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effects of the drug. First, since the drug is an immunosuppressant, it tends to depress the inflammatory response. Second, it interferes with the cross-linkage of collagen, thus inhibiting the formation of scar tissue. Finally, it allows copper (which accumulates in the diseased liver) to be mobilized and excreted in the urine.

Recent work suggests that primary biliary cirrhosis may be an autoimmune disease. Researchers have found lymphocyte abnormalities associated with the disease that resemble those found in scleroderma, Sjögren's syndrome, and other autoimmune disorders.

Penicillamine's effectiveness provides further support for this thesis.

Currently, penicillamine is approved for use in the treatment of metal poisoning, Wilson's disease, and rheumatoid arthritis. If and when primary biliary cirrhosis joins the list, Dickson believes the agent may help improve the results of liver transplantation in the disease because of its apparent ability to extend life and improve liver function. Discussions and a cooperative effort in this direction have begun with transplant surgeon Thomas E. Starzl, MD, of the University of Pittsburgh School of Medicine.

—by MICHAEL REED

TV report on DTP galvanizes US pediatricians

Television viewers were terrified. Physicians' phones were ringing off the hook. To Harry Jennison, MD, executive director of the American Academy of Pediatrics (AAP), Evanston, Ill, it was reminiscent of the polio scare in the early 1950s. "Parents were hysterical," he says.

In the Cleveland, Ohio area, "it was devastating in every pediatrician's office," according to Shaker Heights pediatrician Leonard P. Rome, MD, chairman of the AAP's Chapter Chairmen's Committee. "Doctors were calling each other and saying, 'Are you still giving pertussis [vaccine]?' " (Some physicians actually did halt pertussis immunizations temporarily.)

In the mountains of northern New Mexico, "inquiries about the vaccine have increased 25%," estimates Española pediatrician James D. Waltner, MD.

And as far west as the Pacific coast, "we have had a lot more explaining to do," says Robert Meehan, MD, professor of pediatrics at the Oregon Health Sciences University in Portland and director of the university's pediatric outpatient department, where approximately 75 children are immunized every week.

The alarm was sounded by reporter-producer Lea Thompson's 60-minute documentary entitled "DPT: Vaccine Roulette," which aired in April on WRC-TV, a National Broadcasting Company-owned-and-operated station in Washington, DC. A 13-minute excerpt from the program subsequently ran on the "Today Show," and the original program or parts of it were broadcast by NBC affiliates around the nation.

Thompson's report focused on neurological damage allegedly resulting from the pertussis component of the diphtheria-tetanus-pertussis vaccine, DTP or DPT for short. (She got the idea for the program, she says, from a concerned parent whose two children developed neurological disease after DTP immunization.) Children routinely receive the series of immunizations at 2, 4, and 6 months of age, with one booster dose at age 18 months and another before school entry.

Thompson's message: "Shots, we are told, will protect every child from a dread disease: pertussis. It's whooping cough. But the DPT shot can also

damage to a devastating degree." Her report, many people felt, intimated that physicians, vaccine manufacturers, and the Food and Drug Administration have engaged in a cover-up vis-à-vis adverse reactions to the vaccine.

Some physicians featured on the program argued for the benefits of the vaccine; others, such as Robert Mendelsohn, MD, argued its risks. (Mendelsohn asserted that "the danger is far greater than any doctors here have ever been willing to admit.") However, viewers may have been most affected by heartrending footage of damaged children—accompanied by audio heartbeats—and statements from the children's parents:

"She's a joy to be around because she's such a sweet-natured girl. But we've been told that she probably will never walk on her own, and she probably will never talk."

"... and then he gave her the shot. And the next following morning when I was feeding her she went into a grand mal seizure ... I thought she was dying in my arms is what it amounted to."

The program ended, chillingly, with a crying child receiving an injection and the child's father saying, "See ... it's all gone already."

