistry/UK	436	8.4	26.6
9	Robert Gallo/Cell Biology/USA	428	8.5	86.0
10	Genrikh Tolstikov/Chemistry/USSR	427	8.5	1.2
11	John Huffman/Crystallography/USA	403	9.1	13.2
12	Alan Katritzky/Chemistry/USA	403	9.1	4.5
13	David Greenblatt/Pharmacology/USA	383	9.5	17.1
14	John Najarian/Surgery/USA	345	10.6	14.6
15	Willy Jean Malaisse/Endocrinology/Belgium	344	10.6	10.9
16	Charles Marsden/Neurology/UK	339	10.8	15.0
17	Anthony Fauci/Immunology/USA	338	10.8	52.5
18	E. Donnall Thomas/Oncology/USA	328	11.1	37.5
19	Noboru Yanaihara/Biochemistry/Japan	322	11.3	14.0
20	Timothy Peters/Biochemistry/UK	322	11.3	9.5

Source: ISI's Science Indicators Database 1981-90.

* papers defined as articles, reviews, notes and proceeding papers; abstracts, letters, corrections, etc. were not counted.

The record Paul Erdös 1400 papers, 500 co-authors?

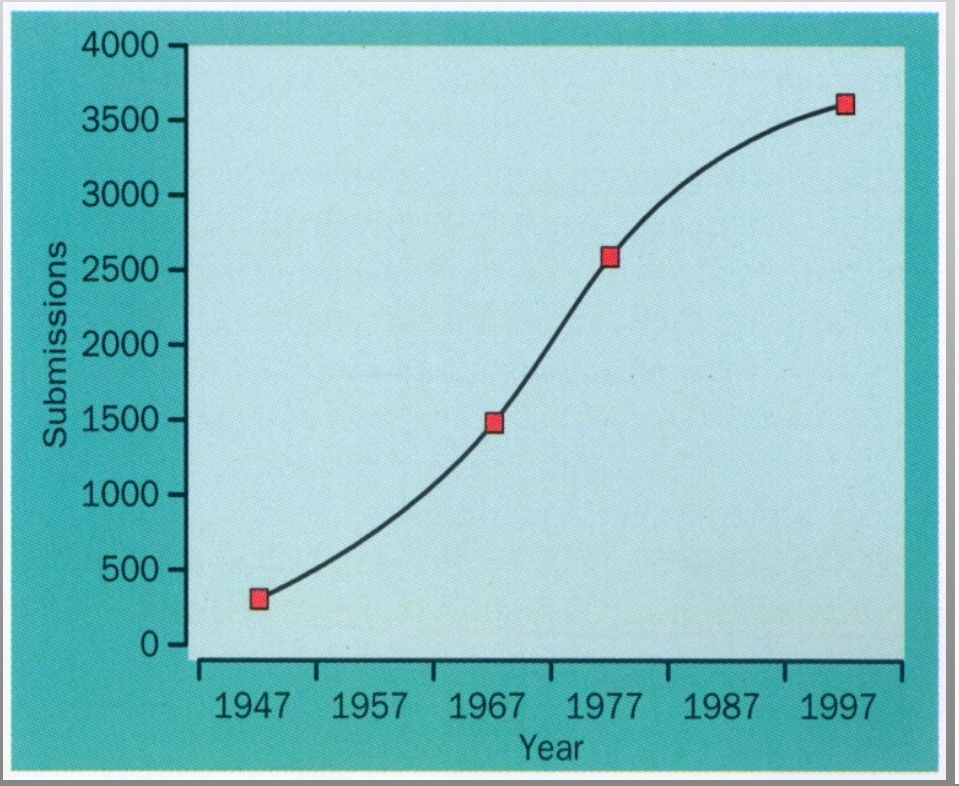
A few interesting numbers…

- 27% of the scientific papers are never cited
- Papers published 1955 – 1987 30 million
  55.7% 1 citation
  79,9% no more than 4
- Papers published in Nature 1999
  citations in 2001 – 10 % (80 papers) = half of citations

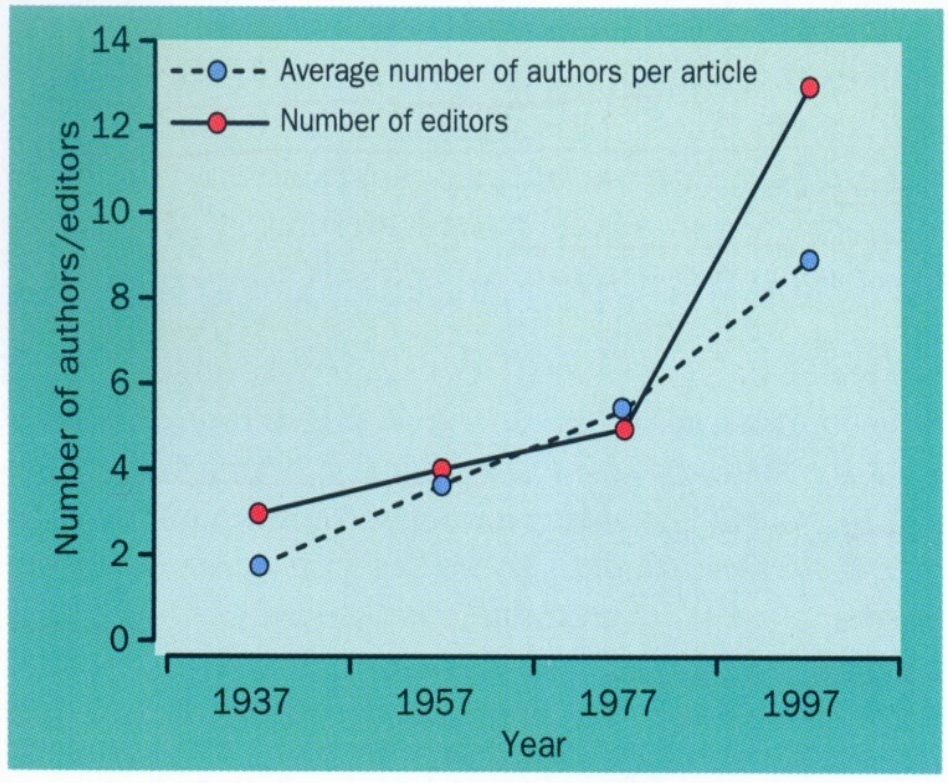
If 2/3 of accepted papers were replaced by 2/3 of the rejected, the quality of the journal would not alter
(Adair et al. Phys Rev Letters 43:1969, 1979)

