# *Pathophysiology and Management of Bronchiolitis*

IN THIS ISSUE of the Journal Downes and his colleagues describe the pathophysiology and management of 30 infants, aged 1–18 months, who had bronchiolitis.

The causative agent in bronchiolitis is usually viral [1] but it may be of bacterial or mixed origin. There is probably a spectrum of involvement of the respiratory tract, from simple tracheobronchitis in which only the larger bronchi are affected to diffuse infection of the bronchiolar tree, which has a more serious prognosis. The degree of illness and mortality varies with the severity of involvement and the type of etiological agent—particularly under epidemic conditions.

Mortality rates from 2 to 7 per cent have been reported, though anatomic and pathogenetic considerations render comparisons of mortality among different series of limited value. It is important, therefore, that Downes and his co-workers have objective evidence of the gravity of of their patients' conditions in the form of blood gas and acid-base values, combined with clinical criteria. Their patients were classified into three groups: 19 with "adequate ventilation ($Pa_{CO_2} < 65$ mm. Hg); five with "impending respiratory failure" ($Pa_{CO_2} > 65$ mm. Hg), but not satisfying certain defined clinical criteria); and six with "acute respiratory failure" ($Pa_{CO_2} > 65$ mm. Hg, with three well-defined clinical criteria present for longer than one hour.

As others have shown,[2] the main feature of bronchiolitis is an uncompensated respiratory acidosis, the degree of which parallels the severity of the clinical signs. Metabolic acidosis is usually minimal, presumably a reflection of the acuteness of the onset of respiratory decompensation and, more important, of the satisfactory tissue oxygenation achieved with supplemental oxygen. Downes and his coworkers make two interesting points in this connection. First, supplemental oxygen apparently does not result in increased $CO_2$ retention, in contradistinction to the situation in some adults with chronic hypercarbia; second, while the patient is breathing air, there is an inverse relationship between the degree of $CO_2$ retention and the level of oxygenation. This has also been reported by Reynolds.[3] From these observations one may deduce that the hypoxemia has a hypoventilatory component.

Downes and his colleagues also report results of physiologic studies of five of their patients. Hypoxemia could be corrected with supplemental oxygen; however, in four patients in their "adequate ventilation" group, sufficient alveolar ventilation could be maintained only at the catabolic and fatiguing expense of increases of as much as 317 per cent in minute volumes, apparently because of increases in deadspace ventilation ($V_{D_P}/V_T$ ratios up to 0.69). The fifth case studied, belonging to their group of "impending respiratory failures," had a $V_{D_P}/V_T$ ratio of 0.76, a $Pa_{CO_2}$ of 70 mm. Hg; a minute volume 113 per cent and a $CO_2$ production 74 per cent of predicted values, indicating marked alveolar hypoventilation. It is plausibly argued that most patients are able to maintain adequate alveolar ventilation only by considerable increases in minute volume. When they are unable to sustain the increased work involved in ventilating lungs with considerably decreased dynamic compliances at up to threefold increases in minute volume, decompensation occurs. This results in falling total and alveolar ventilation, a reduced $CO_2$ output and rising $Pa_{CO_2}$, with clinical signs of "respiratory failure." Five of their patients fell into this category on the basis of serial $Pa_{CO_2}$ estimations and clinical observations.

One would like to have seen an extension of the ventilatory observations to this group, but the difficulties of studying seriously-ill infants, especially by a method that involves adding an additional mask deadspace (6.3 ml.) of the same order of magnitude as the subject's own anatomical deadspace, should not be underestimated.

The authors argue logically that for the patients with respiratory failure intermittent positive-pressure ventilation (IPPV) via a

nasotracheal tube is the treatment of choice. Their expert application, involving curarization, in fact resulted in recoveries in all six of their patients despite three potentially serious complications—pneumothorax, *Klebsiella* pneumonia and mild subglottic stenosis. It is difficult not to agree that the authors have made out a good case for this form of treatment, bearing in mind that the mean $P_{CO_2}$ at the height of the illness in their ventilated group was 103 mm. Hg. However, simultaneous $Pa_{O_2}$ values are not given. Experience with infants in this age group has shown that, providing oxygenation is maintained, as apparently it was in these patients, in the absence of significant metabolic acidosis, even relatively long periods of severe hypercarbia can be survived. The correct criteria for intervention are elusive, but those set by Downes and his associates seem reasonable.

The hazards of assisted ventilation in the infant age group are by no means negligible, as evidenced by the occurrence of three potentially lethal complications in the six cases ventilated. The decision to ventilate must be based on an assessment of the relative risks of progressive respiratory failure compared with the potential complications of IPPV. More experimental results are needed, but the authors of this paper are to be congratulated on a useful addition to our knowledge of the pathophysiologic correlates of the clinical condition in bronchiolitis, and for demonstrating a method of management based rationally on the functional disturbance.

