recommendations to optimize therapy in ARDS by minimizing “shunt” with positive end-expiratory pressure, but to reduce FIO₂ to avoid oxygen toxicity, conflicting choices may arise. Conversely, a decreasing FIO₂ may cause a rise in "shunt" that may be interpreted as clinical worsening just as a rise in "shunt" at an FIO₂ of 1.0. Finally, should the same degree of venous admixture in two patients, caused in one by true right-to-left shunt and in the other by ventilation-perfusion mismatching, be considered identical when contemplating prognosis or recommending modes of therapy? Expressing it another way, does the same venous admixture in two patients at markedly different FIO₂ have the same meaning? If "shunt" or calculated venous admixture is selected as a variable to monitor in large cooperative prospective studies in adult respiratory distress syndrome, these issues will need to be addressed.

I agree that observations and theoretical considerations make it unsatisfactory to measure true right-to-left shunt during 100 percent oxygen breathing. However, in view of the above, it may be just as unsatisfactory to measure venous admixture at lower arbitrary oxygen concentrations. Since only multiple arterial PO₂ measurements on a series of inspired oxygen concentrations spanning a range of FIO₂ could provide an estimate of the behavior of venous admixture in an individual patient, I would suggest caution in the interpretation of "shunt" measured at any single FIO₂, including 1.0.

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To the Editor:
The questions posed in Dr. Sue's letter are in part related to the semantics of the term "intrapulmonary shunt." The calculated shunt ratio (Qsp/Qt) expresses a theoretical percentage of total cardiac output returned to the left heart without change in oxygen content from its value in the pulmonary artery. This calculation allows no distinction between the two components of intrapulmonary shunting: 1) "true shunt"—lung areas where the V/A/Q = O₂; and 2) "shunt effect" or "venous admixture"—lung areas where the V/A/Q is low, but greater than zero. A semiquantitative clinical distinction between these two components can frequently be made by noting the changes in calculated shunt that occur with varying FIO₂ concentrations. However, it must be emphasized that a precise quantitative differentiation between "true shunt" and "venous admixture" cannot be clinically delineated at present.

Historically, attempts to resolve this dilemma have been directed towards attempting to eliminate the component of "venous admixture" by administering 100 percent oxygen. Our study clearly documented that calculated intrapulmonary shunt measurements (Qsp/Qt) are significantly increased with 100 percent oxygen administration independent of the patient's disease state or respiratory care support. With that fact established, the clinical intent of isolating the component of true intrapulmonary shunt by administering 100 percent oxygen is invalid and our statement "there is no clinical advantage to making this measurement at an FIO₂ of 1.0" is justified.

Our studies reveal that the (Qsp/Qt) decreases in most patients as the FIO₂ is increased from maintenance to .5, and that the (Qsp/Qt) is increased as the FIO₂ is raised from .5 to 1.0. These data were not included in our publication since they had been previously reported. This information is consistent with our previously published concept that the optimal maintenance FIO₂ is the minimal oxygen concentration that achieves an arterial Po₂ of at least 60 mm Hg.

The clinical relevance of comparing a shunt measurement at a maintenance FIO₂ to one at an FIO₂ of 0.5 frequently allows for reasonable clinical assessment of changes in "calculated venous admixture." Although this information is frequently less than optimal, in many patients it is often helpful therapeutically by delineating whether the major component of the intrapulmonary shunt is true shunt or venous admixture.

In summary, we would agree with Dr. Sue that it may turn out to be as unsatisfactory to measure intrapulmonary shunting at a reference FIO₂ of .5 as it is an FIO₂ of 1.0. However, 50 percent oxygen does not appear to create the increases in shunt calculations produced by 100 percent oxygen administration, and furthermore, these iatrogenic increases in "intrapulmonary shunting" are not only misleading, but potentially detrimental to the patients.

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To the Editor:
In a recent article by Shapiro et al, it was demonstrated that intrapulmonary shunting (Qsp) increased with the administration of 100 percent oxygen. The mean Qsp at the maintenance inspired oxygen (FIO₂) in patients in whom it was directly measured in their study was 19.4 ± 8.3 (SD) percent. This is similar to data we have previously reported in which Qsp increased with 100 percent oxygen in 26/40 studies. However, in contrast to the data by Shapiro et al, in 14/40 studies in patients with more severe respiratory insufficiency, Qsp with 100 percent oxygen did not change or decrease. Mean Qsp at the maintenance FIO₂ in the group whose Qsp increased with 100 percent oxygen was lower.
than in the group in which \( Q_{sp} \) did not increase (13.3 ± 1.2 vs 27.5 ± 3.1 percent, mean ± SE, \( p < .001 \)).