There are more >16000 medical journals

Manuscripts submitted to NEJM



Authors/article and Editors do NEJM



Drummond Rennie. Lancet 1998;352:SII18

The New England
Journal of Medicine

Volume 329 SEPTEMBER 2, 1993 Number 10

AN INTERNATIONAL RANDOMIZED TRIAL COMPARING FOUR THROMBOLYTIC STRATEGIES FOR ACUTE MYOCARDIAL INFARCTION

THE GUSTO INVESTIGATORS*

Abstract *Background.* The relative efficacy of streptokinase and tissue plasminogen activator and the roles of intravenous as compared with subcutaneous heparin as adjunctive therapy in acute myocardial infarction are unresolved questions. The current trial was designed to compare new, aggressive thrombolytic strategies with standard thrombolytic regimens in the treatment of acute myocardial infarction. Our hypothesis was that newer thrombolytic strategies that produce earlier and sustained reperfusion would improve survival.

Methods. In 15 countries and 1081 hospitals, 41,021 patients with evolving myocardial infarction were randomly assigned to four different thrombolytic strategies, consisting of the use of streptokinase and subcutaneous heparin, streptokinase and intravenous heparin, accelerated tissue plasminogen activator (t-PA) and intravenous heparin, or a combination of streptokinase plus t-PA with intravenous heparin. ("Accelerated" refers to the administration of t-PA over a period of 1½ hours — with two thirds of the dose given in the first 30 minutes — rather than the conventional period of 3 hours.) The primary end point was 30-day mortality.

Results. The mo

groups were as follows: streptokinase and subcutaneous heparin, 7.2 percent; streptokinase and intravenous heparin, 7.4 percent; accelerated t-PA and intravenous heparin, 6.3 percent; and the combination of both thrombolytic agents with intravenous heparin, 7.0 percent. This represented a 14 percent reduction (95 percent confidence interval, 5.9 to 21.3 percent) in mortality for accelerated t-PA as compared with the two streptokinase-only strategies ($P = 0.001$). The rates of hemorrhagic stroke were 0.49 percent, 0.54 percent, 0.72 percent, and 0.94 percent in the four groups, respectively, which represented a significant excess of hemorrhagic strokes for accelerated t-PA ($P = 0.03$) and for the combination strategy ($P<0.001$), as compared with streptokinase only. A combined end point of death or disabling stroke was significantly lower in the accelerated–t-PA group than in the streptokinase-only groups (6.9 percent vs. 7.8 percent, $P = 0.006$).

Conclusions. The findings of this large-scale trial indicate that accelerated t-PA given with intravenous heparin provides a survival benefit over previous standard thrombolytic regimens. (N Engl J Med 1993;329:

972 authors

2 words/author

SINCE the landm
nase by the Gr
Streptochinasi nell'
1986,[1] there has b
thrombolytic regim
benefit in patients
except for the important addition of aspirin.[2] Collectively, the large trials of thrombolytic therapy demonstrated a 25 percent reduction in 30-to-35-day mortality in patients presenting to the hospital within six hours of the onset of symptoms.[3] Neither the GISSI-2/International trial nor the Third International Study of Infarct Survival (ISIS-3) trial[4-6] of

tients found a difference in associ-
een the use of streptokinase and
asminogen activator (t-PA)[4,5] or
these agents and that of anistre-
, the addition of subcutaneous
nens did not significantly reduce mortality as compared with no use of heparin.[5,6] Although clear differences between thrombolytic agents are evident in the speed with which the agents achieve reperfusion, the similar survival rates in these previous trials suggested that factors other than rapid or sustained coronary reperfusion might be important in reducing mortality.

Recent data suggest that more rapid and effective infarct-artery patency can be achieved with accelerated t-PA,[7-9] that lower rates of reocclusion are observed with the use of combination thrombolytic therapy,[10-12] and that infarct-artery patency can be sustained longer with the use of intravenous heparin as an adjunct to thrombolytic therapy.[13-15] ("Accelerated" t-PA refers to the rapid intravenous administra-

Address reprint requests to Dr. Eric Topol at the Department of Cardiology, One Clinic Center, Cleveland Clinic Foundation, Cleveland, OH 44195.

Supported by a combined grant from Bayer, CIBA-Corning, Genentech, ICI Pharmaceuticals, and Sanofi Pharmaceuticals.

Dr. Topol, as chairman of the study, assumes full responsibility for the overall content and integrity of the manuscript.

*A list of the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) investigators appears in the Appendix.

