efforts to warn of the hazard of Laetrile use, I would prefer to be able to say that we will never again see a medical fraud of this magnitude perpetrated on the American public. Unfortunately, I cannot.

The drug regulatory system administered under law by the FDA, like any other system carried out by Government in a free society, functions only so long and so far as the public will allow. Survey after survey shows that there is overwhelming support by the American people for the consumer health protection activities of the FDA. But, as the case of Laetrile proves, that support is neither absolute nor permanent. It can be selectively or totally withdrawn.

In those circumstances, it would seem that the best, perhaps the only, recourse in a free society is for those institutions and groups that have a responsibility for protection of the public health—institutions outside Government as well as within it—to identify, expose, and halt quackery that threatens the public health and welfare. Their weapons in such a struggle are facts as well as laws, credibility as well as confidence, compassion as well as the scientific method. Arrayed against them are cunning deception on the part of the promoters of quackery and the fear and ignorance of desperate people, coupled often with a conviction that the "establishment" is bent on crushing those who oppose it.

While the role of a drug regulatory agency may be limited, submission of scientific data (as part of an application for an investigational permit) should be encouraged. If a promoter of an unproven remedy does not follow the usual channels to demonstrate safety and efficacy, consideration must be given by others to sponsoring such studies; however, concurrent regulatory (enforcement) and public education activities are to be encouraged and should not be seen as conflicting. It is noteworthy that at the same time FDA was permitting a clinical trial of Laetrile, it issued a nationwide Public Warning about the use of Laetrile. Both actions were viewed as responsible, salutary, and not inconsistent.

The challenge of quackery is formidable and seemingly unending. Experience tells us that a successor to Laetrile is almost surely on the horizon, if not in our midst. It is to be hoped that those of us in medicine and science, in and out of Government, will be better able to meet the next challenge of quackery.

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The Story of 'Joseph M.'—Mass Media Against 'Medical Bureaucracy'

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THE PHENOMENON OF QUACK MEDICINE in Western culture presents a special problem for medical authorities because of its increasing popularity among the public. Although legal procedures provide appropriate mechanisms to enforce routines for the regulation of new drugs, major difficulties are repeatedly encountered by the authorities in suppressing the promotion of quack medicine and calming public dissent against such action by the

medical establishment. In order to enforce the law more effectively, it is necessary to better understand the modes of operation of promoters of quack medicine.

We have recently encountered an event that can be used as a model to study the nature of the propagation of this phenomenon and its deep strongholds among the general public. A brief summary and analysis follow.

History

In 1976, a young Israeli physician visited the Contrera Clinic in Tijuana, Mexico, to explore the possibility of using Laetrile for the treatment of his mother's terminal breast cancer. Upon his return to Israel, he wrote a report in which he expressed disappointment with the results of the treatment, ascribing its failure to low dosage. During the ensuing 2 years, he claimed, both in Israel and in the United States, that high-dose Laetrile is efficient and that excellent therapeutic effects had been observed in 40 patients he had treated with such a regimen.

In mid-1977, while being interviewed on the KBBF-TV "Cross-Talk" show in San Diego, the young physician suggested that the active component of Laetrile is not amygdalin, which is a diglucoside of mandelonitrile, but rather DMBG (dimandelonitrile-beta-glucuronic acid), which had been previously introduced by Krebs as the universal cure for cancer.

The theoretical basis for the selective curative effect of DMBG on cancer cells is that tumor cells contain an enzyme, beta-glucuronidase, that can hydrolize DMBG into glucuronic acid and mandelonitrile, and that this enzyme is activated only at low pH, which prevails in malignant cells but not in normal ones. The mandelonitrile produced within tumor cells is further hydrolized, either spontaneously or by benzocyanaze, into benzaldehyde and cyanide, the latter leading to an immediate cell death.

According to this "innovator," the reason DMBG had not been used before was the failure to synthesize it. However, he claimed that if goats and donkeys are fed bitter almond leaves, which contain large quantities of prunansin, the glycoside is hydrolized by beta-glucosidase, in gastrointestinal epithelial cells, into glucose and mandelonitrile. The latter is then transferred via the portal system to the liver, where it undergoes glucuronation, with the aid of hepatic UDP glucuron transferase, to produce DMBG within the liver cells. The DMBG can then be extracted from the urine in relatively large quantities.