Official Reactions

Ensuing concern among parents was such that on May 7, 1982, the US Senate Subcommittee on Investigations and General Oversight, chaired by Sen Paula Hawkins of Florida, devoted a hearing (originally planned to examine continued funding for immunization) to the topic of DTP, with testimony from health authorities, parents of damaged children, and the lawyer involved in one of the damage suits. Persons who believe their children were injured by the vaccine formed a group called DPT (Dissatisfied Parents Together), and the House Commerce Committee approved an amendment to a National Institutes of Health reauthorization bill that called for a two-year study of the safety and efficacy of DTP.



Photograph courtesy of Centers for Disease Control

Response from government research facilities and the medical community was equally vigorous. The FDA is currently preparing a document that reviews the "inaccuracies of the program," according to John Robbins, MD, director of its Division of Bacterial Products, Bureau of Biologics. The Centers for Disease Control (CDC) in Atlanta and the AAP issued press releases reaffirming the necessity of continued routine pertussis immunization and indicating that the benefits of such immunization greatly outweigh the risks. The latter organization also sent out voluminous mailings to its members and chapter chairmen, informing them about the NBC program and providing materials to help them in promoting immunization to parents and communities.

What the pediatricians feared was a repeat of the dismal experience in other countries. In England, where unfavorable publicity of the same sort turned much of the populace against DTP, immunization rates decreased from 79% in 1973 to 31% in 1978. From 1977 through 1980, 102,500 individuals contracted whooping cough, 5,000 were hospitalized with the disease, 200 developed secondary pneumonia, 83 experienced seizures, and 28 died. Although immunization is once again on the upswing in that country, thousands of new cases of pertussis were still being reported there early this year. In Japan, where public opinion and government action interrupted the DTP immunization program, and in Sweden, where vaccine production problems put a temporary stop to immunization and where anti-DTP sentiment also existed, similar epidemics occurred. These outbreaks of disease generally could be traced to parents' fear that their children would suffer brain damage or death from the vaccine.

Hardly Hot News

To health professionals, of course, the dangers of DTP are nothing new. The "D" and "T" components, which were given long before the "P" was added in the late 1940s, are partially purified toxoids considered to carry little risk. The whole-cell "P" component, consisting of 4 units of protective pertussis antigen per 0.5 mL of DTP, is universally acknowl-

edged to be relatively crude and toxic, and the advent of a safer version is eagerly awaited (see page 22).

Almost from the inception of widespread DTP immunization, severe reactions have been reported, beginning with Byers's and Moll's study of vaccine-associated encephalopathy in 1948 (*Pediatrics* 1948; 1:437). The incidence of such reactions has not been firmly established. It does seem fairly certain that vaccine-associated seizures, rare as they are, are considerably more common than brain damage or residual impairment secondary to such seizures.

Endeavoring to rebut certain charges made on the NBC program and disputing Thompson's statistics (she had said that "serious reactions" could occur in as many as 1 out of 700 children vaccinated), Vincent A. Fulginiti, MD, chairman of the AAP Committee on Infectious Diseases, noted in his testimony before the Hawkins subcommittee that different studies have placed the incidence of convulsions or collapse syndrome at 1 per 1,750 to 13,000 injections and the rate of permanent brain damage at 1 per 168,000 to 310,000 injections. (In two studies, the rates of brain damage were zero per 80,000 injections and zero per 180,000 injections, respectively.)

He also mentioned a specific prospective UCLA study, misinterpreted or somehow misrepresented by Thompson, that found convulsions in nine children and hypotonic hyporesponsive episodes in nine children following 15,752 DTP immunizations, but no evidence of permanent brain damage. In addition, there was persistent crying in 398 children and unusual crying in 22 children. Serious neurological reactions did not occur, and persistent crying was much less frequent, following 784 DT immunizations (*Pediatrics* 1981;68:650-660).

