decreased both in the trabecular meshwork and Schlemm's canal. Of course the changes may be incidental and not related to the primary pathology, but these observations do highlight the growing importance of the contractile meshwork cell and the importance of NO in the regulation of IOP. They also perhaps point to a new direction in treatment of this common condition.

Ian Grierson

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Playing with smoke, but not without fire

Hungary has one of the world's highest rates of necropsy examination, partly because it is their custom to perform post-mortems and partly because the law demands it. A team of Hungarian and British researchers took advantage of this practice to analyse the accuracy of tumour diagnosis (or rather the lack of it) at two university hospitals in Budapest.[1] Their findings are important. But there is one perplexing anxiety about this report published in the *European Journal of Cancer*. The research it describes was sponsored by Philip Morris Europe.

From 2000 consecutive deaths Szende and colleagues correlated final pathological diagnosis with admission and clinical diagnoses. The overall false-negative rate for tumour diagnosis was 37% and 9%, respectively. Family physicians and hospital doctors alike misidentified the primary tumour site in 20% of patients. Mistakes were especially common for cancers of the lung, liver, ovary, and gallbladder.

The immediate lessons of this research are very simple. The misdiagnoses could have had profoundly damaging effects on the course of investigation and treatment for the patient. Only necropsy will isolate past clinical errors and provide a means to prevent these mistakes from being repeated in future cases. Also, death certificates written by general practitioners will provide extremely unreliable mortality statistics. Health-service planning could go badly awry if these flawed data became the basis for strategic decisions about service provision. The necropsy must be retained as a vital component in hospital audit and not dismissed, as it sometimes is, as the curio of the overzealous pathologist.

More complex questions arise from the sponsorship of this research by a leading tobacco manufacturer. In cancer medicine, one is hard-pressed to find an opportunity to thank the tobacco industry. Is there reason to cheer Philip Morris for funding this work? If the paper by Szende's group had been submitted to the *American Journal of Respiratory and Critical Care Medicine*, the editor would have rejected it on grounds of its funding alone since that is the policy established by the journal's publishers. Should the editor of the *European Journal of Cancer*, or its publishers Elsevier, have taken the same action? Some ethicists have argued that this strict approach is vital if we are serious about eliminating tobacco as a prevalent human carcinogen. It is, these philosophers claim, a matter of the journal's credibility.

Certainly, Philip Morris sees countries like Hungary as ripe territory for its products. It would be naive to deny that the company's support for medical research has a dual motive. Massing[2] has chronicled how Philip Morris rose from obscurity to become "the largest private tobacco company in the world and the second most admired corporation in America", and how its "strategic philanthropy" of the arts, sport, and politics has sought to sweeten its noxious commercial mission. But as drug-company sponsorship amply proves, the pursuit of ideological purity in medical research is a nonsense. So does the argument against the tobacco industry simply turn on degree? Smoking, after all, accounts for a third of deaths in the industrialised world.

In truth, logic has little place in these debates. For instance, Roberts and Smith[3] appeal to notions of free speech when they argue strongly that the American journals concerned should avoid accusations of censorship by reversing their decision. The justification of an uncompromising corporate agenda with a civil libertarian defence strangely fuses two powerful social forces into a virtually unassailable political axis. Yet in the same magazine, and equally convincingly, Carnall later drew a parallel between a tobacco company and a cocaine cartel to claim that the funding of a chair at Cambridge University by British American Tobacco was a piece of "audacious tobacco advertising".[4] The issue is the same—tobacco money in the setting of academic research—but the conclusions are diametrically opposed. Our views about the rights or wrongs of tobacco sponsorship in medicine are straightforward outbursts of emotion that serve not only to express feeling but also to arouse feeling and so provoke action.

The research by Szende et al is welcome, irrespective of its provenance. Still, we should ensure that our desire to decry censorship does not assist those tobacco manufacturers who wish to mine new markets. Of course, the terrible paradox is that it will. What effective steps we can take to protect people from persuasive cigarette advertising in countries such as Hungary remain obscure to me. And that feeling of impotence makes me anxious about the consequences and so the validity of the libertarian argument.

