Communications for this section will be published as space and priorities permit. The comments should not exceed 350 words in length, with a maximum of five references; one figure or table can be printed. Exceptions may occur under particular circumstances. Contributions may include comments on articles published in this periodical, or they may be reports of unique educational character. Please submit letters online at http://mc.manuscriptcentral.com/CHEST. Please include a cover letter with a complete list of authors (including full first and last names and highest degree), corresponding author’s address, phone number, fax number, and e-mail address (if applicable). Specific permission to publish should be cited in the cover letter or appended as a postscript. CHEST reserves the right to edit letters for length and clarity.

Communications to the Editor

Transthoracic Echocardiography Is Not Proven To Be the Principal Echocardiographic Test in the ICU

To the Editor:

Dr. Joseph and his group1 recently reported data in CHEST (November 2004) on the role of transthoracic echocardiography (TTE) in identifying cardiac etiologies of shock in the ICU. I congratulate the authors on their high rate of “adequate” TTE images (99%), but I find that it is a rate far exceeding the more common 80% “adequate” rate that is seen in many clinical practices, even with tissue harmonic imaging. Of note, the authors do not strictly define their criteria for image “adequacy,” which is the crux of the study. Further, there is no mention of the role of echogenic contrast agents, which have been shown to consistently improve image quality in difficult-to-image patients.2 Cardiac index, certainly a key value in patients who are in shock, was only able to be measured by TTE in 46% of the patients, whereas transesophageal echocardiography (TEE) studies can routinely derive this value in at least 90% of patients.3 Post-cardiac surgery patients were excluded from this study, as the authors note, but this is a very important group of patients who are at high risk for cardiogenic shock in whom TEE has been well-validated. Further, this study does not directly compare TTE to TEE. All of these points make me a bit hesitant to agree with the authors’ concluding statement, “TTE should be considered not only the initial, but also the principal echocardiographic test in the critical care environment.” As TTE technologies improve, this indeed may become the case, but the data presented here do not yet support such a change in clinical practice.

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Carbon Dioxide Kinetics

To the Editor:

In his editorial on the pitfalls of the routine use of pulse oximetry in the ICU in a recent issue of CHEST (November 2004), Demers’ related an anecdote regarding a young female patient with an acute drug overdose who was receiving mechanical ventilatory support and in whom a delayed arterial blood gas measurement revealed a Paco2 less than half the normal value. We are told that a repeat blood gas measurement 2 h after halving the respiratory rate (and therefore the minute ventilation) was basically unchanged and that only after an additional 7 h was the arterial Paco2 in the mid-40 mm Hg range. The author argued that this reflected the large-body CO2 stores (stated as 25 L) in series with the CO2 present in alveolar gas.

These results seem to be at odds with published information on the kinetics of CO2 clearance. Sullivan et al4 hyperventilated sedated, paralyzed, healthy male subjects for 2 h until their Paco2 reached plateau values between 13 and 25 mm Hg, and then decreased minute ventilation to between 25% and 53% of the baseline values for the five subjects. The response in Paco2 was rapid, with an increase to half the final asymptotic value in approximately 10 min. The data fit best a two-component exponential model with a fast-space rate constant of 0.58 min⁻¹ and a slow-space rate constant of 0.034 min⁻¹, corresponding to half-times of 1.5 and 23 min, respectively. The estimate given in the editorial for CO2 storage space seems to have been considerably higher than the estimates in the literature (2.05 to 3.17 mL/kg/mm Hg, or 5.7 to 8.9 L for an individual weighing 70-kg with a Paco2 of 40 mm Hg). The observed lack of rise in Paco2 over an extended period of time might represent unappreciated

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extra ventilatory efforts or some clinical situation in which the metabolic production of CO₂ was decreasing over time.

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On Some Analyses

To the Editor:

There are methodological errors being made in statistical analyses, resulting in flawed results. Examples are in the studies by Hiasa et al1 and Oudiz et al.2 The problem is the authors' use of two-sample t tests, analysis of variance, or analysis of covariance to compare means, which assumes the normality and equality of unknown variances in the groups considered. The Central Limit Theorem justifies normality for mean inferences, but unknown variances need not be equal, making these methods not generally applicable to comparing means. This problem is not removed by futilely3 testing for the equality of variances.

Avoiding normality and nuisance variances with rank tests such as the Wilcoxon test4 means that, if significant, they do not specifically say anything about the mean, median, mode, or any specific moment by Hiasa et al1 and Oudiz et al.2 The problem is the authors' use of rank tests, analysis of variance, or analysis of covariance to compare means, which assumes the normality and equality of unknown variances in the groups considered. The Central Limit Theorem justifies normality for mean inferences, but unknown variances need not be equal, making these methods not generally applicable to comparing means. This problem is not removed by futilely3 testing for the equality of variances.