In a reference to the UCLA study during her program, Thompson repeated her 1-in-700 figure: "Also, the study estimates 1 in every 700 children had a convulsion or went into shock." But one of the investigators on the study, James D. Cherry, MD, professor of pediatrics and chief, Division of Pediatric Infectious Diseases, Center for Health Sciences, UCLA, affirms instead that "1 in 875 had either a convulsion or a hypotonic hyporesponsive episode." Furthermore, Cherry stresses, "None of the 18 children with one of these reactions had any residual," indicating that "in almost 6,000 children, there was no evidence of neurological damage." He echoes the general sentiment of pediatricians: "The program was totally distorted and gave no perspective on the benefit in contrast to the risk" of DTP.

In testimony similar to Fulginiti's, Robert H. Parrott, MD, director of the Children's Hospital National Medical Center in Washington, DC, cited a decision analysis of the risks, benefits, and costs of pertussis immunization carried out by Jeffrey P. Koplan, MD, and co-workers at the CDC and Harvard Medical School (*N Engl J Med* 1979;301:906-911). The investigators projected 6,745 cases of pertussis, 7.6

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pertussis deaths, and 2.3 cases of encephalitis secondary to the disease in each cohort of 1 million children if immunization were discontinued. In contrast, they projected 95 cases of pertussis, 0.3 pertussis deaths, 0.1 case of disease-associated encephalitis, and five cases of immunization-associated encephalitis (with 1.7 deaths) per cohort of 1 million if the program continued. Koplan and colleagues used pessimistic estimates for all of the factors they examined. In the case of reactions to pertussis vaccine, for example, they incorporated in their analysis unpublished data from the Netherlands that place the risk of shock at 1 per 3,500 children, the risk of at least one convulsion (including benign febrile seizures) at 1 per 2,150, of persistent screaming at 1 per 3,500, and of encephalitis at 4 per 190,000.

Finally, there are figures from the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) Collaborative Perinatal Project which has looked at the incidence of seizures between birth and age 7 years among the offspring of 54,000

pregnant women. At the American Academy of Neurology meeting in Washington, DC, this spring, Deborah G. Hirtz, MD, of the Developmental Neurology Branch of NINCDS, reported on recently analyzed data from that study showing that 39 of the children had seizures within two weeks of immunization. Of those, ten had seizures following DTP. One of the ten children sustained a speech defect and a focal EEG abnormality, but there were no sequelae among the rest. Hirtz told *JAMA MEDICAL NEWS*, "The main focus of our study was to show that the outcome of almost all children with immunization-associated seizures was very good, and that the seizures for the most part resembled the benign febrile seizures of childhood."

Why the conflicting statistics on incidence of CNS effects from "P"? Underreporting may be part of the problem, but the major factor is the difficulty of establishing more than a temporal relationship—usually assumed when problems occur within 48 or 72 hours after immunization—between DTP and neurological symptoms. Confounding variables include such

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According to the just-published American Academy of Pediatrics (AAP) "Red Book" (*Report of the Committee on Infectious Diseases*; ed. 19. Evanston, Ill, American Academy of Pediatrics, 1982, pp 200-202), children who have any of the following reactions to DTP should not receive the "P" component again:

- Convulsions
- Encephalitis
- Focal neurologic signs
- Collapse

Scientific staff at the Food and Drug Administration's Bureau of Biologics point out that two distinctly different types of seizures can occur after DTP vaccination: benign febrile seizures and more serious nonfebrile seizures. They speculate that two different surface antigens of the whole *Bordetella pertussis* organism contained in the vaccine are responsible. Nevertheless, a child who experiences any type of seizure after DTP immunization should receive only diphtheria-tetanus (DT) vaccine subsequently.

Certain other reactions probably contraindicate further "P" administration, says the Red Book, although the significance of these reactions is unknown:

- Excessive somnolence
- Excessive screaming (persistent crying or screaming for three or more hours)
- Temperature higher than 105 °F (40.5 °C)

In some cases, the clinician must use his or her best judgment as to whether one of these reactions has occurred. Leonard P. Rome, MD, chairman of the AAP's Chapter Chairmen's Committee, points out that "excessive somnolence," for instance, refers to a state of sleep from which the infant cannot be aroused; a drowsy child who wakes up to eat is not experiencing this reaction. As for "excessive scream-

ing," some clinicians have reported a "high-pitched, unusual cry," not necessarily continuous.