The Politics of Publication*

- The journal more important than the message
- The craze for publicity

Short letter to Nature or report to Science better than full article in a more specialized journal

- Salami publication – Minimal Publishable Unit (MPU)
- Some tips – trendy stock phrases (“paradigm”)
  – tenous link to human disease

* Peter Lawrence.
Nature 422:259, 2003

The Malefices of Covert Duplicate Publication

Example

Ondasetron on post-operative emesis

9 trials published in 14 further reports duplicating data from 3325 patients

Inclusion of duplicate data in meta-analysis led to a 23% overestimation of the drugs antiemetic efficacy

Tramer et al. Brit Med J 315:635, 1997

- Pub Med 2000-2002

- 400,000 78 retracted articles (0.02%)

Table 1 | Percentage of scientists who say that they engaged in the behaviour listed within the previous three years ($n = 3,247$)

Top ten behaviours	All	Mid-career	Early-career
1. Falsifying or 'cooking' research data	0.3	0.2	0.5
2. Ignoring major aspects of human-subject requirements	0.3	0.3	0.4
3. Not properly disclosing involvement in firms whose products are based on one's own research	0.3	0.4	0.3
4. Relationships with students, research subjects or clients that may be interpreted as questionable	1.4	1.3	1.4
5. Using another's ideas without obtaining permission or giving due credit	1.4	1.7	1.0
6. Unauthorized use of confidential information in connection with one's own research	1.7	2.4	0.8 ***
7. Failing to present data that contradict one's own previous research	6.0	6.5	5.3
8. Circumventing certain minor aspects of human-subject requirements	7.6	9.0	6.0 **
9. Overlooking others' use of flawed data or questionable interpretation of data	12.5	12.2	12.8
10. Changing the design, methodology or results of a study in response to pressure from a funding source	15.5	20.6	9.5 ***
Other behaviours			
11. Publishing the same data or results in two or more publications	4.7	5.9	3.4 **
12. Inappropriately assigning authorship credit	10.0	12.3	7.4 ***
13. Withholding details of methodology or results in papers or proposals	10.8	12.4	8.9 **
14. Using inadequate or inappropriate research designs	13.5	14.6	12.2
15. Dropping observations or data points from analyses based on a gut feeling that they were inaccurate	15.3	14.3	16.5
16. Inadequate record keeping related to research projects	27.5	27.7	27.3

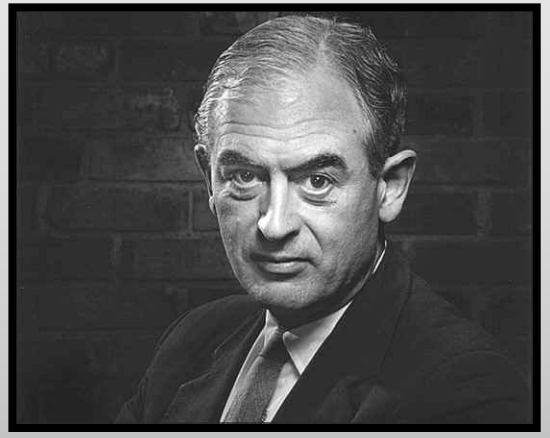
Note: significance of χ^2 tests of differences between mid- and early-career scientists are noted by ** ($P < 0.01$) and *** ($P < 0.001$).

33% admitted one or more of the top 10

Response rate Mid career 52% Early career 43%

B. C. Martinson et al Scientists behaving badly Nature 435:737, 2005

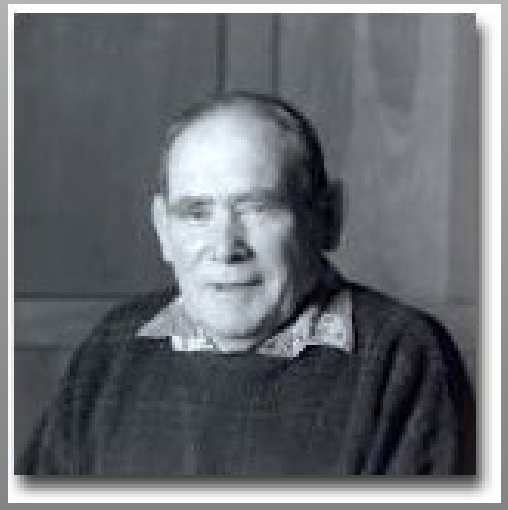
Why do they cheat



1915-1987

- Hunger for scientific reputation and the esteem of colleagues
- The passionate belief in the truth and significance of a theory or hypothesis which is disregarded or not believed

Peter Medawar “Scientific Fraud”
In “The threat and the Glory”



1927-

- Is the product of the work structure, because we now have a managerial structure
- There is the problem of the scientist who gets hold of an idea that he then falls in love with and can’t let go

Sidney Brenner “My life in Science”

Gate-Keepers
The Peer-review system

Rate of acceptance JAMA 9%
Academic Medicine 15%
Nature 5%

Remote
Mysteriously
Crude
Understudied

but indispensable

The pitfalls – Confirmatory bias

Bias against negative results

86% of unpublished trials have negative results

45% of published trials have negative results

Give disproportionate credit to the already famous

Orientation and theoretical persuasion

The politically correct

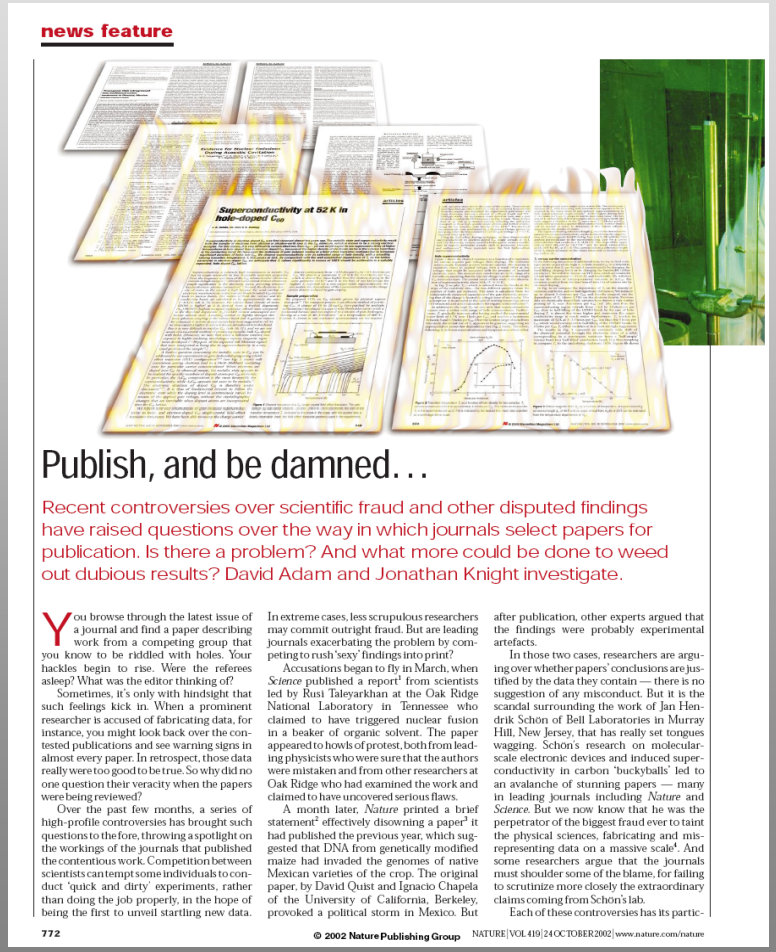
Conflicts of interest [competitors antagonists]

