Ethics in science

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Science and evolution

Living creatures have evolved the ability

(a) to act in ways that further their own interests; and

(b) in order to provide a reliable basis for action, to construct rational explanations of the world.

2

Science is a social activity

Doing science involves learning from others

and

communicating with others

3

Modern science is a peculiarly human activity

It is a form of goal-directed behaviour
undertaken for many reasons:

curiosity, need, acclaim, rewards…

4

As with social behaviour in general,
notions of Nyâya and Neeti
enter into discussions of scientific activity.

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Why has scientific ethics not attracted much attention until recently?

Ethical conduct has been assumed to be intrinsic to science. At the same time, because of the supposed self-correcting nature of scientific activity, lapses from ethical behaviour are assumed not to have serious consequences.

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Implicitly accepted norms

1. Honesty in communication.
2. Not copying from someone else – or from oneself.
3. Giving appropriate credit to others.

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Examples of unethical behaviour

Research misconduct is defined as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT GLOBAL SCIENCE FORUM
Unofficial Report on Best Practices for Ensuring Scientific Integrity and Preventing Misconduct

Based on a Workshop held on 22-23 February, 2007, in Tokyo, Japan
[ALSO: Grant review, Peer review, Manipulating funds,…]

"Even on the rare occasions when scientists do falsify data, they almost never do so with the active intent to introduce false information into the body of scientific knowledge. Rather, they intend to introduce a fact that they believe is true, without going to the trouble and difficulty of actually performing the experiments required."

(http://en.wikipedia.org/wiki/Scientific_misconduct)

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Andrea Pozzi* & Paul A. David**

**Stanford University* : pozzi@stanford.edu*

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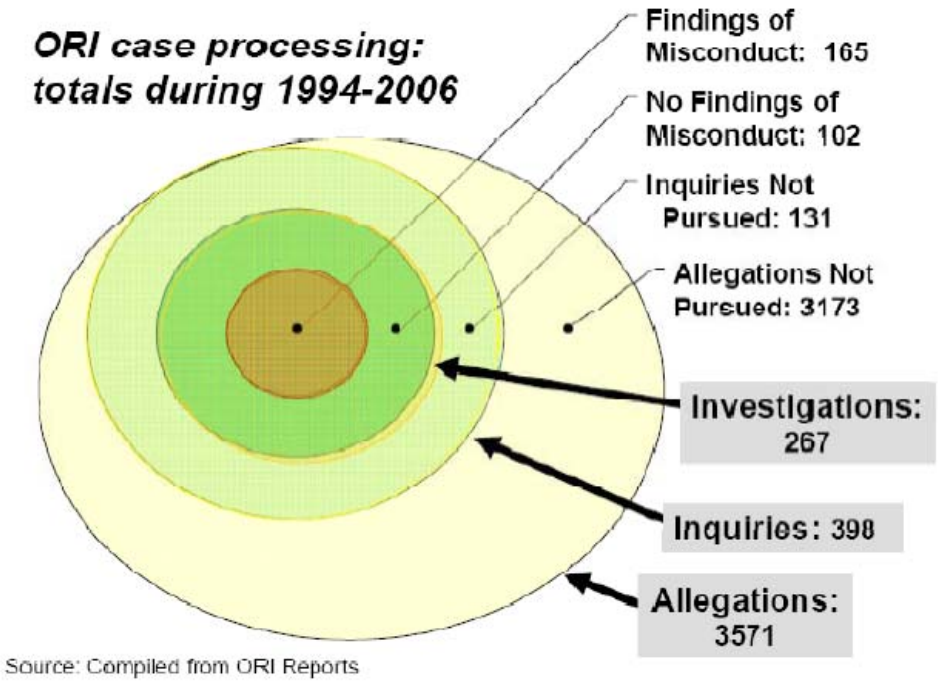

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Major focus of RRI = Misconduct (FFP)