In other cases, when a worrisome reaction occurs that does not actually contraindicate further pertussis immunization—for example, considerable drowsiness from which the child can be aroused, with moderate fever persisting for two days—some pediatricians prefer to include only half the normal dose of pertussis vaccine in the next immunization. If the reaction recurs, they administer DT from then on.

With regard to preexisting neurological disorders, the Red Book says that pertussis vaccine is not contraindicated when seizures "are infrequent, occurred months or years ago, or are well controlled." Most children with developmental retardation and those with nonprogressive disorders (eg, cerebral palsy) also may receive the vaccine.

Progressive or evolving disease (eg, progressive encephalomyelopathy) is a contraindication, however, "if only because confusion might occur regarding the relationship of the vaccine to disease progression," the Red Book states. A family history of neurological illness, including seizures, is not a contraindication.

The following mild side effects of DTP are common and temporary, and generally do not contraindicate further immunization:

- Induration, sometimes with tenderness, at the injection site
- Malaise
- Slight to moderate fever

Normally, persons older than age 7 do not require the vaccine, says the AAP, but during whooping cough epidemics, adolescents and heavily exposed health care workers may be given a booster dose of 0.25 mL of pertussis vaccine, adsorbed.—E. R. G.

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conditions as infectious illnesses and occult underlying neurological disorders.

Even if incidence could be determined, the problem of identifying which children are vulnerable would remain. Seizures associated with DTP can be febrile or afebrile and can occur unexpectedly after any shot in the series, even when a child has not shown a previous reaction to the vaccine. The mechanism(s) of such reactions are unknown.

Thompson told *JAMA MEDICAL NEWS* that she has heard from hundreds of parents who believe that DTP damaged their children. She therefore speculates that the rate of such damage may be higher than previously suspected. Fulginiti, who is professor and chairman, Department of Pediatrics, University of Arizona College of Medicine, Tucson, likewise continues to hear from parents but has been able to reassure some of them that their children's health problems are unrelated to DTP.

What everyone agrees is that a child who has experienced a major reaction to one of the DTP injections should not receive the "P" component again (see page 14)—although Thompson says some parents have told her that their physicians insisted on giving a second shot despite convulsions or high fever after the first one.

Thompson also contends that until now, many physicians in private practice, unlike public health clinics, have not informed parents about the risks of DTP. Pediatricians concede that discussions of the vaccine with parents may have been less frequent or thorough before the NBC report. In its recent mailing, the AAP included the information sheet that public health clinics issue as part of their informed consent procedure. This sheet explains, "About 1 out of every 7,000 children who get the shots will have a more serious side effect such as high fever, convulsions, abnormal crying for several hours, or going into shock and getting pale. Rarely, about once in every 100,000 shots, inflammation of the brain (encephalitis) or other brain damage may occur. Sudden unexplained infant deaths have occurred rarely after vaccination, but it is not known whether this has been caused by the vaccine." (Most authorities now believe that there is no demonstrable association between DTP immunization and sudden infant death syndrome [SIDS].)

Information regarding deaths allegedly resulting from DTP-associated neurological damage is almost completely anecdotal. The FDA Bureau of Biologics has received no reports of such deaths during the past five years. Since the CDC instituted its monitoring system in 1978, says Alan Hinman, MD, director of the centers' Immunization Division, "we have received reports of 44 deaths occurring within four weeks of DTP immunization. Thirty-two of the deaths were SIDS. Of the other 12, in only one was there autopsy or clinical information that would indicate that this was a neurologic or encephalopathic response to DTP."