Agreement between referees 10-15%

Blinding is not the solution. The authors can be guessed in 46% of manuscripts!

(JAMA 272: 143, 1994)

Pressure to publish
Unhealthy competition?



news feature

Publish, and be damned…

Recent controversies over scientific fraud and other disputed findings have raised questions over the way in which journals select papers for publication. Is there a problem? And what more could be done to weed out dubious results? David Adam and Jonathan Knight investigate.

You browse through the latest issue of a journal and find a paper describing work from a competing group that you know to be riddled with holes. Your hackles begin to rise. Were the referees asleep? What was the editor thinking of?

Sometimes, it's only with hindsight that such feelings kick in. When a prominent researcher is accused of fabricating data, for instance, you might look back over the contested publications and see warning signs in almost every paper. In retrospect, those data really were too good to be true. So why did no one question their veracity when the papers were being reviewed?

Over the past few months, a series of high-profile controversies has brought such questions to the fore, throwing a spotlight on the workings of the journals that published the contentious work. Competition between scientists can tempt some individuals to conduct 'quick and dirty' experiments, rather than doing the job properly, in the hope of being the first to unveil startling new data. In extreme cases, less scrupulous researchers may commit outright fraud. But are leading journals exacerbating the problem by competing to rush 'sexy' findings into print?

Accusations began to fly in March, when *Science* published a report[1] from scientists led by Rusi Taleyarkhan at the Oak Ridge National Laboratory in Tennessee who claimed to have triggered nuclear fusion in a beaker of organic solvent. The paper appeared to howls of protest, both from leading physicists who were sure that the authors were mistaken and from other researchers at Oak Ridge who had examined the work and claimed to have uncovered serious flaws.

A month later, *Nature* printed a brief statement[2] effectively disowning a paper[3] it had published the previous year, which suggested that DNA from genetically modified maize had invaded the genomes of native Mexican varieties of the crop. The original paper, by David Quist and Ignacio Chapela of the University of California, Berkeley, provoked a political storm in Mexico. But after publication, other experts argued that the findings were probably experimental artefacts.

In those two cases, researchers are arguing over whether papers' conclusions are justified by the data they contain — there is no suggestion of any misconduct. But it is the scandal surrounding the work of Jan Hendrik Schön of Bell Laboratories in Murray Hill, New Jersey, that has really set tongues wagging. Schön's research on molecular-scale electronic devices and induced superconductivity in carbon 'buckyballs' led to an avalanche of stunning papers — many in leading journals including *Nature* and *Science*. But we now know that he was the perpetrator of the biggest fraud ever to taint the physical sciences, fabricating and misrepresenting data on a massive scale[4]. And some researchers argue that the journals must shoulder some of the blame, for failing to scrutinize more closely the extraordinary claims coming from Schön's lab.

Each of these controversies has its partic-

The Schön Scandal

- "They chose reviewers who they knew to be positive (...) They did not allow their experiments to be reproduced"

  Robert Laughtin

  (Nobel Prize physics)

- "Given the exciting claims made by the papers, we were certainly hoping that the outcomes would be positive"

  Karl Ziemeli

  (Chief physical sciences editor, Nature)

The Editors' Pressure

Manipulation of the impact factor of the journal, encouraging the citation of other papers published in the journal (*)

and yet

"Impact factors tell you more about sociology of science than about science itself"

S. Brenner

(*) (M. Farthing, Science and Engineering Ethics 12:45-52, 2006)

Pressures To Delay or Prevent Publication

The values

- Communalism
- Shared ownership
- Free exchange of methods and results

The pressures

- Personal – competion for priority, recognition and funding
- External – commercial patenting