- JM Ranstam, (2000, *Control Clin Trials* 21, 5:415-27)
  - – Survey, 442 biostatisticians, 37% response
  - – 51% knew about fraud in medical research
    - 26% involved FF
    - 31% directly involved in projects with misconduct
  - – Estimates of rate, 0.69% –> 0.80% (0.25% standard)

"What do we know?" Nicholas Steneck, Office of Research Integrity, USA

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Geggie, *(2001, J Med Ethics* 27, 5:344-6)

Survey, 305 new medical consultants, 64% response

55.7% observed misconduct (FF lower)

5.7% committed misconduct in the past

18% would commit in future

17% had research ethics training

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Conclusions:

Evidence does not support view that misconduct is "rare"

Most research misconduct is not detected, reported and investigated

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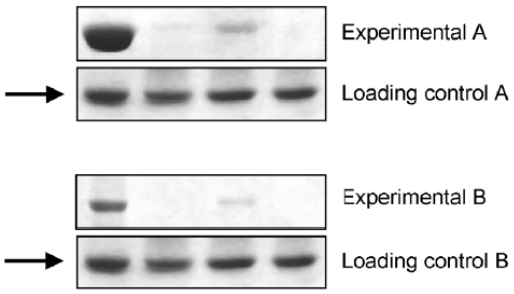
- Duplicating Data:



Courtesy Editor, Journal of Cell Biology

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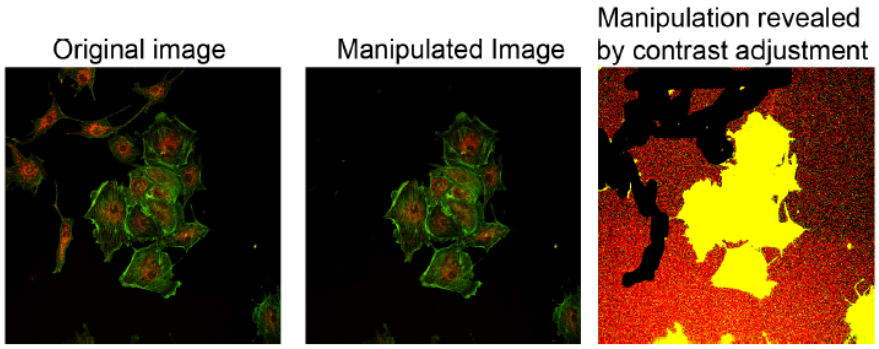
Inappropriate Manipulation Examples

- Cleaning up background – adjustment of a specific feature



Courtesy Editor, Journal of Cell Biology

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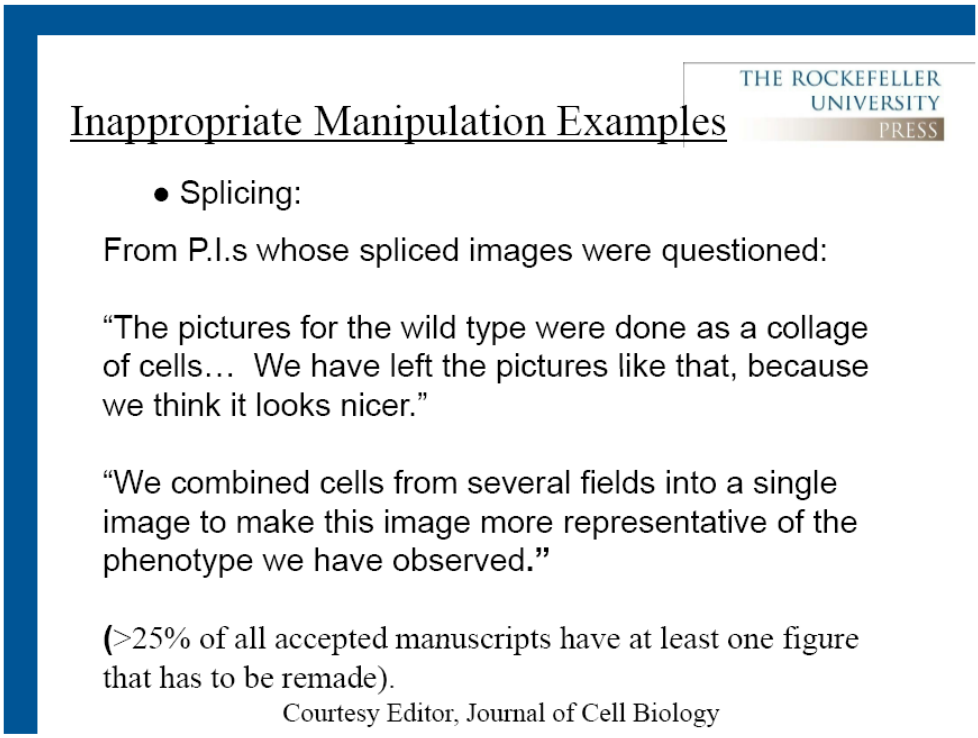