The Deleted Disease

What Thompson's report failed to cover adequately, say incensed pediatricians, was the ravages of pertussis itself. They point out that many parents of young children who saw the program have little knowledge of the disease because they were born after improved living conditions and, much more importantly (as indicated by epidemiologic research), DTP immunization virtually eradicated whooping cough in the United States. During the 1930s, up to 265,000 cases and 7,000 deaths were reported annually. At present, reported cases average 1,000 to 3,000 per year and deaths, five to 20 per year.

In his testimony before the subcommittee, Fulginiti noted that children who fall prey to the illness "cough unmercifully, choking in the process and gasping for air. They often vomit and become acutely undernourished and dehydrated. They may destroy parts of their lungs and brain from hemorrhage, lack of oxygen, or both." Added Parrott, "Perhaps we need more testimony from grandparents who remember."

The NBC report did include a verbal description of the disease, along with an old training film on the subject, but claimed that whooping cough "is no longer a killer . . . except in infants who are probably too young to receive the vaccine." It is true that treatment of whooping cough is better than in the past. But it remains "a horrible disease" (and sometimes a fatal one), emphasize scientific staff members at the FDA Bureau of Biologics. Patients in England had many more seizures than one could expect in association with DTP vaccination, and 3% of Swedish patients fractured their ribs as a result of coughing.

Morbidity and mortality are highest in persons under 6 months of age; at present, the only way of protecting such infants adequately is to immunize their prospective contacts. (Immunity to pertussis is not acquired through the placenta or from breast milk, either because a mother's own DTP-induced immunity has not persisted into adulthood or because the mechanism of immunity is not the formation of serum antibodies.)

In defense of the minimal attention she devoted to the illness, Thompson says that she would have liked nothing better than to show an afflicted child. She complains, however, that she could not obtain any current material for such a segment from the CDC, the FDA, or 20 different medical institutions—because of the lack of whooping cough cases in this country. She adds that she is still trying to obtain such material. A CDC official, she says, told her, "You should show the English children dying," but she considers a trip to England an unreasonable request in view of her station's limited budget.

The AAP was especially concerned about this lack of balance in Thompson's report. Josephine Schuda, director of the AAP's Division of Communications, relates that Jennison and Fulginiti approached NBC with "a request for the airing of a program that

would present the benefits and risks of the vaccine in a more balanced and accurate way."

The network responded by granting a brief, live segment on the May 24 "Today Show," consisting of an interview of Fulginiti by Thompson. Of this concession Fulginiti says gloomily, "The lead-in was footage of a damaged child." Comments Jean Lockhart, MD, director of the AAP's Department of Health Care and Pediatric Practice, "The interview followed a long segment about a male centerfold. The whole thing was so poor."

On the Cutting Room Floor?

Tendentious interviewing, highly selective editing, and the sacrifice of ethical scruples to personal ambition were criticisms leveled at Thompson and NBC by proponents of immunization who participated in the original program.

For example, Edward A. Mortimer, Jr, MD, member and former chairman of the Red Book Committee, says that Thompson interviewed him for about five hours, asking him the same question "repeatedly in slightly different ways, apparently to develop or obtain an answer that fitted with the general tone of the program." He adds that "by cutting and splicing, remarks taken out of context gave a very different meaning from what I intended or what I believe." Thompson says that Mortimer got "one and a half minutes, which is a long time for television," adding: "I am not going to risk my reputation by moving someone's words around. That speaks to my journalistic integrity."

Additionally, say the program's critics, Thompson chose dubious "experts" to badmouth the vaccine and endowed them with false credentials. Mendelsohn, for instance, has a consulting practice in pediatrics and family practice in Evanston, Ill, and has held some academic appointments in the past, but the program's identification of him as a former head of pediatrics at the University of Illinois School of Medicine was incorrect. Moreover, the show failed to mention that Mendelsohn opposes not only DTP, but all other immunizations as well.

Another prominently featured authority was Dr Gordon T. Stewart of Glasgow, Scotland, who has maintained that pertussis vaccine does not confer immunity and that the rates of whooping cough have declined largely as a result of improved socioeconomic conditions (*Lancet* 1977;1:234-237).

