

verse reactions of primary vaccinations with DTP-OPV; however, to be effective the patient needed 3 doses of acetaminophen immediately, 4 and 8 hours after vaccination. This administration schedule is not suitable for our policy of vaccination in children. In Taiwan, each child receives an oral polio vaccine (Sabin) and DTP vaccine, so the ideal first dose of acetaminophen should be 30 min after immunization. As in Japan, increased adverse reactions reduced the vaccinated rate in 1975, and reported pertussis cases and deaths increased approximately 20-fold over the next 5 year.<sup>2-3</sup> If prophylactic acetaminophen administration can be shown to reduce fever or eliminate other adverse reactions, it may lessen the parents' anxiety about the painful experience of the babies. Therefore, we conducted a randomized, placebo-controlled, double-blind study of acetaminophen prophylaxis of adverse reactions to diphtheria-tetanus-pertussis and oral polio vaccine in 412 infants aged 2, 4, 6, and 18 months.

## METHODS

### Subjects

Infants who received regularly scheduled DTP-polio vaccinations were prospectively enrolled in this study. We collected data from the subjects from 18 May 1996 through 28 February 1997. They all had visited the well-baby OPD at Taipei Medical College Hospital for routine vaccinations at 2, 4, 6, or 18 months of age. Only children who were receiving their appropriate immunizations for their ages were eligible for this study. Infants with febrile illnesses, close family history of seizures, upper respiratory tract infections, chronic illnesses, or previous severe reactions to DTP-P vaccination were excluded. Informed consent was obtained from the parents prior to vaccination.

### Vaccine

Commercially available licensed diphtheria and tetanus toxoids with adsorbed pertussis vaccine, DTP vaccine (Pasteur Merieux), and oral polio vaccine (SmithKline Beecham Biologicals) were used for this study. These are the standard vaccines used in Taiwan.

**Table 1. Number of Subjects Receiving Either a Placebo or Acetaminophen for Various Doses of DTP-OPV Vaccine**

Dose	Placebo	Acetaminophen	Total
1	60	66	126
2	55	50	105
3	46	44	90
Booster	42	49	91
Total	203	209	412

The recommended dose of 0.5 ml was administered via deep intramuscular injection into the upper lateral thigh (primary series, 1-3 doses) or buttock (booster).

### Prophylactic Acetaminophen

Four groups were designated based on age at DTP-P vaccine receipt: 2, 4, 6, and 18 months of age. There were approximately equal numbers of subjects in each age group who received acetaminophen or a placebo (Table 1). Both the placebo and acetaminophen were supplied by a pharmacist in 2 packages labeled only with the study identification number. The acetaminophen was given as a pink powder. The placebo consisted of pink sugar powder and Biofermin, which looks and tastes the same as acetaminophen. The packages of medication were given at random; neither the parents nor the pediatricians in charge knew the contents of individual packages.

Each dosage of acetaminophen was 15 mg/kg. The first dose of medication was given 30 min after the vaccination. The second dose was given 4 hours after the first dose. All subjects totally received 2 doses of acetaminophen or placebo, respectively.

### Evaluation of Reactions

Rectal thermometers were provided and parents received detailed instructions on obtaining rectal temperature, including holding the thermometer in place for 2 min. The rectal temperatures of the infants were recorded at 4, 6, 16, 24, and 48 hours after vaccination. Parents were also provided with a plastic ruler to measure redness and swelling at the injection site at 24 and 48 hours post vaccination. If the diameter of local redness, or swelling was more than 2 cm, it was recorded