Richard Horton

The Lancet, London, UK

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INDEPENDENT ON SUNDAY
21 JULY 1996

Tobacco firm's gift starts row

By Clare Garner

THE Cancer Research Campaign is threatening to withhold future funding from Cambridge University after its decision to accept a £1.6m gift from the world's second largest tobacco company.

Professor Gordon McVie, director of the CRC, said yesterday he felt "bitter disappointment" at the university's decision to accept the endowment from BAT Industries, whose brands include Benson and Hedges, Silk Cut and Lucky Strike, and said the campaign's relationship with the university could become less "intimate" as a result.

While unlikely to be able to withdraw existing funding, the campaign would think hard about future support, he said. "We fund some of the best science in the UK at Cambridge, but we have gone to great lengths to purge our investment portfolio of any tobacco shares, and we won't accept money, despite the fact that we desperately need money for research, from tobacco. This is our stand, and our supporters support that stand."

Members of the university's parliamentary body, Regent House, last week voted by 1,128 votes to 583 in favour of the controversial Sir Patrick Sheehy Professorship of International Relations, named after BAT's retiring chairman. Professor Sir David Williams, the vice-chancellor, said the decision "did not endorse" BAT's products.

Professor Sir Keith Peters, head of the university's clinical school where cancer is a priority, was among the 538 academics who voted against taking the money. "There are potential consequences," he said yesterday.

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...sterday morning, ...
...out in Omagh, foll

Umbrellas come

Fans at the Phoenix Fes

Blai

TONY BLAIR, the Lal
leader, issued a veiled war
to senior members of the S
ow Cabinet yesterday, callin
more "unity and discipl
amid rising tensions over p
towards striking London
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Sources say he was ann
by the lukewarm endorse
of his opposition to the strik
fered by Labour front-benc
including Robin Cook, Sha
Foreign Secretary.

Mr Cook was asked in a ...
interview if he backed Mr B
demand that the strikers ca

Cancer "challenge" to limited-resource countries

Seven research commitments were made at the second meeting of "Challenge"—the fight against cancer in countries with limited resources—which was held in Cairo on Aug 21–22. They were:

- **research into behavioural and psychological factors that perpetuate tobacco use and ways to control it;**
- **research into the possibility of identifying common cancer prevention recommendations that are relevant to countries with limited resources;**
- **research into simple and inexpensive methods of early detection of cancers, such as those of the cervix, breast, head and neck, and bladder through the use of randomised trials;**
- **research into treatment of childhood cancers in countries with limited resources—children form a disproportionately large proportions of these countries' populations;**
- **compilation of a list of effective and affordable anticancer drugs;**
- **a comparative study of various cultural, psychosocial, and behavioural factors that influence therapeutic practices and their outcome on quality of life; and**
- **research into the feasibility of facilitating easy access to up-to-date treatment recommendations through the Internet, and the possibility of adapting existing cancer information databases to the needs of clinicians in countries with limited resources.**

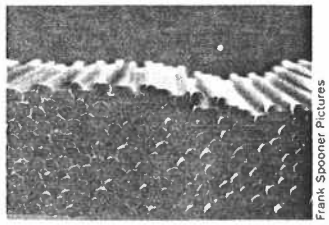
"Challenge", an initiative of the European School of Oncology, started last year as a newsletter for exchange of information on cancer in countries with limited resources. Unlike WHO and the International Union Against Cancer, which operate mainly through governments and cancer organisations, Challenge is working with individual clinicians and members of the public.

Challenge will hold yearly meetings in different countries and work towards a world conference on the fight against cancer in countries with limited resources to be held in the year 2000.