On the program, Stewart was identified as having served on the United Kingdom's Committee on Safety of Medicines. Actually he was not a member, but he did provide data to the committee. These data were examined by an ad hoc panel (on which Stewart served), established by the committee, which concluded that the rate of brain damage might be approximately 1 case per 53,000 children vaccinated. The committee declined to accept these data without further evidence from other studies, including the

UK's National Childhood Encephalopathy Study (NCES). As it turned out, the NCES placed the risk of permanent brain damage at 1 case per 110,000 injections (not, as Thompson reported, at 1 case per 100,000 children). The NBC program made much of the fact that British authorities favored the NCES over the study with which Stewart was associated. But the program did not mention that the NCES was a case-control study that examined the first 1,000 cases of serious neurological illness occurring in England, Scotland, and Wales among children aged 2 to 36 months during a three-year period, whereas Stewart's data consisted of retrospective material from the Association of Parents of Vaccine Damaged Children. In fact, some of his reports were submitted to the government in claims for compensation of vaccine damage.

Both Stewart and Mendelsohn (the former on the program and the latter in an interview with *JAMA MEDICAL NEWS*) referred to the outbreak of whooping cough in England as the "so-called epidemic." Mendelsohn says he will not be convinced until he sees bacteriologic proof of pertussis in the reported victims, adding that British physicians are diagnosing the disease "every time someone clears his throat."

Thompson also focused on the late Bobby Young, PhD, who was billed as a former vaccine researcher at the FDA and the University of Maryland, College Park. Young was a former contracts officer at the FDA's Bureau of Biologics who also had a laboratory at the bureau but was involved, as far as anyone there can ascertain now, only with viral vaccines. When he later moved on to Maryland, he was chairman of the undergraduate microbiology department; again, he had no known involvement, says that department, with pertussis vaccine research.

On the program, Young said he feared that few infants escape some kind of neurological damage from DTP. He used such elliptical language as "I mean, if the child isn't frankly rendered a vegetable and yet has a fever. . . ." And, following a reference that Thompson made to persistent or high-pitched crying in the UCLA study, Young stated, "This may be indicative of brain damage in the recipient child." No association between such crying and brain damage has ever been established, however. Moreover, UCLA's Cherry points out, such juxtapositions made it appear that Young was commenting on the study—which was not completed until after his death.

In sum, officially acknowledged experts on pertussis and DTP describe the NBC presentation as "the most frightening bit of show business sensationalism I've ever seen," "biased, histrionic, and inaccurate," and even "amoral and psychopathic."

Whether the show will have a lasting impact remains to be seen. No data on current DTP immunization rates are available, but anecdotal impressions suggest that they have not changed substantially since the broadcast. Ohio's Rome believes that the

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country's pediatricians probably have averted mass rejection of the vaccine and a consequent increase in cases of pertussis. Others, however, are not so sure.

Hinman points out that a 30% drop in immunizations lasting only a week after the broadcast would not cause an epidemic, but a lesser decrease over a longer period could have serious repercussions.

Much will depend on whether—and how—the broadcast media keep the issue alive in people's minds. Physicians who support continuing DTP immunization have been fairly successful in getting airtime, at least in some cities. Rome has confronted Thompson on a PBS radio call-in program in Washington, DC. Mortimer, who is also chairman of the Department of Epidemiology and Community Health at Cleveland's Case Western Reserve University School of Medicine, has appeared on a number of broadcasts and says he was treated well by the NBC affiliate station in Cleveland, which permitted him to criticize Thompson's program on the air.

Mendelsohn also is appearing on broadcasts coast to coast, to discuss the dangers of DPT. He told *JAMA MEDICAL NEWS* that he regards Thompson's report as "the greatest thing since apple pie. For the first time the American people got the truth about pertussis vaccine."

In addition, NBC affiliate stations have the option

of continuing to show "DTP: Vaccine Roulette." To the charges of reportorial irresponsibility and distortion that the program continues to provoke, Thompson responds, "I obviously categorically deny that." Her report, she insists, was "extremely responsible" and "anything but distorted," and was not intended to stop parents from having their children immunized.