During 1979 and 1980, while busy with attempts to produce large quantities of DMBG by this method, the young physician performed some preliminary acute toxicity studies as well as therapeutic experiments in mice injected with goat urine extracts. He also succeeded in recruiting a well-known Israeli professor of chemistry, who agreed to try to synthesize DMBG chemically, and a well-known Israeli professor of medicine (noted for his unconventional approach toward the medical establishment), who agreed to carry out Phase I clinical studies with the drug as soon as it became available.

'. . . of the 110 reports and 50 editorials and articles written on the issue, only 6 were in favor of the Ministry of Health's position. This indicates that the Ministry of Health did not handle the problem of the media very efficiently.'

As a consequence, but without any scientific basis, an impressive article entitled "The Drug of Great Hope" appeared in March 1980 on page one of the most popular national morning newspaper. The article stated that DMBG can cure 85 percent of all cancer.

The effect of this article was shocking. The public was extremely impressed, and people in Israel and abroad were anxiously calling the Israeli Ministry of Health for information on availability of the drug. Although the Ministry of Health discredited the claims, the power of the media was evident.

During the next 2 years, this group continuously negotiated with the Ministry of Health's authorities, trying to minimize the toxicological experiments required for approval of the drug for Phase I clinical studies. In fact, these toxicity tests have never been carried out.

In October 1981, by a brilliant chemical procedure, DMBG was indeed synthesized in small quantities for the first time. The substance was apparently prescribed for three patients abroad—one in Australia, one in Portugal, and one in an undisclosed place. According to claims, the treatment did not produce acute or lethal side effects. Neither the successful synthesis nor the facts related to treatment were disclosed at the time to the Ministry of Health.

Enter "Joseph M."

The person who will be referred to here as "Joseph M." was a 54-year-old journalist with advanced metastatic, anaplastic carcinoma of the lung that had failed to respond to radiation and chemotherapy. In late 1981, the patient was hospitalized with pleural effusion and shortness of breath at one of the largest medical centers in Israel, where he received supportive care only.

On December 25, 1981, the patient's wife submitted a personal application to the Director General of the Minis-

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try of Health for a special permit for use of DMBG for her husband's terminal and intractable disease. According to Israeli law, no such permit could be given, and the request was reluctantly denied.

Concurrently, requests for special licenses to use DMBG and to carry out Phase I clinical studies were submitted to the Ministry of Health by the young physician and his colleague the professor of medicine, despite the lack of obligatory toxicity studies or of data demonstrating effectiveness of the drug. These requests also had to be denied.

On January 17, 1982, Joseph M., his wife, and his daughter appealed to the Israeli Supreme Court for an Order Nisi, requiring the Ministry of Health to explain why it should not permit saving of the patient's life by allowing him to be treated with DMBG.

Enter the Media

On the following day, a massive campaign was initiated in the media. The story received extensive coverage—with headlines such as "Cancer Researcher Hits Absurd Ministry Demands"—in all major Israeli newspapers.

The request for a special permit was denied by the Supreme Court, although the judges in their statement noted that "if the court was to decide according to its feeling and sympathy, the petition would have been granted." However, the judges said, they were "obliged to consider not only the petition of the immediate painful problem, but also the far-reaching consequences of the court's decision in the first case of its kind to be brought before Israeli courts."

This decision resulted in a major outpouring of articles in the daily press, persisting for 3 days, that mostly sympathized with the petition and criticized the medical authorities.

Gradually, the public's interest decreased and relevant articles dwindled. But at this point the patient himself decided to appear on prime-time evening television. During the interview, his shortness of breath intensified the desperate appeal of a clearly dying, intelligent person who strongly criticized the establishment, including the Supreme Court, for denying his chance to live. His rhetorical question—"Why not recognize my right to do something for my body so that I can live? I merely ask to save a life which is in question today"—remained, of course, unanswered.

The patient's appearance had an electrifying effect on the nation. Because of the late hour of the program, the press could not respond immediately, but one day later multiple essays appeared in every newspaper edition. Again, most of the media favored Joseph M.'s appeal, using headlines such as "Opening Up the Cancer Debate," "Inescapable Conclusion," "The Right to Hope," and so on. Only a minority of reporters expressed the concern that the "terminally ill should not be guinea pigs."