Forbidden knowedge

Competing goals in medical research

Academic investigators – Publication in peer-reviewed journals

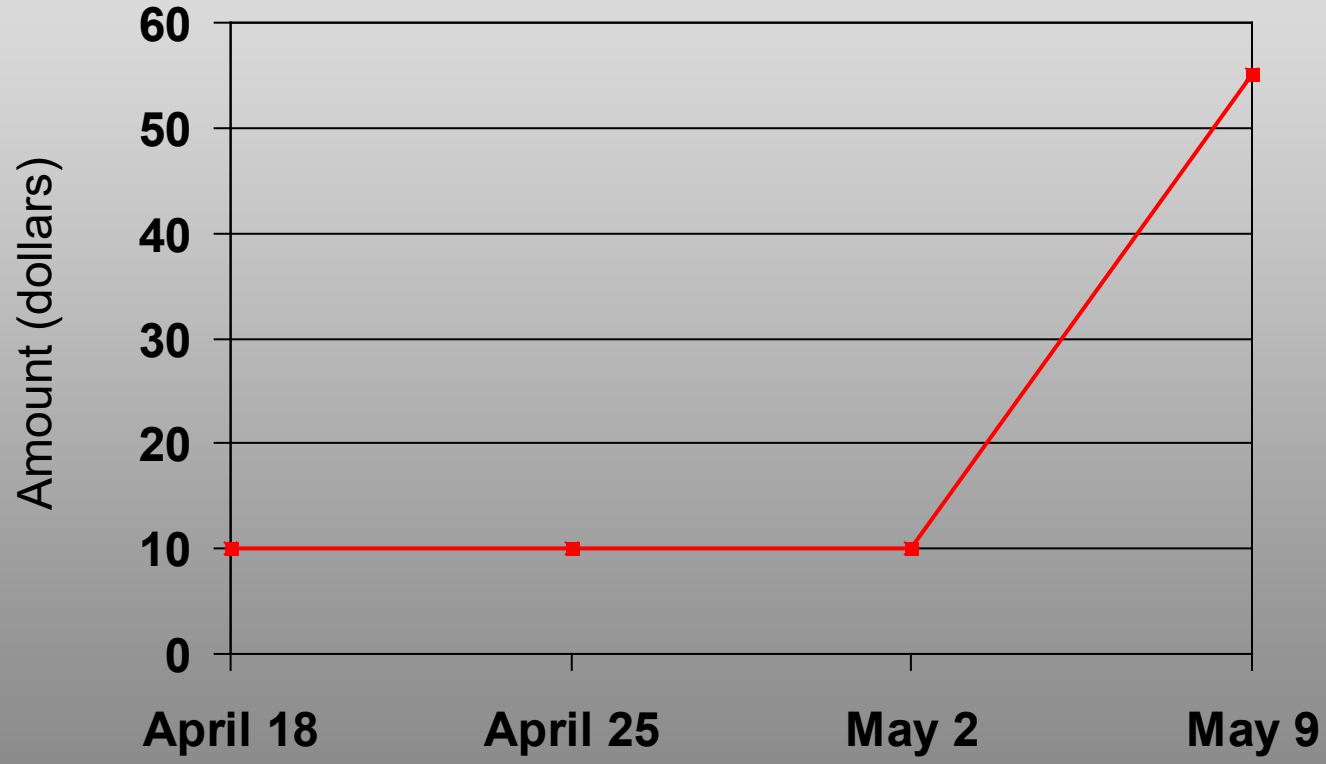
Industry – Approval and marketing of drug.
Without approval, publication is not worth a cent.
Publication in prestigious journals important for the marketing

No drug company gives away its stockholders' money in an act of desinterested generosity

Journal of Commercial Molecular Biology

Journal of Commercial Neurobiology

Sidney Brenner "My life in Science"



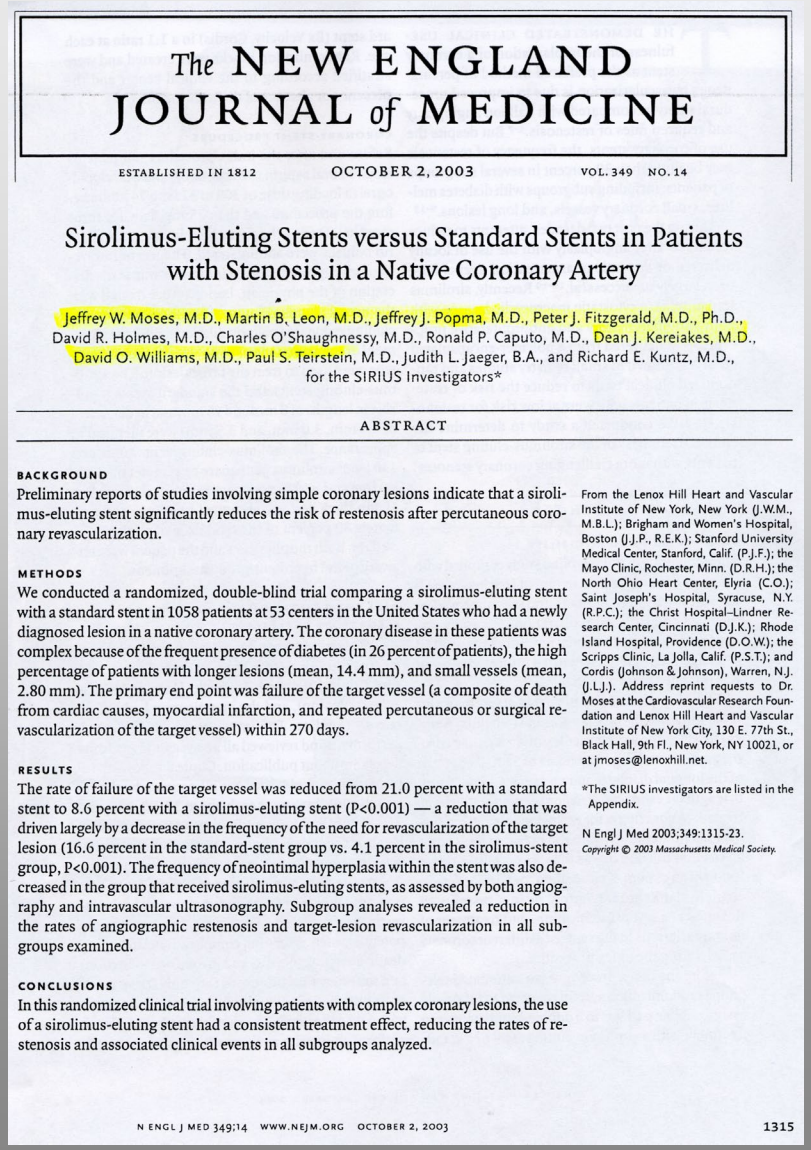
Therapeutic effect. A news report on angiostatin and endostatin's promise did wonders for WEntreMed's stock

Industry support of biomedical research

USA
1980 32%
2000 62%

- Lead authors 1 every 3 articles hold relevant financial interests.*
- In biomedicine, with rare exceptions, is the private sector, not academics that develops diagnostic, therapeutic and preventive products and brings them to market.
- 2/3 of academic institutions hold equity in “start-up” businesses that sponsor research by their faculty

* Quoted in Bekelman et al. JAMA 289:454, 2003



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 2, 2003 VOL. 349 NO. 14

Sirolimus-Eluting Stents versus Standard Stents in Patients with Stenosis in a Native Coronary Artery

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ABSTRACT

BACKGROUND

Preliminary reports of studies involving simple coronary lesions indicate that a sirolimus-eluting stent significantly reduces the risk of restenosis after percutaneous coronary revascularization.