Nazli Gad EL-Mawla

UK MRC and Cambridge inhale tobacco profits

A UK Sunday newspaper's revelation that a Medical Research Council unit is using research funding derived from tobacco sales has forced the Council to review its funding procedures and left its head of public communications contemplating her future. The *Sunday Times* article revealed that work at the Neurochemical Pathology Unit in Newcastle is being sponsored by BAT Industries, owner of British American Tobacco. (The company is also sponsoring research at the MRC Toxicology Unit in Leicester.) MRC head of public communications Mary Rice, who was quoted as saying "I didn't think [the funding] could be justified", is now on paid leave and has been advised by the MRC not to take any further calls from the media.


Frank Spooner Pictures

Money to burn

Jane Lee, MRC director of corporate affairs, explained that the MRC Council approves broad policy guidelines on what the business relations between the MRC and external funders should be. Within those conditions, research directors of MRC units are free to make contact with potential sources of external support. The MRC will now, however, be reviewing the guidance given to research units, she said.

BAT's beneficence may also have unwelcome repercussions for medical research at Cambridge University, whose senior members voted 1128 to 583 in July to accept £1·6 million from the company to fund a chair in international relations and various bursaries and scholarships. Disquiet over acceptance of the money has been widespread, leading the Cancer Research Campaign, which currently funds Cambridge research to the tune of £2·25 million a year, to hint that it may take its money elsewhere. In a statement, Prof Gordon McVie of the CRC said "The charity will of course honour its existing funding of research projects at Cambridge but we will be reviewing our future relationship with the university in the light of this decision". The CRC's reaction is in stark contrast to the Wellcome Trust, another of Cambridge's major medical-research benefactors, which has no plans to review its relation with the university.

The company's previous involvement in international education includes supporting the building of two primary schools in China and sponsorship of two British secondary schools.

Sarah Ramsay

Canadian doctors vote for two systems

In a state of apparent confusion prompted by frustration over Medicare cuts, Canadian doctors endorsed support for a publicly funded health-care system while urging their leaders to launch a "national public discussion and debates on the appropriate place of regulated private insurance for medical services".

At last month's 129th annual meeting of the Canadian Medical Association, delegates passed contradictory resolutions providing support for publicly funded, as well as tentative approval of a private, two-tiered system in which wealthier Canadians can obtain optional, speedier treatment for their ailments.

But delegates stopped short of wholesale endorsement of parallel health-care systems, voting by a 104–76 margin to reject privatisation after outgoing CMA president Jack Armstrong pleaded that they step back from the abyss of greed for fear of Canadian's wrath. "If we become the first out of the trenches advocating a private system, we are going to get shot down in flames", Armstrong argued. "It will be totally perceived as money in the pockets of doctors".

However, delegates did urge re-examination of the principles of the Canada Health Act, as well as the implementation of strict limits on the nature of medical services paid for by the public system. They also approved a motion to discuss "the appropriate balance of the roles of the public and private sectors in the funding and delivery of medical services".

Wayne Kondro

Public opinion sought on UK tobacco money

The UK cancer charity, the Cancer Research Campaign announced on Sept 27 that it is commissioning a major new study on public knowledge and attitudes towards tobacco and the tobacco industry. The CRC also intends to develop a code, in conjunction with the institutions it funds, to ensure that "Campaign grants and intellectual scientific property are not tainted with tobacco money".

The Campaign's decision was taken after a major row which centred on whether Cambridge University should accept a £1·5 million chair endowment in International Relations (see *Lancet*, Sept 7, p 677). Initially, the CRC said that although the university's current funding (£2 million) was not in jeopardy, future plans needed discussion.

Prof Gordon McVie of CRC said "the development of a code of practise will need substantial time spending on it". Defining tobacco money association may be difficult but the CRC are adamant that they will not co-sponsor research. McVie says that CRC-sponsored scientists at Cambridge agree with the CRC's stand, which he hopes other charities and the UK Medical Research Council will emulate.

Jane Bradbury

Austrian confidentiality

Austrian Chancellor Franz Vranitzky strongly criticised the medical staff treating President Thomas Klestil for not informing the government that Klestil was unable to fulfil his duties on 3 days.