V J Gupta

Dr V J Gupta, Professor of Geology at Punjab University… India's most celebrated fossil scientist, for 25 years stunning the geological world with intriguing fossil finds that turned the accepted picture of the Himalayas on its head….

It wasn't until 1987, when Professor John Talent went to Paris, that he concluded that Gupta's fraud was not just one or two papers – it was *vast*. With a few hours to kill before his flight back to Sydney, Professor Talent stopped by a local rock shop. There he found some interesting fossils from Morocco. He bought a handful and caught his flight. Professor Talent remembered having seen photographs of these exact same fossils in a Gupta paper - except Gupta's identical specimens were supposedly from the Himalayas, not Morocco.

Talent: .McQuarie Univ, Sydney; http://www.abc.net.au/rn/science/ss/stories/s1451250.htm

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Why does it happen?

1. Temptations…of various kinds

Howard Alper,
University of Ottawa

Challenges for those individuals who are honest but, because of …

- National goals,
- Being in the limelight,
- Peer pressure or
- Other factors,

… are tempted to take liberties with results, falsify or fabricate data, plagiarize, etc.

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Commemorative stamp

Why does it happen?

2. Poor mentorship.

(importance of early exposure and formal training)

Why does it happen?

3. Poor regulatory and administrative system.

Why does it happen?

4. Pressure to publish, quantity equated with quality.

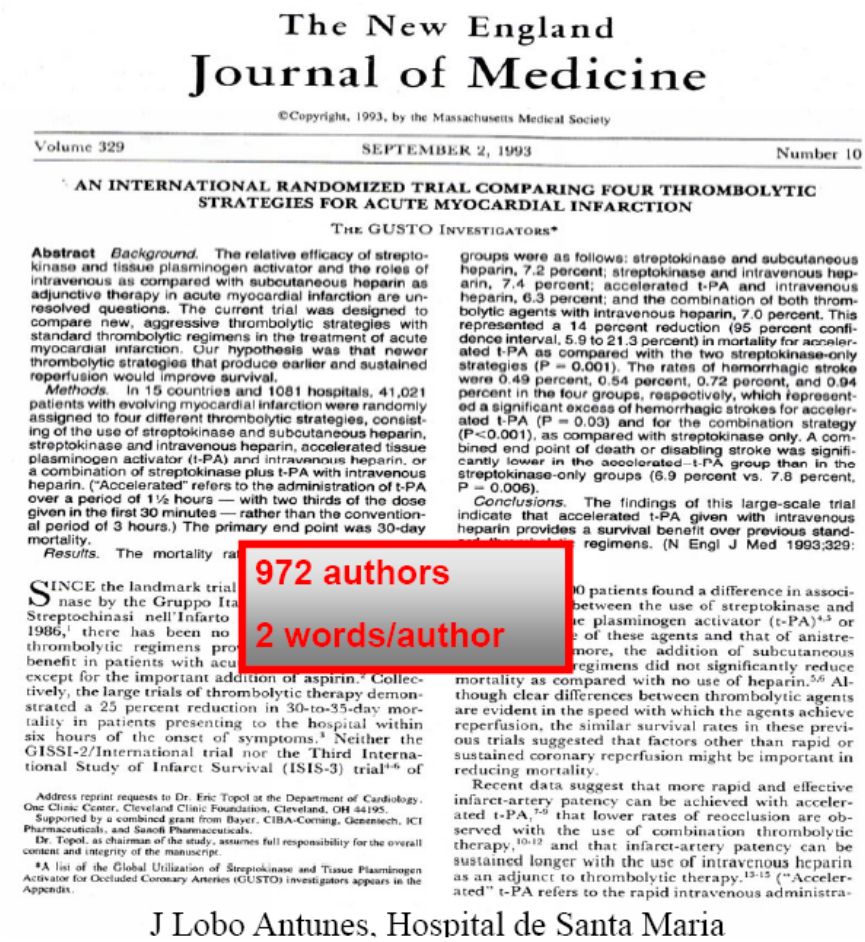
World's twenty most prolific researchers