METHODS

We conducted a randomized, double-blind trial comparing a sirolimus-eluting stent with a standard stent in 1058 patients at 53 centers in the United States who had a newly diagnosed lesion in a native coronary artery. The coronary disease in these patients was complex because of the frequent presence of diabetes (in 26 percent of patients), the high percentage of patients with longer lesions (mean, 14.4 mm), and small vessels (mean, 2.80 mm). The primary end point was failure of the target vessel (a composite of death from cardiac causes, myocardial infarction, and repeated percutaneous or surgical revascularization of the target vessel) within 270 days.

RESULTS

The rate of failure of the target vessel was reduced from 21.0 percent with a standard stent to 8.6 percent with a sirolimus-eluting stent ($P<0.001$) — a reduction that was driven largely by a decrease in the frequency of the need for revascularization of the target lesion (16.6 percent in the standard-stent group vs. 4.1 percent in the sirolimus-stent group, $P<0.001$). The frequency of neointimal hyperplasia within the stent was also decreased in the group that received sirolimus-eluting stents, as assessed by both angiography and intravascular ultrasonography. Subgroup analyses revealed a reduction in the rates of angiographic restenosis and target-lesion revascularization in all subgroups examined.

CONCLUSIONS

In this randomized clinical trial involving patients with complex coronary lesions, the use of a sirolimus-eluting stent had a consistent treatment effect, reducing the rates of restenosis and associated clinical events in all subgroups analyzed.

From the Lenox Hill Heart and Vascular Institute of New York, New York (J.W.M., M.B.L.); Brigham and Women's Hospital, Boston (J.J.P., R.E.K.); Stanford University Medical Center, Stanford, Calif. (P.J.F.); the Mayo Clinic, Rochester, Minn. (D.R.H.); the North Ohio Heart Center, Elyria (C.O.); Saint Joseph's Hospital, Syracuse, N.Y. (R.P.C.); the Christ Hospital–Lindner Research Center, Cincinnati (D.J.K.); Rhode Island Hospital, Providence (D.O.W.); the Scripps Clinic, La Jolla, Calif. (P.S.T.); and Cordis (Johnson & Johnson), Warren, N.J. (J.L.J.). Address reprint requests to Dr. Moses at the Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute of New York City, 130 E. 77th St., Black Hall, 9th Fl., New York, NY 10021, or at jmoses@lenoxhill.net.

*The SIRIUS investigators are listed in the Appendix.

N Engl J Med 2003;349:1315-23.

	Consultant	Speaker	Financing	Stockholder
Moses	+	+		+
Leon	+	+		+
Popma	+	+	+	
Fitzgerald	+	+	+	
Kereiakes		+	+	
Williams	+		+	
Teirstein	+	+		+

Study biases

Companies may design studies more likely to favor their products

- Testing in healthier populations (younger, fewer existing or associated pathologies and milder illnesses)
    - (NSAID – 2.1% of patients younger than 65)*
- Comparing with insufficient doses of competing product
- Include many surrogate endpoints and publish results only of those that favor the product.

* Rochon et al. Arch Intern Med 154:157, 1984

Data withholding

- 58% of life science companies that report academic research refrain to publish for more than 6 months
- Data withholding more frequent in human genetics
- Higher publication rates <> withholding
- Scientists in training are discouraged to show data

42% genetic
38% other life sciences

Blumenthal et al Jama 277: 1220, 1997
Blumenthal et al. Acad Med 81: 137, 2006

Preventing Publication

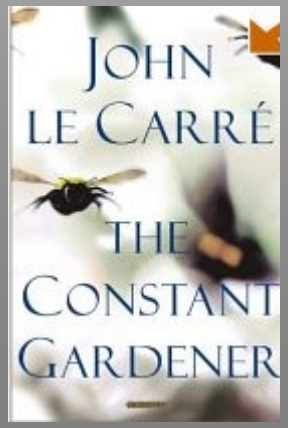
Examples

- The study of bioequivalence of different thyroid preparations (7 year delay)

  Boots – Knoll pharmaceutics (*)

- "The infamous case of Dr. Nancy Olivieri" deferiprone (iron-chelation) in thalassaemia

  Apotex Inc. (**)



(*) Rennie JAMA 277:1238, 1997

(**) Olivieri et al. N Eng Med J 339:417, 1998

A convenient omission

The New England Journal of Medicine

COMPARISON OF UPPER GASTROINTESTINAL TOXICITY OF ROFECOXIB AND NAPROXEN IN PATIENTS WITH RHEUMATOID ARTHRITIS

CLAIRE BOMBARDIER, M.D., LOREN LAINE, M.D., ALISE REICIN, M.D., DEBORAH SHAPIRO, DR.P.H., RUBEN BURGOS-VARGAS, M.D., BARRY DAVIS, M.D., PH.D., RICHARD DAY, M.D., MARCOS BOSI FERRAZ, M.D., PH.D., CHRISTOPHER J. HAWKEY, M.D., MARC C. HOCHBERG, M.D., TORE K. KVIEN, M.D., AND THOMAS J. SCHNITZER, M.D., PH.D., FOR THE VIGOR STUDY GROUP

ABSTRACT

Background Each year, clinical upper gastrointestinal events occur in 2 to 4 percent of patients who are taking nonselective nonsteroidal antiinflammatory drugs (NSAIDs). We assessed whether rofecoxib, a selective inhibitor of cyclooxygenase-2, would be associated with a lower incidence of clinically important upper gastrointestinal events than is the nonselective NSAID naproxen among patients with rheumatoid arthritis.

