correctly point out that this may be due to the manner in which these patients arrived to them (ie, most were receiving mechanical ventilation at hospital admission, had significant underlying disease, and, most importantly, many were receiving antibiotic therapy at the time of diagnosis). Thus, the similar outcomes for patients with monomicrobial and polymicrobial pneumonia are not so surprisingly.

What struck me in reviewing this article was how little attention surgeons pay to the problem of VAP in our patients. The investigative group from Hôpital Bichat (Paris, France) as well as several others1–4 have provided a systematic inquiry into the complex problem of VAP. Most of these studies have focused on medical or mixed populations of critically ill patients and in the process have contributed to our knowledge of VAP in trauma and surgical patients. By comparison, VAP is an enormous problem in trauma patients requiring mechanical ventilation, especially if this condition is combined with a neurologic injury. The incidence of VAP may approach 50 to 80% in certain populations.5,6 Despite this, only a few surgical investigators5–8 have shown any interest in this problem. The proceedings of the first ever Pneumonia Summit held by surgeons were published in 2000.9 I hope that this modest attempt to call attention to the problem of VAP in surgical and trauma patients will lead to a thoughtful investigation similar to the one provided by our medical and pulmonary colleagues.

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Cytokines, Genes, and ARDS

The leading cause of death in patients with ARDS is multiorgan failure (MOF) caused by a systemic inflammatory response. This finding has led to a great evolution in our understanding of ARDS since it was first reported in 1967.1 We have struggled over the last number of years to find the molecular basis for the changes we see in the gross pathology of the lung and other end organs.

Many investigators have begun to develop the relationship between cytokine modulation and cytokine levels in the physiology of ARDS and how this syndrome relates to the systemic inflammatory response and end-organ dysfunction. Donnelly and colleagues2 found that patients at risk for ARDS who had higher levels of interleukin (IL)-8 in BAL fluid subsequently progressed to ARDS, thus providing a potential early marker for the development of this syndrome and some clues as to pathogenesis. The clinical importance of this developing understanding of cytokine modulation has led to studies looking at how the simplest treatment for respiratory failure and ARDS, mechanical ventilation, contributes to MOF through the spread of inflammatory mediators.3,4

In this issue of CHEST (see page 1716), Takatsuka et al report how certain patients who are positive for human leukocyte antigen (HLA)-B51 or B-52 respond to the administration of granulocyte colony-stimulating factor (G-CSF). These patients showed significant increases in tumor necrosis factor (TNF)-α and IL-8 at the onset of ARDS. This data differed from a large group of patients who received G-CSF and did not have respiratory dysfunction develop, but had neither HLA-B51 or B52 antigens. It points out that some groups of patients may be genetically primed to have a multiplied response develop to a trigger, and thus release increased levels of cytokines than other patients.

Work from Moine et al5 showed that patients with ARDS had increased activation of the transcriptional regulatory factor nuclear factor-kB in alveolar macrophages. This work suggests a transcriptional mech-
anism that may be important in maintaining the persistently elevated expression of proinflammatory cytokines and other mediators that characterize ARDS. Regional alterations of proinflammatory and immunoregulatory cytokine gene expression appear, therefore, to greatly contribute to the patient’s response to a trigger and maintenance of response in patients with established ARDS. Persistently elevated levels of cytokines, including TNF-\(\alpha\) and IL-8 in BAL, have been correlated with poor outcome. The patients in this current study showed an elevation of both of these cytokines. We know that a primary trigger for the inflammatory response in circulation is the adhesion of neutrophils to vascular endothelial cells and their migration and infiltration into stroma, and this mechanism plays a basic role in the pathogenesis of ARDS. Both TNF-\(\alpha\) and IL-8 are key to this response.

We must continue to develop the genetic map of patients at risk of having ARDS and systemic inflammatory response develop. In understanding the gene, we may better understand and treat ARDS. Gene therapy represents one of several new technologies that are changing the face of medicine and medical technology. Molecular biology, in general, has greatly advanced our understanding of the pathogenesis of many diseases; gene therapy is poised to implement that new knowledge.

Clinical trials are now under way with a variety of gene therapy approaches for the inherited diseases, but as this research has gone forward, it has become clear that even acquired diseases have a genetic component, which theoretically could be a target for gene therapy. Therefore, our understanding of specific patients at risk may lead to new molecular-based treatments for ARDS. By changing gene expression, we may prevent the elevation of certain inflammatory cytokines, and the reaction of the body to these cytokines.

The article by Takatsuka et al in this issue of CHEST only supports the importance in the interrelationship of both clinical and basic science research and how this work will lead us down the uncharted path of the molecular basis of inflammatory diseases. We must collect data on the genetic makeup of patients with severe ARDS and how these patients are different or similar to patients who do not develop ARDS. This may contribute more to patient care than novel new therapies targeted at only one or more cytokines.

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References

Pulmonary Munchausen Syndrome

Elsewhere in this issue of CHEST (see page 1704), Highland and Flume report their involvement with a patient with cystic fibrosis. They initiated all the appropriate tests but, apparently from the very beginning, had doubts regarding this case: somehow things didn’t add up. They continue by constructing a list of their positive criteria supporting the patient’s true diagnosis, Munchausen syndrome. With the correct diagnosis, they then set out to offer care but, as is the rule with this disorder, the patient escaped from the hospital before help could be implemented. Every case of Munchausen syndrome is different but usually starts with everything being almost too good—the patient helps too much with the diagnosis, armed with a bewildering amount of supporting facts, carrying sheaves of paperwork (to include results from previous diagnostic studies such as in this case), and appearing most helpful and gracious. However, things usually begin to soon fall apart. The patient’s knowledge base, no matter the ruse, soon belies itself, as the facts that the patient has are out of step with that which they have presented so far. Additionally, the personality disorder—most commonly borderline personality—reveals itself in the...