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The problem of comparing the means of normal populations exactly with unknown variances is the Behrens-Fisher problem, which was solved by Tsakok5 in its generalized form. The Tsakok solution is more effective in detecting significant mean differences, even with unknown equal variances. Its exposition6 is available elsewhere.

A statistical software package (GSP; London, UK) implements the Tsakok technique. Some results from Table 1 and Table 2 are given. These appear to have been overlooked. After taking care to obtain the data, they deserve correct analysis.

The article by Tsakok7 on exact, unconditional, uniformly most powerful unbiased tests extends the Tsakok technique to the nonparametric problem of comparing distributions, superseding rank tests or the Fisher exact test (which is neither exact nor unconditional). An extension to dependent samples8 is indicated. The Tsakok articles are reprinted9 with further results.

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Table 1—Some Results of Mean Comparisons From Table 2

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Group A vs Group C</th>
<th>Group B vs Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>123I-MIBG early H/M</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>ECG RV5 + SV1</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Echocardiography LVDd</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>

*S = significant difference between means at 0.02 (one significant figure) significance level; RV5 = voltage of R wave in lead V5; SV1 = voltage of S wave in lead V1; LVDd = left ventricular end-systolic dimension; MIBG = metaiodobenzylguadidine; H/M = heart/mediastinum ratio.

Table 2—Some Results of Mean Comparisons From Table 2

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Treprostinil vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate change</td>
<td>S</td>
</tr>
<tr>
<td>PAPm change</td>
<td>S</td>
</tr>
<tr>
<td>Mean right atrial pressure change</td>
<td>S</td>
</tr>
<tr>
<td>Mean pulmonary capillary wedge pressure change</td>
<td>S</td>
</tr>
</tbody>
</table>

*PAPm = mean pulmonary arterial pressure. See Table 1 for abbreviation not used in the text.

Function of the Günther Tulip Vena Caval Filter

To the Editor:

As an interventional radiologist with a strong interest in vena caval filters, I read the evidence-based guidelines of the Seventh
ACCP Conference with careful attention. In the second part of the publication, Antithrombotic Therapy for Venous Thromboembolic Disease, Dr. Buller and colleagues have made a citation error in Section 4.5, vena caval interruption for the initial treatment of pulmonary embolism. They state that the Günther Tulip filter (Cook; Bloomington, IN) appears to be “less satisfactory.” To support this they provide a reference from 1992. This reference is to the Günther Basket filter (which has been withdrawn from sale), not the Günther Tulip filter. Although the similarity of the names could cause confusion, the Günther Tulip filter is a completely different device. It functions well as both a permanent vena caval filter, and as a retrievable device. The maximum window between implantation and retrieval is not known, but successful retrieval has been reported after implantation periods of up to 126 days.3

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References

Peak Expiratory Flow Time in Amyotrophic Lateral Sclerosis*

To the Editor:

I read with interest the recent article in CHEST (January 2005) by Wilson et al1 on peak expiratory flow time (PEFT) in amyotrophic lateral sclerosis (ALS). They reported increasing PEFT with time, with the rate of increase in PEFT being greater than the rate of decline in either FVC or peak expiratory flow rate (PEFR).

The authors did not measure maximal expiratory pressure (Pmax). Since Pmax correlates with PEFR in patients with ALS,2 the interpretation of the PEFT data in the absence of respiratory muscle strength measurements creates more questions than it gives answers. The PEFT reflects in large part the ability of the expiratory muscles to develop rapid (explosive) force and is related to the rate of pressure rise. It is also related to the Pmax because the capacity of skeletal muscles for rapid force development declines in proportion to the ability to generate maximal force.3 If this is not the case for ALS patients, the measurement of Pmax would establish the superiority of PEFT in monitoring respiratory function in these patients. If, on the other hand, changes in PEFT relate to Pmax, then the measurement of Pmax is preferable to that of PEFT. Pmax, as for all indexes of rapid force development, is less reliable and less reproducible than PEFT.4,5 In addition, the measurement of PEF will require the standardization of the forced expiratory maneuver and, specifically, the speed of inspiration prior to exhalation, which was not controlled for in the study of Wilson et al.4 A fast inspiration to total lung capacity will prestretch (eccentric contraction) the expiratory muscles, which will then develop greater pressure (and a greater rate of pressure rise) during the subsequent forceful (concentric) contraction.6,7 The property of skeletal muscles to produce greater force when a concentric contraction is immediately preceded by an eccentric contraction is known as the stretch-shortening cycle. Therefore, standardizing the expiratory maneuver used for measuring PEFT will help to minimize the variability of the PEFT.