Methods We randomly assigned 8076 patients who were at least 50 years of age (or at least 40 years of age and receiving long-term glucocorticoid therapy) and who had rheumatoid arthritis to receive either 50 mg of rofecoxib daily or 500 mg of naproxen twice daily. The primary end point was confirmed clinical upper gastrointestinal events (gastroduodenal perforation or obstruction, upper gastrointestinal bleeding, and symptomatic gastroduodenal ulcers).

Results Rofecoxib and naproxen had similar efficacy against rheumatoid arthritis. During a median follow-up of 9.0 months, 2.1 confirmed gastrointestinal events per 100 patient-years occurred with rofecoxib, as compared with 4.5 per 100 patient-years with naproxen (relative risk, 0.5; 95 percent confidence interval, 0.3 to 0.6; $P<0.001$). The respective rates of complicated confirmed events (perforation, obstruction, and severe upper gastrointestinal bleeding) were 0.6 per 100 patient-years and 1.4 per 100 patient-years (relative risk, 0.4; 95 percent confidence interval, 0.2 to 0.8; $P=0.005$). The incidence of myocardial infarction was lower among patients in the naproxen group than among those in the rofecoxib group (0.1 percent vs. 0.4 percent; relative risk, 0.2; 95 percent confidence interval, 0.1 to 0.7); the overall mortality rate and the rate of death from cardiovascular causes were similar in the two groups.

Conclusions In patients with rheumatoid arthritis, treatment with rofecoxib, a selective inhibitor of cyclooxygenase-2, is associated with significantly fewer clinically important upper gastrointestinal events than treatment with naproxen, a nonselective inhibitor. (N Engl J Med 2000;343:1520-8.)

NONSTEROIDAL antiinflammatory drugs (NSAIDs) are among the most commonly used medications in the world.[1] A major factor limiting their use is gastrointestinal toxicity. Although endoscopic studies reveal that gastric or duodenal ulcers develop in 15 to 30 percent of patients who regularly take NSAIDs,[2] the chief concern is clinically important gastrointestinal problems, such as bleeding. It has been estimated that more than 100,000 patients are hospitalized and 16,500 die each year in the United States as a result of NSAID-associated gastrointestinal events.[3,4]

Most NSAIDs inhibit both cyclooxygenase-1 and cyclooxygenase-2, isoenzymes involved in the synthesis of prostaglandins.[5] Cyclooxygenase-1 is constitutively expressed and generates prostanoids involved in the maintenance of the integrity of gastrointestinal mucosa and platelet aggregation,[6] whereas at sites of inflammation, cyclooxygenase-2 is induced to generate prostaglandins that mediate inflammation and pain.[7] The antiinflammatory effects of nonselective NSAIDs (those that inhibit both cyclooxygenase-1 and cyclooxygenase-2) therefore appear to be mediated through the inhibition of cyclooxygenase-2,[8] whereas their harmful effects in the gastrointestinal tract as well as their antiplatelet effects are believed to occur primarily through the inhibition of cyclooxygenase-1.[5]

Agents that selectively inhibit cyclooxygenase-2 have antiinflammatory and analgesic effects that are simi-

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Arthur Weaver, M.D., Arthritis Center of Nebraska, Lincoln, was another author.

A 4x increase in heart atacks was ommitted

The journal sold 929.000 offprints (Revenue $ 679.000 to $ 836,000)

Sponsorship, authorship, and accountability

(The Editors of Ann Int Med, JAMA, New England J Med, Canad MAJ, J Danish M A, Lancet, Medline, etc, Sep 2001)

- When authors submit manuscript they are responsible for disclosing all financial and personal relationships that might bias their work
- Researchers should not enter in agreements that interfere
  - Their access to the data
  - Ability to analyze data independently
  - Prepare manuscripts
  - Publish them