It is presently impossible to be dogmatic about the treatment of bronchiolitis. Because of the possibility of a bacterial or mixed bacterial-and-viral etiology, broad-spectrum antibiotics should usually be employed, but they carry the risk of selection of resistant organisms such as *Klebsiella pneumoniae*. Clinical impressions have suggested that steroids[4, 5] are beneficial, but controlled statistical evidence is lacking. Using the physiologic data reported by Downes *et al.* and by Reynolds,[2, 3, 6] a number of further recommendations can be made.

The maintenance of full oxygenation is usually possible with inspired oxygen concentrations up to 40 per cent, particularly as there is no risk of precipitating further $CO_2$ retention. A small plastic hood can be used for the infant, thus avoiding cumbersome tents. The flow of humidified air–oxygen mix should be at 5–10 liters per minute. Inspired oxygen concentrations should be checked frequently until the desired level is stabilized; then at two-hour intervals. In critical cases the required oxygen concentration may be guided by measurement of arterial oxygen tension.[6] Dehydration and the maintenance of fluid and electrolyte balance usually necessitate intravenous therapy. If the physical signs suggest bronchospasm, a trial of bronchodilator drugs is justifiable; however, in small infants the danger of toxicity of agents such as aminophylline exists. Usually these measures will suffice, but if the clinical signs of respiratory failure supervene, accompanied by a fall in $Pa_{O_2}$ and a rise in $Pa_{CO_2}$, then tracheal toilet via bronchoscopy should be performed. Others have advocated tracheostomy.[8] It seems likely that the associated tracheobronchial toilet was responsible for the improvement reported, though reduction in anatomical dead-space ventliation may have played a part. If, after bronchoscopy, there is no clinical improvement, IPPV as advocated by Downes *et al.*, should be undertaken, provided adequate facilities are available for this highly demanding form of treatment.

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# *Barbiturates Combined with Local Anesthetics*

FATALITIES from reactions to local anesthetics have been reported since the first introduction of these drugs to clinical medicine. Physicians appear to have been nonchalant about the lethal potentials of these drugs, perhaps because the deaths seem to occur at infrequent intervals. What is not realized is that deaths occur sporadically in many areas simultaneously, and that the mortality actually is much higher than it appears from the incidental, seemingly infrequent deaths within the experience of the individual physician. In addition, many fatal and nonfatal reactions occur which are not reported and therefore pass unnoticed. The number of fatalities or near-fatalities is unknown, and will remain so because physicians not thoroughly familiar with these drugs often are not aware of tragic experiences they barely miss. Therefore, it is gratifying to observe an increasing awareness of the lethal potential of these drugs. Much of the credit for this can be given to those anesthesiologists who have waged a vigorous campaign during the past decade to emphasize the lethal nature of the drugs when they are not used with caution. The occasional user is the one least aware of the hazards of the systemic effects of local anesthetics, although seasoned workers have had their difficulties, too.

The fact that systemic reactions are due to high plasma levels is now universally accepted. The effects of high plasma levels on the central nervous system have been emphasized, and attention has been drawn to the convulsions which follow rapid absorption of the drug. Less emphasis has been placed upon the fact that the action of local anesthetics on the nervous system is biphasic; stimulation occurs initially, followed by depression. Indeed, the depressant effects have been utilized for the treatment of epilepsy by Bernhard and Bohn,[1] in electroshock therapy by Usubiaga,[2] and for convulsions resulting from tetanus, by Godman and Adriani.[3] Central excitation may be short-lived. Certain areas of the brain may be undergoing excitation while neurons in other parts are depressed.

The classic experiments of Tatum,[4] showing that barbiturates antagonize the convulsive manifestations of cocaine, led to their adoption and widespread use, not only for treatment of convulsions, but also for prophylaxis. The prophylactic use of sedative doses of barbiturate to counteract convulsions was ineffective; their use for this purpose has been abandoned. Although they continue to be used for their anticonvulsant effects this use has recently been challenged. Moore and Bridenbaugh [5] advocated oxygen as an antidote and suggested the use of muscle relaxants to overcome the convulsive effects. Although the threshold intravenous convulsive doses of local anesthetics are not altered by inhalation of oxygen, the relief of any attendant anoxia is without a doubt beneficial, since the minimal convulsive dose is decreased by anoxia.[6] However, the excitation of the nervous system continues during the paralysis produced by the neuromuscular blocker. Whether continued excitation injures the neurons is debatable.

The conjecture that barbiturates may augment the depression of cardiovascular activity resulting from the local anesthetic has been