

felt that this publication legitimized what we had been doing. Of great importance, it also led to increased resources and space within academic pediatric departments. This occurred at a time when federal monies available for hospital construction supported the building of inpatient units for adolescent patients.

The most valuable result of this redefinition of the age limits of pediatrics was, undoubtedly, the opportunity to teach a growing number of trainees interested in adolescents. The creation of the Section on Adolescence by the AAP also was an outgrowth of the recognition of the need for continuing medical education of pediatricians in practice. Because the Society for Adolescent Medicine had been formed in 1968, primarily by pediatricians and a few internists, and held its early national scientific meetings in concert with those of the AAP, there was synergy in the training effort.

The impact of publication of this Statement also can be felt in the increasing requirements by the Residency Review Committee for inclusion of formalized training in adolescent medicine in pediatric programs.

Most recently, the force of this statement was felt in the documentation for the need for subspecialty certification in adolescent medicine by the American Board of Pediatrics. The establishment of subspecialty certification ensures that there will be academicians capable of training generalist pediatricians to provide primary care to teenagers. It also is significant that this was a conjoint SubBoard with the American Board of Internal Medicine, paving the way for eventual improvement in management of the transition of health care from adolescent to adult settings as they mature.

The issue of interface with internal medicine was critical in the deliberations that led to the setting of

the upper age limit of adolescence at 21 years. According to Sherrel Hammar, MD (personal communication), this reflected acknowledgment of the difficulty faced by teenagers with chronic illnesses in finding appropriate care providers when they reached adulthood. The improved longevity of many of these patients is, happily, leading to efforts to train internists and family practitioners in their care.

Despite the importance of this definitional Statement to the care of teenagers by pediatricians, it is sobering to find that only 7% of office visits to all physicians are by adolescents, despite the fact that they constitute almost 20% of the population. Moreover, more family practitioners than pediatricians are providing the care. The sad reality is that 25 years after this Statement was published, most teenagers still are not getting any care, let alone the care they deserve.

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## COMMENTARY

### *A Controlled Trial of Antepartum Glucocorticoid Treatment for Prevention of the Respiratory Distress Syndrome in Premature Infants,* by G. C. Liggins, MB, PhD, FRCOG, and R. N. Howie, MB, MRACP, *Pediatrics*, 1972;50:515-525

Comments by Mary Ellen Avery, MD

**ABSTRACT OF ORIGINAL ARTICLE.** A controlled trial of betamethasone therapy was carried out in 282 mothers in whom premature delivery threatened or was

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planned before 37 weeks' gestation, in the hope of reducing the incidence of neonatal respiratory distress syndrome by accelerating functional maturation of the fetal lung. A total of 213 mothers were in spontaneous premature labor. When necessary, ethanol or salbutamol infusions were used to delay delivery while steroid or placebo therapy was given. Delay for at least 24 hours was achieved in 77% of the mothers. In these unplanned deliveries, early neonatal mortality was 3.2% in the treated group and 15.0% in the control subjects. There

were no deaths with hyaline membrane disease or intraventricular cerebral hemorrhage in infants of mothers who had received betamethasone for at least 24 hours before delivery. The respiratory distress syndrome occurred less often in treated babies (9.0%) than in controls (25.8%), but the difference was confined to babies of <32 weeks' gestation who had been treated for at least 24 hours before delivery (11.8% of the treated babies compared with 69.6% of the control babies). There may be an increased risk of fetal death in pregnancies complicated by severe hypertension–edema–proteinuria syndromes and treated with betamethasone, but no other hazard of steroid therapy was noted.

We conclude that this preliminary evidence justifies additional trials, but that additional work is needed before any new routine procedure is established.

#### COMMENTARY

The first controlled trial of antepartum glucocorticoids for prevention of respiratory distress syndrome launched more than 25 years of exploration of the hormonal regulation of lung maturation and the optimal means of achieving it in premature infants. Sir Graham Liggins, an obstetrician, and Ross Howie, a neonatologist, in Auckland, New Zealand, tested whether antenatal glucocorticoids given to the mother within 48 to 72 hours before a planned delivery could accelerate fetal lung maturation and prevent deaths from respiratory distress syndrome (also known as hyaline membrane disease).<sup>1</sup> From December 1969 to early 1972, they embarked on a prospective, blinded, controlled, clinical trial based on Liggins' experience with premature delivery of fetal lambs infused with glucocorticoids. In 1969, Liggins had published the observation that such an intervention promoted early onset of labor in the ewe, but the newborn premature lambs, delivered at 117 to 123 days' gestation, had partial aeration of lungs from spontaneous ventilation.<sup>2</sup>

Meanwhile, deLemos and colleagues at Johns Hopkins, confirmed the observation of Liggins in twin fetal lambs, one of which received dexamethasone and the other saline. The dexamethasone-treated animals all had lungs with accelerated appearance of pulmonary surfactants at least a week earlier than did controls.<sup>3</sup>

The translation of these findings in lambs to the clinical setting accomplished in New Zealand in 1972, to routine care elsewhere, was slow, for readily understood reasons.<sup>4</sup> Most obstetricians were concerned about the appearance of delayed adverse effects on fetal tissues and were reluctant to use steroids before follow-up studies could be reviewed. There also was a question of efficacy in infants born before 32 weeks' gestation, who were not represented in the New Zealand study (average gestational age at delivery, 249 days in treated group, 225 in controls). Many other groups, including the Bal-

lards, found synthetic steroid administration optimal between 26 and 34 weeks.<sup>5</sup>

Another reason for delay in acceptance of antenatal glucocorticoid therapy was failure of the Collaborative Group on Antenatal Steroid Therapy in 1981 to show efficacy in males or in Caucasian subgroups. Overall, no complications were cited, but the limited benefit in a large multicenter study was discouraging. By 1982, the New Zealand group provided the crucial follow-up of 6-year-old children whose mothers had been treated antenatally with betamethasone,<sup>6</sup> and by 1984, the Collaborative Group on Antenatal Steroid Therapy reported that no detectable growth or physical, motor, or developmental deficiencies were identified in the first 3 years of life that could be attributed to steroid therapy.<sup>7</sup>

In the 1990s, additional perspectives on antenatal glucocorticoids, summarized by Jobe and co-workers in 1993,<sup>8</sup> showed that the combined use of antenatal glucocorticoids and surfactant replacement therapy was better than either alone, and if a choice had to be made, glucocorticoids conferred the greater benefit. By 1994, the National Institutes of Health Consensus Conference, complete with meta-analyses, established the efficacy of glucocorticoids as well as their cost benefit.<sup>9</sup> By 1996, the impact on survival of preterm infants by glucocorticoids and surfactant replacement therapy contributed to the lowest neonatal mortality in the United States in history.<sup>10</sup>

It was a long road from the publication by a New Zealand obstetrician/endocrinologist interested in parturition to life-saving interventions on behalf of preterm infants. The next step will be to reduce preterm births.

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