The doctors decided on Sept 27 to put Klestil into a coma to relieve pain from medical examinations for an undisclosed condition. Klestil spent the weekend in an intensive care unit, but Vranitzky was only informed of this on Monday. The doctors say that had an important decision been required, they could have easily woken the President. Many politicians consider Austria not to have had a formal head of state at this time and want a law to avoid such a repetition. Vranitzky is officially replacing Klestil until his discharge from hospital.

Denis Durand de Bousingen

Homoeopathy celebrates 200th birthday

Two hundred years ago Samuel Hahnemann published his first treatise about a new principle of medication. Treating the individual patient with very low doses of drugs that provoke the same symptoms and signs as the illness was as much disputed by his medical contemporaries as it is today by orthodox medicine. The current exhibition in the German Hygiene Museum in Dresden, which runs until Oct 20, shows the evolution and history of homoeopathy.

Deutsches Hygiene-Museum

Samuel Hahnemann

In Germany there are about 3000 qualified homoeopathic practitioners who have undergone specialist training. However, homoeopathic drugs are frequently used by many general practitioners, at the request of their patients. It is estimated that 1·5 million patients per year are treated in Germany with homoeopathic drugs. Orthodox medicine is divided on the issue. The Society of Pharmacologists denies that the treatments have pharmacological value, whereas the Federal Medical Council (despite a sceptical attitude) has accepted homoeopathy as an additional medical qualification because of its high acceptability to patients.

Annette Tuffs

Dutch euthanasia society solicits complaints

The Dutch voluntary euthanasia society (NVVE) received 600 calls last week after a telephone number for complaints about the behaviour of doctors in cases of physician-assisted euthanasia was given on national television. The NVVE wants to counterbalance the official government inquiry evaluating the euthanasia guidelines which became law in 1994. The results of both studies will be published in December.

One-quarter of the callers complained that their doctors would not co-operate with their wishes. Another quarter said their doctors had promised to help them end their lives but had not. Yet another 25% of the negative experiences were due to misunderstandings between different doctors caring for the patient. The remaining callers were inpatients who complained about doctors who hide behind protocols, procedures, colleagues, and teachers to avoid participating in euthanasia.

The Verwy-Jonker Institute in Utrecht will analyse the response and conduct a follow-up study on 200 of the cases. Senior researcher Riki van Overbeek said "It is important to know the clients perspective in cases of requests for euthanasia or assisted death, whether the life-terminating actions happened, or what exactly happened if doctors did not do what they promised".

NVVE press officer Jonne Boesjes said that some individuals, most of whom have terminal cancer, are suffering because the written NVVE euthanasia declaration does not guarantee the cooperation of doctors. "Euthanasia is not easy. In fact the declarations seem to have no worth at all in hospitals", Boesjes said. The 86 000 members of the society and their relatives are involved in a research programme on the process of life-terminating actions. Boesjes said that "The Ministers of Justice and of Public Health are going to evaluate their policies on the basis of a large survey in which doctors and judicial professionals are participating. We are convinced it is unthinkable to reconsider this matter without knowing the patients views".

The government survey aims to document to what extent euthanasia is underreported and is looking at both officially registered cases of assisted deaths and 1000 randomly sampled deaths as well as completed court cases in which a wish to die could not be expressed. The official number of euthanasia and assisted suicide cases has been static at 1400 per year over the past few years. The real numbers are thought to be higher—due to a political climate that does not encourage reporting. The NVVE hopes to identify the main problems for clients and relatives with a wish to die.

Marjanke Spanjer

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Editor's choice

Tobacco money, the *BMJ*, and guilt by association

Bans against smoking in public are ubiquitous. Cigarette smoke is irritating, and passive inhalation increases tobacco-related morbidity and mortality. Or perhaps not, say Enstrom and Kabat (p 369). Based on an analysis of data from the American Cancer Society, they conclude that the association "may be considerably weaker than generally believed." A firestorm erupted when the *BMJ* published this article in May. The American Cancer Society released a stinging press statement. The *BMJ* received 130 Rapid Responses and was advised to issue a retraction. Two main concerns predominated. First, the authors acknowledged being funded by an organization tied to tobacco interests. At least one author had been a tobacco industry consultant.