Finally, the authors state that the PEFR is determined by the force-velocity characteristics of the respiratory muscles rather than by the mechanical properties of the lung. The current notion is that PEFR is determined by a flow-limiting mechanism. Some studies8 using the negative expiratory pressure technique,9 calculating PEFR on the basis of wave speed theory10 or employing specific maneuvers to augment expiratory effort through the stretch-shortening cycle, have shown that PEFR is not limited by the velocity of muscle shortening.

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9 Tantucci C, Duguet A, Giampicollo P, et al. The best peak expiratory flow is flow-limited and effort-independent in...
Delivery of β-Agonists in the Emergency Department Setting

Metered-Dose Inhalers or Nebulizers?

To the Editor:

In a recent issue of CHEST (January 2005), Dolovich et al. reported on evidence-based guidelines for device selection and the outcomes of aerosol therapy. Overall, I agree with the authors in the equivalence of using nebulizers and metered-dose inhalers (MDIs) with holding chamber in the emergency department (ED) setting. Nevertheless, the recommendation that both methods are appropriate for the delivery of short-acting β-agonists in the ED is not entirely supported by the evidence. There are important potential limitations to this assertion. (1) Compared with nebulizers, MDIs with spacers provide a quicker and more cost-effective way to delivered β-agonists, with fewer adverse effects. (2) Nebulizers are more expensive (both in terms of equipment cost and personnel time), require a power source, need regular maintenance, and represent a potential cause of cross-infection. (3) The output can be highly variable. It is very dependent on the technique used by the operator, and small variations in the gas flow and filling alter the performance significantly. Not surprisingly, larger doses of the aerosol must be administered during acute episodes of severe asthma to achieve the maximal effect. (4) A systematic revision recently published has demonstrated that the use of an MDI with a spacer is more effective in terms of decreasing the duration of hospitalization and improving clinical scores than the use of a nebulizer in the ED. Nevertheless, the recommendation that both MDIs and nebulizers are appropriate for the delivery of short-acting β-agonists in the ED is not entirely supported by the evidence. Therefore, these recommendations were applied only to the subpopulation of patients without life-threatening asthma. All studies reviewed in these guidelines excluded patients with life-threatening acute asthma. Therefore, these recommendations were applied only to the subpopulation of patients without these characteristics. The fact that each treatment can take 15 to 20 min instead of 1 to 2 min is a very important aspect of the treatment of patients with life-threatening asthma. In our experience, the use of a pressurized pMDI plus spacer can be the only way to deliver high doses of bronchodilators quickly to patients with acute severe asthma with a reduced level of consciousness. In any case, the assertion that “in acute asthma with life threatening features the nebulized route (oxygen-driven) is recommended” does not have support from the evidence.

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REFERENCES

Sodium Bicarbonate in Life-Threatening Asthma

Not So Soon!

To the Editor:

We read with interest the article by Buysse et al (March 2005), who evaluated the clinical effect of sodium bicarbonate (NaHCO3) on carbon dioxide levels in 17 children with life-threatening asthma. They show a significant decrease of Pco2 after NaHCO3 infusion and improvement of respiratory distress in the majority. However, certain points need clarification. First, the authors claim that NaHCO3 per se has beneficial effects in asthma. The authors assume that other therapies remained unchanged during the time period between the blood gas analysis before and after the administration of NaHCO3 and attribute this to clinical improvement secondary to NaHCO3. However, one should also remember that the patients had received glucocorticoids, and the improvement during that time could be due to the latent period of onset of action of glucocorticoids. Hence, this is only a crude estimate of the efficacy of NaHCO3, and it requires adjustment for other variables, such as salbutamol, ipratropium, and glucocorticoids, by a multivariable analysis. Second, the fear of administration of NaHCO3 is mainly (or only) in patients with pure respiratory acidosis and not mixed metabolic and respiratory acidosis. In the present study, the majority of patients had mixed metabolic and respiratory acidosis, which otherwise is not an absolute contraindication. Although several risks are associated with NaHCO3, the most prominent concern is an acute worsening of intracellular acidosis. Approximately 10 to 15% of HCO3-I immediately converts to carbon dioxide, so that a typical 1 mEq/kg dose administered rapidly results in approximately 200 mL of carbon dioxide (equivalent to 1 min of carbon dioxide production for an average-size adult). In general, treating primary respiratory acidosis with NaHCO3 should be discouraged, and should be administered to patients with acute severe asthma who have mixed metabolic and respiratory acidosis pending larger trials or in strict trial conditions.