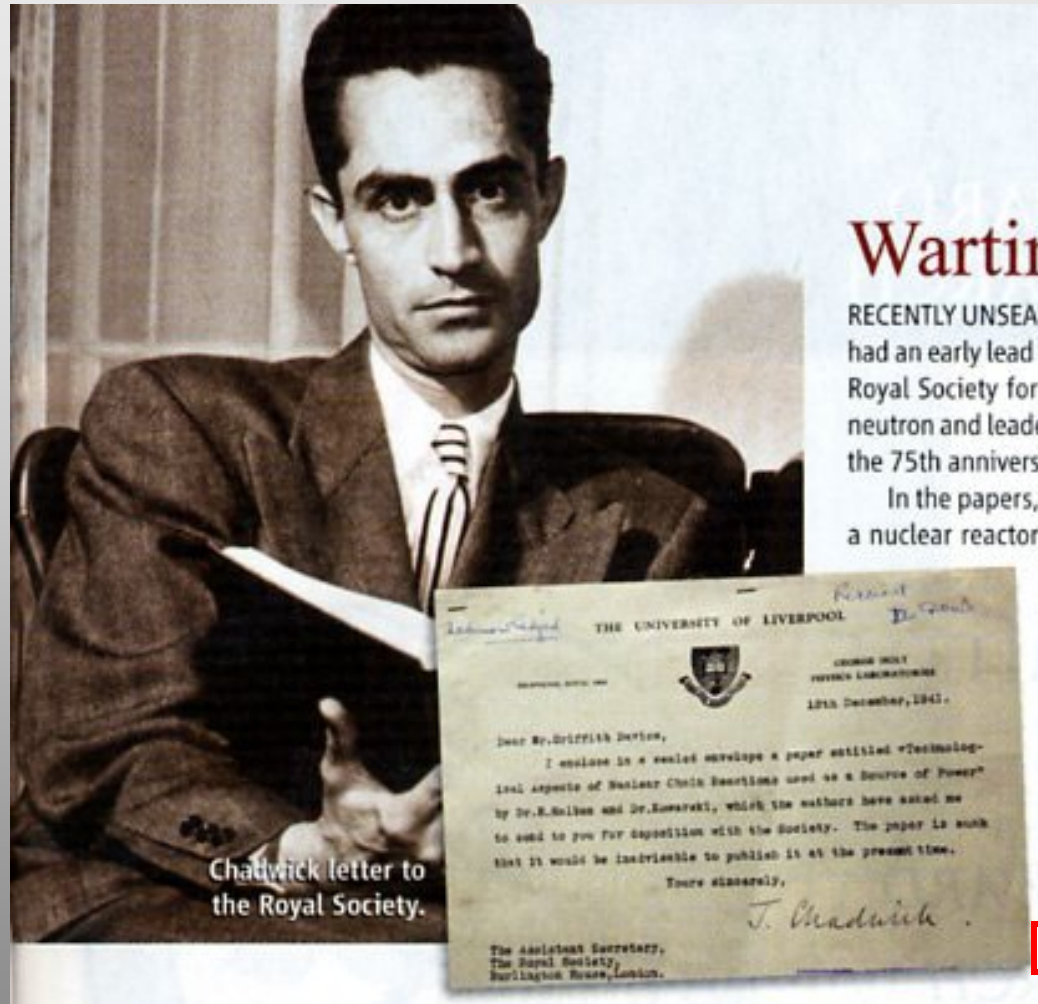
EDITED BY CONSTANCE HOLDEN

Wartime Memories

RECENTLY UNSEALED DOCUMENTS FROM WORLD WAR II ILLUSTRATE that French physicists had an early lead in the race to produce a nuclear reactor. The papers were given to Britain's Royal Society for safekeeping in 1940 and 1941 by James Chadwick, discoverer of the neutron and leader of Britain's wartime nuclear research. The society opened them to honor the 75th anniversary of Chadwick's Nobel Prize–winning discovery.

In the papers, French citizens Hans von Halban and Lew Kowarski discuss how to make a nuclear reactor and generate plutonium. Before fleeing to Britain, the pair worked in Paris with Frédéric Joliot-Curie. After German scientists discovered nuclear fission in 1939, the three realized it should be possible to make a reactor to generate power and patented the idea.

Halban and Kowarski likely gave the papers to Chadwick to establish the priority of their findings, says Chadwick biographer Andrew Brown, a research fellow at Harvard's John F. Kennedy School of Government. During the war, researchers couldn't publish results for fear of revealing secrets, and many looked to Chadwick, known for his integrity, to keep tabs on their work. Ironically, Brown says, Chadwick took a dim view of priority squabbles: "He thought that people shouldn't be concerned with their reputations when the survival of the country was at stake."



Chadwick letter to the Royal Society.

Science June 8th 2007

Forbidden knowledge

Articles we would rather not see published

- How to build your own atomic bomb *
- How to modify Influenza virus to relase snake venom
- Ten easy modifications of the E.coli genome
- How to modify small pox to counteract the smallpox vaccine
- How to build self guiding, low flying air plane using inexpensive aircraft computer, GPS and a notebook computer

* Nate Ciccolo, 15 year-old high school student built a papier-maché model very accurate. He found 563 web pages on atomic bomb design!

(Adapted from Ray Kurzweil: “Promise and Peril” in “Living with the Genie, ed Alen Ligthman et al. 2003)

Forbidden Knowledge

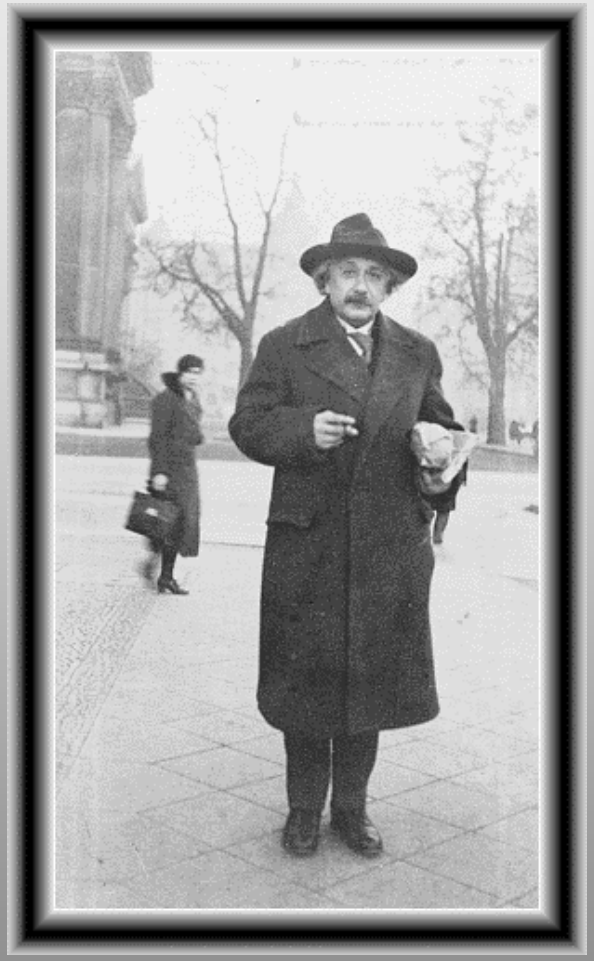
- Inacessible, unattainable
- Prohibited by religious, moral or secular authority
- Dangerous, destructive
- Fragile, delicate
- Double – bound
- Ambiguous
- Consciousness, free will
- Reproductive clonning, stem cell research
- Atomic bomb, bioweapons
- Particles & waves afected by the act of observation
- “Knowledge about a thing is not the thing itself” (W.James)
- The “political” science

(adapted from Roger Shattuck “Forbidden Knowledge”, 1996)

"Scientific" has become an all purpose term of epistemic praise meaning "strong, reliable, good"

and yet...

like all human enterprises it is thoroughly fallible, imperfect, uneven in its achievements, often fumbling, sometimes corrupt, and of course incomplete



Albert Einstein

“Many people say that is the intellect which makes a great scientist.

They are wrong: it is character”