Death of the Patient

In the midst of this furor, the patient died. During the following 2 days, the newspapers were again full of reports of the event and the subsequent funeral ceremonies. Eulogies at the gravesite were also amply reported, with headlines pointing sharply at the establishment: "A Shocking Case of a Sick Man Who Sought But Was Denied a High Court Order Because of Legalistic Formalities," "An Injustice Was Committed—Somewhere Along the Arteriosclerotic Channels of the Health Ministry Bureaucracy," "Acts of the Health Ministry Flew the Black Flag of Inhumanity," and "The Death Points an Accusing Finger and This Desperate Voice Will Haunt Us for Some Time to Come; It Is in the Direction of the Executive Branch Represented in This Case by the Ministry of Health."

With such comments in the newspapers, reactions by governmental bodies were unavoidable. Knesset members asked the Judicial Committee to draft legislation to create a special appeals body and thus deny the Ministry of Health its full authority for a professional judgment on drug regulation. The Prime Minister, during the weekly Cabinet meeting, expressed his deep regret that "a sick man had been denied a High Court order because of legalistic formalities."

In response, the Minister of Health, without consulting his advisory board, was inclined to approve DMBG experimental therapy for cancer patients. This was immediately misinterpreted as a "green light" for the drug. This announcement on the evening news intensified the media reaction. When, on the following morning, the Minister of Health reassessed the legal "state-of-the-art" and courageously retreated, the bonfire started anew.

Finally, the Knesset, after a prolonged and vociferous discussion, turned the case over to the Social Affairs Committee. With this move, the stream of publication stopped almost immediately.

The committee investigated the matter for almost 6 months. In their final conclusion, they clearly supported the procedures and decisions of the Ministry of Health, admitting that the permit for the use of DMBG should *not* have been issued. The final paragraph of their report is of special interest:

> The committee feels that communications with the public and the transfer of information and decisions to the public knowledge were inadequate. Lack of sufficient information regarding policy and procedures created confusion in the media, in the public and among members of the government and the Knesset.

A summary of this final conclusion was printed in two newspapers—in a hidden corner of an inner page.

Analysis

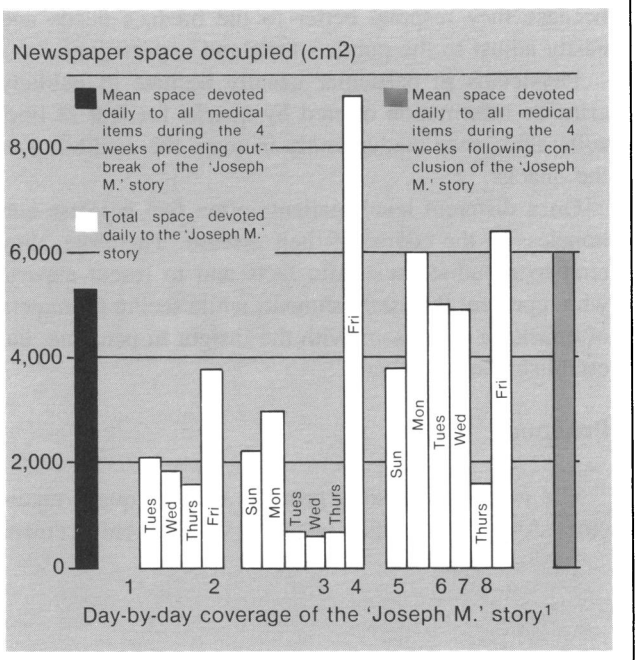
In an attempt to quantify involvement of the press, the total space, in square centimeters per day, devoted to the "Joseph M." story in six of the most important Israeli daily newspapers was compared with the mean space devoted daily to all medical items during the 4 weeks preceding the outbreak of the story and the 4 weeks following its conclusion.

The chart presents the distribution of newspaper space allocated to the story each day in the six dailies, starting with the date Joseph M.'s appeal was submitted to the Supreme Court. It is evident that within 4 days the space devoted to news items and editorials on this topic almost exceeded the mean daily coverage of all medical items combined. The response time following the occurrence of specific events was extremely short. As expected, the weekend papers devoted greatest coverage to the issue.

The following points in time, depicted on the chart, illustrate the sequence of events (numbers correspond with numbers in the chart):

- An abrupt increase in media coverage following submission of the appeal to the Supreme Court, 1;
- reaction to the court's rejection of the appeal, 2;
- an extreme peak of media coverage following the patient's television appearance, superimposed on the previously mentioned weekend peak, 3, 4;
- the response to the patient's death, 5;
- combination of the reporting on gravesite eulogies, government deliberations, and response to the Minister of Health's misinterpreted order, 6;
- reaction to the Minister's "change of mind," 7;
- discussions at the Knesset during the following 2 days, 8; and, finally,
- the sharp turn-off.