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Inadequate LVEDV is the very basis of DHF, and its additional primary lowering by positive pressure could only further limit stroke volume, and hence cardiac output, because of the steep curve for left ventricular diastolic pressure in relation to volume. Hence, caution must be used because patients with DHF are sensitive to the preload reduction and may become hypotensive or have severe prerenal azotemia. In this context, there may be a theoretical superiority of bilevel positive airway pressure over CPAP because of varying inspiratory and expiratory pressures. But the authors did show improvement in the clinical condition of the patients?

We believe that improvement because of CPAP is probably due to the reduction in heart rate (101 ± 19 beats/min at baseline vs 83 ± 11 beats/min after CPAP). Tachycardia causes an increase in demand for myocardial oxygen and a decrease in coronary perfusion time, which may lead to myocardial ischemia, even in the absence of obstructive coronary artery disease. In addition, there may be insufficient time for complete relaxation, with a resultant increase in diastolic pressure that compromises ventricular filling. CPAP causes a significant decrease in the heart rate, resulting from increased parasympathetic tone in response to CPAP-induced lung inflation.

However, because of small numbers it is difficult to draw any firm conclusions, unlike systolic dysfunction, in which a recent metaanalysis of almost 500 patients conducted showed significant decrease in rates of intubation and mortality, and the numbers needed to treat to prevent one intubation and one death are six and eight, respectively. Thus, pending larger data, CPAP in DHF should be used only under strict experimental conditions with the potential of clinical deterioration due to CPAP per se kept in mind.

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REFERENCES

To the Editor:

We read with great interest the comments by Drs. Agarwal and Gupta regarding our article (March 2005) entitled “Does Continuous Positive Airway Pressure (CPAP) by Face Mask Improve Patients With Acute Cardiogenic Pulmonary Edema (ACPE) Due to Left Ventricular Diastolic Dysfunction?” The authors do not agree with the proposed mechanism of CPAP in patients presenting with ACPE that was illustrated by our study.
I would like to make the following remarks about their comments. First, the authors should read the introduction to our article in order to appreciate that, as was also the case for them, our expectation prior to performing the study was the contrary of what we actually found.1,2 Second, they stated that inadequate left ventricular end-diastolic volume (LVEDV) is the basis of diastolic heart failure, and they expected that positive pressure could limit left ventricular filling and cardiac output. However, chronic diastolic heart failure is different from ACPE due to diastolic dysfunction. Indeed, keeping in mind that transthoracic echocardiography underestimates LVEDV,3 in our study,1 as in the study by Ghandi et al.,4 patients presenting with ACPE had a normal mean (± SD) LVEDV (107 ± 4 and 109 ± 43 mL, respectively). These results render the authors’ argument irrelevant as inadequate LVEDV was not observed in patients with ACPE due to diastolic dysfunction.

Second, the authors believe that bilevel positive airway pressure should theoretically be more efficient than CPAP for treating patients with ACPE due to diastolic dysfunction. How could additional intrathoracic pressure be better for left ventricular filling, excluding the role of assistance to the respiratory muscles? Moreover, in a recent study,5 therapy with bilevel positive airway pressure did not offer any advantage over CPAP therapy in the treatment of ACPE.

Third, the authors believe that the improvement related to CPAP seen in patients with ACPE due to diastolic dysfunction in our study is due to the reduction in heart rate that causes less myocardial work and better coronary perfusion and left ventricular filling. However, even if this theoretical assumption may be agreed upon, our study does not confirm it, as no increase in ejection fraction and LVEDV was observed during CPAP (Starling curve).1

Finally, Agarwal and Gupta misunderstood our conclusions to mean that the decrease in LVEDV is a helpful mechanism of action of CPAP therapy in patients with ACPE due to diastolic dysfunction. As explained in the “Discussion” section, we think that CPAP, by decreasing respiratory work in patients with cardiopulmonary edema, unloads the heart from the large amount of cardiac output that supplies the respiratory muscles and improves oxygen delivery for other tissues. Physicians should keep in mind that it is not because ACPE is a heart disease affecting the lung that the beneficial effect of CPAP is mandatory related to its hemodynamic effects on the pump. Indeed, as we have already stated in others articles,6,7 supporting the lung by positive pressure acts as a pulmonary circulatory drive.8

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