	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?

[Haldane, Medawar]



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 mortality ra

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 regimens. (N Engl J Med 1993;329:

972 authors

2 words/author

SINCE the landmark trial
nase by the Gruppo Ita
Streptochinasi nell'Infarto
1986,[1] there has been no
thrombolytic regimens pro
benefit in patients with acu
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

0 patients found a difference in associ-
between the use of streptokinase and
plasminogen activator (t-PA)[4,5] or
of these agents and that of anistre-
more, the addition of subcutaneous
regimens 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.

J Lobo Antunes, Hospital de Santa Maria

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

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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)

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Why does it happen?

5. Financial interests.

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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

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 anti-inflammatory 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,[7] 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-

From the Institute for Work and Health, Mount Sinai Hospital, and the University Health Network, Toronto (C.B.); the Gastrointestinal Division, Department of Medicine, University of Southern California School of Medicine, Los Angeles (L.L.); Merck, Rahway, N.J. (A.R., D.S.); the Faculty of Medicine and Research Division, Universidad National Autonoma de Mexico, and Hospital General de Mexico, Mexico City, Mexico (R.B.-V.); University of Texas–Houston School of Public Health, Houston (B.D.); the Department of Clinical Pharmacology, University of New South Wales and St. Vincent's Hospital, Sydney, Australia (R.D.); the Division of Rheumatology, Department of Medicine, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil (M.B.F.); the Division of Gastroenterology, School of Medical and Surgical Sciences, University Hospital, Nottingham, United Kingdom (C.J.H.); the Division of Rheumatology and Clinical Immunology, University of Maryland, Baltimore (M.C.H.); Oslo City Department of Rheumatology, and Diakonhjemmet Hospital, Oslo, Norway (T.K.K.); and the Office of Clinical Research and Training, Northwestern University School of Medicine, Chicago (T.J.S.). Address reprint requests to Dr. Bombardier at the Institute for Work and Health, 250 Bloor St. E., Suite 702, Toronto, ON M4W 1E6, Canada, or at claire.bombardier@utoronto.ca.

Author Weaver, M.D., Arkansas 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)

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Séralini et al. (2012)

"Long term toxicity of a Roundup herbicide and a Rounduptolerant genetically modified maize".

Food and Chemical Toxicology 50(11): 4221–4231.

"The health effects –2 years – rats - females, all treated groups died 2–3 times more than controls, and more rapidly ..." .

-November 2013 – Elsevier – publisher - announced retraction – "..concluded that, after an in-depth look at the raw data of the study, no definitive conclusions can be reached regarding the role of ..NK603...in overall mortality or tumor rates.."

http://en.wikipedia.org/wiki/Séralini_affair

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Trivers (2014; ongoing)

"Report of the Rutgers Research Advisory Board
Investigations into allegations of research misconduct
against Dr. William Brown

April 25, 2012"

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Irrationality needs advanced brains...
unscientific attitudes are possible only in human beings.

Only we can get away with it.

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Features of the Indian situation

1. Strongly hierarchical; people more significant than issues; group loyalty.
2. Honours and Awards (the economisation of science).
3. "Shame culture" versus "Guilt culture".