\( Q_{sp} \) with 100 percent oxygen may increase as a result of absorption atelectasis and redistribution of regional pulmonary blood flow to poorly or nonventilated lung areas. However, a decline in \( Q_{sp} \) with 100 percent oxygen may result from a decrease in "shunt like" effects produced by low \( V/Q \) areas or diffusion impairment. It has been suggested that the change in \( Q_{sp} \) with increasing \( FIO_2 \) is a result of the interaction between those factors which will increase and those which will decrease \( Q_{sp} \). Our data suggest that this interaction favors an increase in \( Q_{sp} \) with 100 percent oxygen in those patients where \( Q_{sp} \) at the maintenance \( FIO_2 \) is low, but does not in more severely ill patients where \( Q_{sp} \) at the maintenance \( FIO_2 \) is higher.

We agree that measurement of \( Q_{sp} \) after administration of 100 percent oxygen may be misleading and may result in overestimation of \( Q_{sp} \). However, measurement of \( Q_{sp} \) at the maintenance \( FIO_2 \) and with 100 percent oxygen may give an estimate of the net effect of factors influencing the change in \( Q_{sp} \) with 100 percent oxygen and provide some insight into the pathophysiology of the underlying respiratory failure.

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To the Editor:

Undoubtedly some differences exist between our data and yours, but we agree this is most likely related to the severity of pulmonary pathology studied. Our study avoided patients with extremely high intrapulmonary shunts because we were interested in evaluating the effects of 100 percent oxygen on shunt measurements with moderate disease.

The concept that 100 percent oxygen may increase shunting as a result of absorption atelectasis and/or redistribution of regional pulmonary blood flow is well recognized. Equally well accepted is the phenomenon that appropriate increases in \( FIO_2 \) will decrease the shunt effect (venous admixture) component of a shunt measurement. Douglas et al demonstrated that a reduction of maximum effect in venous admixture was generally achieved at oxygen concentrations in the 40 to 50 percent range. Further increases in oxygen concentration resulted in increased shunt measurements. While we can conceptualize severe degrees of shunt effect (venous admixture) requiring oxygen concentrations higher than 40 to 50 percent, it is difficult to conceive that these severe \( V/Q \) imbalances require 100 percent oxygen in order to be adequately compensated.

We can find no basis for your statement that measurements of shunt at 100 percent oxygen may provide insight into the pathophysiology of the underlying respiratory failure. You have conceded that the administration of oxygen can result in overestimation of the shunt measurement; therefore, such a measurement may reflect either the underlying pulmonary pathophysiology or iatrogenic changes attributable to the methodology. At present, there is no way to ascertain the degree to which these two possibilities are occurring and therefore, this approach is clinically of little value in evaluating the existing pulmonary pathology.

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Conjunctival and Tonsillar Biopsies in Sarcoidosis

To the Editor:

We have studied the suitability of conjunctival and tonsillar biopsies for histologic diagnosis of sarcoidosis in 146 consecutive white patients (mean age 37 years, 87 women and 59 men). In 139, the clinico-radiologic diagnosis of sarcoidosis was confirmed histologically, mainly (127) from mediastinal lymph nodes. Seventy-one had extrathoracic sarcoid changes also. The disease was active in 49.

Conjunctival biopsy was taken from the lower fornix of 136 patients, using the method of Crick et al. If microscopy revealed nodules, the specimen was taken from them. Tonsillar biopsy was taken from 50 patients (unselected), after applying surface anesthesia with 1 percent lidocaine spray, from the upper pole of the left tonsil which always looked normal macroscopically. The procedures involved no complications.

Conjunctival biopsy revealed epithelioid cell granulomas in 23 patients (17 percent). Of the 35 with conjunctival nodules suggestive of sarcoidosis on slit-lamp examination, 14 (40 percent) showed granulomas on biopsy. Granulomas were found more often in the active (13/44) than in the inactive (10/92) phase of the disease, and more often in generalized (17/69) than in intrathoracically restricted disease (6/67). Tonsillar biopsy revealed granulomas in five patients (10 percent), all with active disease (5/17). Three of these had generalized (3/19) disease. At least one of the two biopsies showed granulomas in 11 (28 percent), again more often in those with active (6/11) or generalized (8/17) than with inactive (5/30) or restricted intrathoracic (3/24) disease.

Our study shows that conjunctival sarcoid lesions are fairly common also in white patients, although opposing opinions have been expressed. The relation of conjunctival sarcoid...