were comparable to those produced by the higher dose of either drug alone.

These findings suggest: (1) therapeutic advantages of the combination of high doses of theophylline and an oral β-adrenergic agonist in asthmatic patients who are not well controlled on a high dose of either drug alone and (2) advantages of the combination of these drugs in lower doses in patients who experience intolerable side effects from a high dose of either drug alone.

112. Serum terbutaline assay by high-pressure liquid chromatography.

James M. Pugely, M.D., and O. L. Frick, M.D., San Francisco, Calif.

There is a need for an easy, reproducible assay of terbutaline in the blood. With such an assay it would be possible to better evaluate dose-response relationships and drug interactions, especially in lowering doses of theophylline which has a narrow therapeutic-toxic blood level range. It has been possible to obtain a dose versus time curve in a rabbit model by the use of high-pressure liquid chromatography. A Bondapak C 18 column with 5% acetonitrile in 95% sodium acetate buffer, pH 4.0 was used. Terbutaline sulfate was injected subcutaneously in rabbits at 0.1 mg/kg and 0.4 mg/kg. Baseline blood samples were drawn and then serial samples at 30 mm 1 hr, 2 hr, 4 hr, 6 hr, and 8 hr were obtained. A standard composed of equal volumes of injectible terbutaline sulfate, and buffer was prepared, run on the same column and compared in time and proportion to the serum samples.

In 8 New Zealand rabbits, the terbutaline serum peaked in ranges 50 to 200 μg/ml for 0.1 mg/kg dosage and 200 to 600 μg/ml for the 0.4 mg/kg dosage. The peak values were obtained at 1 to 2 hr with a second variable peak in a few animals at 6 hr. The mean half-life was 6½ hr in most rabbits.

Terbutaline in human serum after oral ingestion is measurable by the same method. However, a natural metabolite, has a similar chromatographic peak; resolution of this problem should permit serum terbutaline assay for clinical use.

113. Salbutamol vs theophylline in asthmatic children age 2 to 6 yr.

W. E. Pierson, M.D., C. T. Furukawa, M.D., G. G. Shapiro, M.D., and C. W. Bierman, M.D., Seattle, Wash.

The effectiveness of theophylline and several newer beta-2 adrenergic agonists has been shown in adults and youths. However the effectiveness of the agents given separately or simultaneously has not been examined in very young asthmatic children (ages 2 to 6).

Seventeen patients were studied for a 7-wk period that included a serum theophylline standardized dosage and a 2-wk double-blind crossover period of salbutamol or placebo. Each patient was given placebo or salbutamol, a 10-mg/kg along with regular theophylline. The theophylline levels during both treatment periods with salbutamol and/or placebo averaged 7.1 μg/ml.

The patients were examined weekly and performed pulmonary function tests including peak expiratory flow rate (PEFR) and forced oscillation measurement of total respiratory resistance (TRR). The results are shown in Table I.

TABLE I.

	PEFR (1/min)		TRR (CmH_2O/1 sec)	
(N = 17)	Baseline	2 hr	Baseline	2 hr
Placebo	195	(NS) 189	1.72	(NS) 1.75
Salbutamol	188	216 (p = 0.01)	1.80	1.35 (p = 0.02)

Results

The results of both PEFR and forced oscillatory resistance showed a significant improvement with salbutamol. There were few side effects and tremor was notably absent.

In conclusion we determined that salbutamol offers significant bronchodilating effectiveness independent of concomitant theophylline treatment in very young asthmatic children.

114. The effect of metaproterenol in chronic asthmatic children receiving therapeutic doses of theophylline.

S. Duriseti, M.D., C. E. Groncy, M.D., S. P. Galant, M.D., and L. Strick, M.D., Irvine, Calif.

The effect of metaproterenol added to therapeutic doses of theophylline was compared with a combination of placebo and theophylline by measurement of the 1-sec forced expiratory volume (FEV_1), forced vital capacity (FVC), and maximal midexpiratory flow rate (MMEFR) in 17 asthmatic children in a double-blind crossover study. Plasma theophylline levels were measured at 1.5 hr (peak) and 6 hr (trough) after drug administration on all test days. Children weighing less than 60 pounds received 10 mg of metaproterenol (1 teaspoon), while those weighing more than 60 pounds received 20 mg every 6 hr.

The mean peak theophylline level for both metaproterenol and placebo treatment days was approximately 10 μg/ml, while the trough was 6 μg/ml. Metaproterenol caused a significantly greater increase in FEV_1 ($p < 0.05$)