Second, the study had an obvious design flaw. The control group meant to represent unexposed persons consisted of spouses of nonsmokers, who in that era encountered cigarette smoke almost everywhere they went. The American Cancer Society had warned Enstrom about this problem beforehand (see p 352). In 1996 *JAMA* rejected what many assume is an earlier version of this study. Some believe the *BMJ* would have done the same if its peer reviewer had been an expert on the topic.

The decision to reprint this study in *BMJ USA* was difficult. The editors oppose Big Tobacco and poor research but are also committed to open scientific discourse. The study suffers from an imperfect control group and overstated conclusions, but hundreds of such studies are published regularly. It would be publication bias to reject a study of similar quality because it reached the "wrong" conclusion.

Some might discard any study tainted by tobacco money, but in 1996 the *BMJ* rejected such a policy, saying that it would intrude on the "open marketplace of ideas." "[A]ll studies undertaken must be available in some form: if some studies are systematically suppressed then we will reach false and biased conclusions when reviewing a body of research" (*BMJ* 1996;312:133-134).

The decisive factor should be study quality, not its financing or even its authors. As one reader put it, "The cogency of an argument should not depend on who makes it" (p 374). Enstrom was faulted for having tried, as early as 1975, to obtain tobacco money for his research. This is suspect, but top researchers do the same with drug companies. A perfectly good study of an unpopular hypothesis may find funding only through industry. The funding does not impugn the methods.

Or does it? The integrity of research depends on trust—that the methods described were followed and the data are complete and undistorted. It would be foolish to trust tobacco companies, which have knowingly promoted a product that kills its users. But can we trust researchers who accept tobacco money, or the journals that publish their work? How far does guilt by association extend? ✦

—Steven H Woolf, MD, MPH

July 2003

BMJ USA
Primary Care Medicine for the American Physician

More misleading science from the tobacco industry

Delaying clean air laws through disinformation

Paper p 369

The article by Enstrom and Kabat (p 369) is the latest in a long series of publications funded by the tobacco industry that report little or no relationship between environmental tobacco smoke (ETS) and disease.[1] The current study has an aura of legitimacy because it is drawn from the American Cancer Society (ACS) Cancer Prevention Study I (CPS-I), a landmark prospective study of the hazards of active smoking,[2] and because the analyses are based on nearly 40 years of data. Despite these apparent strengths, the study by Enstrom and Kabat is uninformative and its conclusions are exaggerated.

Indeed, the negative conclusions were entirely predictable from the outset because of the flawed way in which exposure to ETS was classified. CPS-I collected no information on ETS exposure other than the smoking status of the spouse. The study began in 1959, an era in which secondhand smoke was pervasive; virtually everyone was exposed at work, in social settings, or in other activities of daily living. Enstrom and Kabat therefore could not identify a comparison group of "unexposed" persons. Their analyses essentially compare nonsmokers married to a smoking spouse to nonsmokers with other sources of ETS exposure. This potential for misclassification was further exacerbated in the final 26 years of follow-up after 1972, when no updated information on the smoking status of the spouse was collected. Many of the spouses who reported smoking at the start of the study would have quit, died, or ended the marriage, yet the surviving partner was still classified as "exposed" in the analysis. Enstrom and Kabat could not distinguish persons with continuing exposure to ETS from those with past exposure, or persons with multiple sources of ETS exposure from those exposed only to spousal smoking.