"I think much of the potshooting has come from people who have been burned," Thompson says. "We hit a lot of raw nerves. . . . Many doctors are miffed because they have to talk to their patients now."

But, says Rome, "I tell all parents that one child in three will have a reaction to the shot," including minor reactions, "and I ask them to call me if there is any reaction whatsoever."

Fulginiti stresses that the AAP has long supported the establishment of a national program to compensate persons with vaccine-associated injuries.

Oregon's Meechan and New Mexico's Waltner both speak gravely of the ethical concerns they weigh with respect to immunization. Statistics are meaningless, Meechan reflects, if it's your own child who has a reaction to a vaccine.

Says Robbins, "I keep getting letters from parents of damaged children. I don't know what to say to them. If that happened to my child, I don't know how I'd feel. I guess I'd feel like crying."

—by ELIZABETH RASCHE GONZÁLEZ

Newer pertussis vaccines on horizon

More than 1 million children in Japan have received new and possibly safer pertussis vaccines produced by several different manufacturers. Unlike the classic whole-cell vaccine (the "P" component of the diphtheria-tetanus-pertussis immunization, DTP), the new products are partially purified and detoxified acellular or extract vaccines.

At a recent workshop on new pertussis vaccines held at the National Institutes of Health, Bethesda, Md, M. Kimura, MD, of a similar agency in Japan, reported on clinical trials of the vaccines in 5,000 children. All of the children began their series of two immunizations at 24 months of age (although the series is now begun at 6 months of age).

The vaccines produced a much lower incidence of local reactions and fever than DTP. It is too soon to know whether they also cause less or no CNS irritation, but preliminary evidence indicates that the incidence of serious reactions such as seizures and shocklike states is considerably lower, according to scientific staff at the Food and Drug Administration's Bureau of Biologics. The bureau also reports that the vaccines have substantially lower amounts of pyrogenic material than the whole-cell vaccine currently licensed in the United States.

In addition to analyzing the Japanese vaccines, the

Bureau of Biologics is conducting its own research into individual components of the *Bordetella pertussis* organism, under Ronald D. Sekura, PhD, Charles R. Manclark, PhD, and J. L. Cowell, PhD, as are a number of Japanese and American vaccine manufacturers. All of this work is concentrated on isolating and purifying the 20 or so surface antigens of the *B pertussis* organism and characterizing their ability to induce immune reactions.

Until recently, explains John Robbins, MD, director, Division of Bacterial Products, Bureau of Biologics, researchers did not know how the organism interacts with the host. The turning point was an article (*Rev Infect Dis* 1979;1:401-411) in which Margaret Pittman, PhD, guest scientist at the bureau, proposed that pertussis is a toxin-mediated disease similar to diphtheria and tetanus.

Summarizing the disease process, Robbins explains, "In the first stage, the organism is located on the cilia of the upper respiratory tree, where it causes upper respiratory disease with no distinctive symptoms. During this time the organism can be recovered from the respiratory mucosa and the disease is communicable. After the disease progresses and its distinctive effects—coughing, apnea, profound metabolic alterations, and a remarkable lymphocytosis—become man-

ifest, the organism is no longer easily recoverable," indicating that "the initial infection is mediated by the bacterium, whereas the active disease state is mediated by a toxin elaborated by the bacterium."

Pittman theorized that immunity to pertussis entails the formation of antibodies to both lymphocytosis-promoting factor (LPF), which she designated "pertussis toxin," and another surface antigen, filamentous hemagglutinin (FHA). At present, reported Cowell at the NIH workshop, it is known that administration of either antigen to mice will protect the animals from experimentally induced pertussis. The new Japanese vaccines contain both antigens.