Chronological sequence of coverage by Israeli newspapers of the 'Joseph M.' story, and comparison with coverage of all medical items



[1]Numbers 1 - 8 represent major events. For explanation, see text.
NOTE: No newspapers appear in Israel on Saturdays.

Almost every newspaper published at least one report per day on the story, and one editorial or article every other day. However, of the 110 reports and 50 editorials and articles written on the issue, only 6 were in favor of the Ministry of Health's position. This indicates that the Ministry of Health did not handle the problem of the media very efficiently.

Aftermath

The failure of the authorized officials to counter promotion of quackery in the media is not specific to Israel. While Israel was preoccupied with the DMBG story, The New York Times stated in an editorial summarizing the Laetrile story: "The failure of communication cannot be laid entirely on the public's doorstep—medical authorities were too slow to understand that the Laetrile case required something more than the usual scientific standards of evidence."

In fact, scientists often fail to convince the media because they tend to adhere to strict statistical criteria and rules, whereas for the media even an anecdotal story is a legitimate event, provided that it is of interest to the public. Scientific material consists of dry facts and figures, presented in a boring format, while the media prefer more sensational information, even if it is statistically nonsignificant. Also, scientists tend to use scientific terms and aphorisms that are not well understood by

the general public; therefore, scientists are quite often regarded as presumptuous and arrogant.

In contrast, "quacks" are well accepted by the media because they respond better to the media's needs and easily adjust to the public's taste and expectations.

Physicians in particular usually hesitate to publicly criticize information offered by quacks for fear of libel suits; thus, they inadvertently increase the credibility of the quacks.

On a different level, patients often feel helpless and hopeless in the course of their disease. Therefore, they tend to repudiate scientific facts and to resent experts who represent the establishment, while seeing promoters of quackery as persons with the insight to penetrate the establishment's "fakery."

Prospect

The media can readily promote modern quack medicine. Attempts to fight quackery by law enforcement may be ineffective because laws are amenable to changes, and legislators usually yield to media pressures. On the other hand, scientific rejection may be insufficient in view of the increasing popularity of unconventional medicine. Therefore, quack medicine should be fought on its own grounds—namely, in the media—and the fight should involve media experts.

The issue is still wide open. In the words of the already cited New York Times editorial:

> Because of the continuing intractability of cancer, Laetrile will doubtlessly be resurrected in a new form. Physicians should not again wait for 27 State Legislators to tell them of the crisis of confidence in scientific medicine. The next time around they should start sooner to reason with the desperate.

The story of Joseph M. is but one example.

Toxic Shock Syndrome: Chronology of State and Federal Epidemiologic Studies and Regulatory Decision-Making

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SEVEN CASES OF AN UNUSUAL NEW ILLNESS were reported in the November 25, 1978, issue of Lancet by James Todd, MD, a pediatric infectious disease specialist at the University of Colorado School of Medicine (*1*). The illness was characterized by high fever, low blood pressure, a diffuse erythematous rash with subsequent skin peeling, vomiting, diarrhea, and multiple abnormalities in laboratory findings. These cases had occurred in four girls and three boys between the ages of 8 and 17 years. All five patients studied prospectively had *Staphylococcus aureus* isolated from at least one body site, although not, interestingly, the blood. Todd named this illness toxic shock syndrome (TSS) and suggested that it might be caused by a toxin elaborated by *S. aureus*. Despite this report, there was only infrequent recognition of TSS by the medical community until early 1980.

State Health Agencies

In Late January 1980, the Minnesota Department of Health (MDH) and the Wisconsin Division of Health and Social Services (WDH) officials reported to the Centers for Disease Control (CDC) nine cases of illness compatible with TSS that had occurred in the two States in the preceding 3 months. Unlike the cases reported by Todd, these cases had occurred not in children, but in adult women. In addition, most of the women had become ill during their menstrual period.

Also in January 1980, coincidentally with the first case reports by the two State health agencies, the MDH began an actively defined epidemiologic surveillance system for TSS (*2*). Intensity of surveillance was constant from the beginning through June 1981. Active