This is not the first time that tobacco industry consultants have published misleading reports about ETS exposure based on flawed analyses of ACS cohort studies. In 1995, LeVois and Layard reported no association between ETS exposure and coronary heart disease (CHD) mortality either in CPS-I or in CPS-II, an even larger ACS cohort study begun in 1982.[3] ACS repeatedly communicated to these researchers and to Enstrom that CPS-I was not informative for evaluating ETS because of the deficiencies in the exposure data.[4] Enstrom and Kabat lament the exclusion of the earlier CPS-I report from meta-analyses of ETS exposure and CHD, but they do not discuss the methodologic limitations that led to its exclusion. Nor do the authors cite the reanalysis of the CPS-II data by Steenland et al,[5] the conclusions of which do not support their views or the position of the tobacco industry.

The reviewers at the *BMJ* may have been persuaded that the resurvey of 681 subjects in 1999 ensured the validity of the exposure data, or that the size of the CPS-I cohort provided adequate statistical power to evaluate the relationship between ETS and any disease end point. However, respondents to the 1999 resurvey comprised only 2% of the original 35 561 married lifelong nonsmokers who originally enrolled and 5% of those who were followed after 1972. A close examination of the seemingly extensive data on the 1999 respondents provided in Tables 2 through 6 (available at http://bmj.com/cgi/content/full/326/7398/1057) reveals that the data are actually sparse; these tables include many empty cells or percentages based on fewer than five subjects.

The number of deaths from lung cancer in CPS-I is considerably smaller than in numerous other ETS studies. Enstrom and Kabat based their analysis on married, lifelong nonsmokers drawn from the 10% of subjects who live in California. Because

lung cancer is rare in lifelong nonsmokers, the relatively small number of observed deaths in this subgroup gives rise to wide 95% confidence intervals that in fact overlap with relative risk estimates cited in meta-analyses by the International Agency for Research on Cancer (IARC),[6] the Environmental Protection Agency (EPA),[7] and others.[8,9]

The article selectively omits mention of studies and reviews of ETS published after 1999, as well as reports that addressed the tobacco industry's standard criticisms of the scientific literature on ETS, such as the California EPA report.[10] No mention is made of the 2002 report by IARC that concluded that involuntary exposure to tobacco smoke is carcinogenic.[6] Enstrom and Kabat minimize the extent of the published literature linking ETS exposure to lung cancer. Recent reviews[8,9] list 51 relevant studies, many of which collected information on ETS exposure from other sources, as well as from smoking by the spouse. These studies had been conducted during time periods and in countries where the potential for exposure misclassification was substantially less than in CPS-I. Enstrom and Kabat incorrectly claim that ETS exposure data in CPS-I are comparable in quality to those of most other studies.

> Enstrom and Kabat could not identify a comparison group of "unexposed" persons. Their analyses essentially compare nonsmokers married to a smoking spouse to nonsmokers with other sources of ETS exposure.

ACS does not endorse or agree with the methods and conclusions of the study by Enstrom and Kabat. ACS once collaborated with Enstrom, beginning in 1989, to enable him to extend follow-up of the California subgroup of CPS-I from 1972 forward. The acknowledgments at the end of the article thank two former ACS vice presidents for this assistance but fail to mention that ACS terminated its collaboration with Enstrom several years ago because of his unwillingness to address fundamental methodologic problems with this and other analyses. At no point did Enstrom inform ACS that he had communicated with Philip Morris about the potential value of the CPS-I follow-up in 1990[11] or that he had applied for and received funding from Philip Morris in 1997.[12]

Sadly, the forum in which the study by Enstrom and Kabat will be most influential is not the scientific world—most scientists will recognize the study for what it is—but in the battle for public support in communities that are considering more stringent regulations on smoking in public spaces. Misleading publicity appears repeatedly in newspapers and other community publications wherever clean air laws are being debated.[13] For example, the methodologically flawed study by LeVois and Layard was recently cited in an op-ed piece in a Seattle newspaper in March 2003,[14] eight years after it had been published in an obscure journal.[3] The Enstrom and Kabat paper represents an even more valuable public relations resource for tobacco companies. They can refer not only to the ACS as the data source for the study but also to the prestigious *BMJ* as the journal in which it was published. ✦

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