This new knowledge notwithstanding, work with acellular vaccines is not entirely new. Some 30 years ago, before it was known that the pertussis organism contains more than one surface antigen, Louis Pillemer, PhD, of the Institute of Pathology at what was then Western Reserve University in Cleveland, adsorbed an incompletely characterized extract of *B pertussis* and showed that its protective and hemagglutinating properties arise from two chemically dissimilar structures (*Proc Soc Exp Biol Med* 1950; 75:704-705). In fact, Pillemer actually created an early extract vaccine that appeared efficacious when tested in British field trials. No manufacturer adopted it, but Pillemer's brainchild did illustrate that an acellular vaccine can protect against pertussis.

Only one vaccine emerging from the recent studies has been administered to humans in the United States or seems likely to undergo clinical testing anytime soon. That vaccine, manufactured by Wyeth Laboratories, was given to several hundred infants in Texas and Arizona in a study headed by Philip A. Brunell, MD, professor and head, Department of Pediatrics, University of Texas Medical School at San Antonio. Brunell reported at the workshop that the new product seemed less reactogenic than the whole-cell vaccine. One of the children developed a shocklike syndrome, however, and results of the study were inconclusive overall.

Why were the Japanese vaccines hustled into wide-spread use? Japanese children received DTP for more than 40 years, as mandated by the US Occupation Forces. That immunization program proceeded smoothly until 1974-75, when two children died following immunization. The Japanese Ministry of Health and Welfare suspended immunization for several months; when the program resumed, compliance was poor, and a whooping cough epidemic ensued. In the face of this situation, the government decided to authorize general use of the new vaccines beginning in August 1981. These vaccines are still in short supply. Because of the epidemic, children in Japan are now receiving *any* available vaccine, including DTP.—E. R. G.

Untoward effect of a face peel: toxic shock syndrome

Toxic shock syndrome (TSS) continues to occur in strange situations.

One of the most recent concerns a transsexual Canadian man who contacted the disease while undergoing a full chemical face peel to fight off the ravages of wrinkling, electrolysis scarring, and mild acne.

The case was reported to the annual meeting of the American Academy of Facial Plastic and Reconstructive Surgery in Palm Beach, Fla, by John R. Dmytryshyn, MD, clinical instructor in the Department of Otolaryngology at the University of British Columbia Health Sciences Centre, Vancouver.

Dmytryshyn said that the 42-year-old man underwent a full-thickness chemical peel under general anesthesia. The peel ingredients included 3 mL of 89% phenol, 2 mL of tap water, 7 drops of Septisol, and 3 drops of croton oil.

Postoperative swelling was controlled for the first four days by continuous application of cool compresses and dexamethasone, 12 mg per day. On the fifth day, the patient experienced fever (temperature reaching 39 °C), tachycardia, and hypotension. The facial swelling continued and was accompanied by a malodorous purulent discharge. The trunk and upper arms were marked with a diffuse nonpruritic macular erythroderma, and the patient was confused and somnolent.

Gram's stains of the purulent material from the face showed +4 polymorphonuclear cells and +3 gram positive cocci in clusters. Cultures yielded *Staphylococcus aureus*. The organism was resistant to penicillin and methicillin by standard disk-diffusion susceptibility testing.

The patient was treated with cloxacillin (2 g every four hours), plus penicillin G, 2,000,000 units every four hours, intravenously, and was given 5% dextrose in saline, 200 mL/hr for the first 24 hours, then 125 mL/hr for the next 48 hours. In all, 10 L of crystalloid was administered during the first three days.

The BP returned to normal within eight hours of initiation of fluids. Three days after appearance of the skin rash, skin desquamation—considered highly characteristic of TSS—occurred on the hands and feet.

The patient was discharged well, 15 days after admission to the hospital.

Dmytryshyn noted that possible risk factors in this case may have been colonization of nose, throat, axilla, and perineum with *S aureus*. The large denuded area on the face could have allowed toxin absorption, and the risk for TSS could also have been heightened by use of continuous wet compresses on the infected area of the face and, possibly, by the use of diethylstilbestrol, which was being given to this patient to achieve feminization.—by MILAN KORCOK