Hypoxemia During Extreme Hyperleukocytosis: How Spurious?

Andry Van de Louw MD PhD, Ruchi J Desai MD, Coursen W Schneider MD, and David F Claxton MD

BACKGROUND: Spurious hypoxemia has been described in case reports during extreme hyperleukocytosis and has led to recommendations for immediate cooling and analysis of arterial blood gases (ABGs). We sought to determine, in samples processed as recommended, the magnitude of spurious hypoxemia in acute leukemia subjects with hyperleukocytosis. METHODS: A retrospective chart review was conducted of all subjects admitted between 2003 and July 2014 for acute leukemia, who presented with white blood cell (WBC) count $> 50 \times 10^9$ cells/L and had ABGs performed. For each ABG, we collected $P_{aO_2}$, $S_{aO_2}$, simultaneous WBC count, and $S_{pO_2}$ when available. Bland and Altman analysis was used to assess the agreement between $S_{pO_2}$ and $S_{aO_2}$. RESULTS: One-hundred forty-six samples (from 45 subjects) were included, of which 57 samples (from 18 subjects) had data available for Bland and Altman analysis. Mean $(S_{pO_2} - S_{aO_2})$ was 2.5%, and 95% CI for limits of agreement between $S_{pO_2}$ and $S_{aO_2}$ was $(-10.1,15.1)\%$. The mean $(S_{pO_2} - S_{aO_2})$ was significantly higher for WBC count $> 100 \times 10^9$/L as compared with WBC count $< 100 \times 10^9$/L (3.8% vs 0.4%, $P = .04$), and the 95% CIs for limits of agreement were $(-10.3,18)\%$ versus $(-7.9,8.6)\%$. $S_{pO_2}$ and $S_{aO_2}$ were poorly correlated ($r^2 = 0.19$), whereas the difference $(S_{pO_2} - S_{aO_2})$ was fairly correlated with WBC count ($r^2 = 0.44$). Overall, 11 of 19 samples with WBC count $> 150 \times 10^9$/L had $P_{aO_2} < 55$ mm Hg whereas $S_{pO_2}$ was $> 94\%$, the proportion being 5 of 62 samples for WBC count $< 150 \times 10^9$/L ($P < .001$). Three subjects with WBC count $> 150 \times 10^9$/L exhibited large $S_{aO_2}$ to $S_{pO_2}$ differences (10–20%) before leukapheresis, which decreased to below 5% afterward. CONCLUSIONS: In subjects with acute leukemia and hyperleukocytosis, despite cooling and quickly analyzing the samples, we observed poor correlation and agreement between $S_{pO_2}$ and $S_{aO_2}$, unacceptably low for WBC count $> 100 \times 10^9$/L. Our results suggest that current guidelines may not totally prevent the diagnosis of spurious hypoxemia. Key words: hypoxemia; blood gas analysis; leukocytosis; acute leukemia; oximetry; oxygen. [Respir Care 0;0(0):1–. © 0 Daedalus Enterprises]

**Introduction**

Between 10 and 30% of patients newly diagnosed with acute leukemia present with hyperleukocytosis, usually defined as a white blood cell (WBC) count $> 100 \times 10^9$/L.\(^1\) Hyperleukocytosis not only negatively impacts overall survival but is also associated with increased early mortality, due to cerebral and pulmonary leukostasis.\(^2\) Patients requiring ICU admission and mechanical ventilation for acute respiratory failure have an overall poor survival\(^3\);\(^-\)\(^4\); thus, the respiratory status of acute leukemia patients with hyperleukocytosis is a major concern.

In acute leukemia, early detection of pulmonary compromise may prompt invasive intervention aimed at decreasing WBC count (leukapheresis) or improving gas exchange (mechanical ventilation). As clinical signs and chest x-ray findings may be subtle in immunocompromised hosts, the assessment of patient’s oxygenation via arterial blood gas (ABG) measurement and/or pulse oximetry is crucial. The finding of artifactual decrease in $P_{aO_2}$ due to increased...
oxygen consumption by WBCs in collected samples, has been described and referred to as spurious hypoxemia.\[^5\] A clinically relevant decay in Pa\textsubscript{O\textsubscript{2}} may occur as soon as 2 min in samples with WBC count as low as 55 × 10\textsuperscript{9}/L and seems proportional to WBC count.\[^5\] Several case reports have been published,\[^6-9\] but other authors have emphasized that the hypoxemia observed during hyperleukocytosis might actually be real and reflect subtle pulmonary leukostasis.\[^10\] Published data come from small series, but no study has ever systematically investigated the reliability of Pa\textsubscript{O\textsubscript{2}} and Sa\textsubscript{O\textsubscript{2}} in this setting, probably because of the relative rarity of extreme hyperleukocytosis. Although the American Association for Respiratory Care (AARC) has recommended immediate cooling and analysis of ABG for hyperleukocytic patients,\[^11\] these guidelines rely on limited data, and their effect on the magnitude of spurious hypoxemia has never been evaluated.

Given the limited published data, we included a large series of acute leukemia subjects with hyperleukocytosis in this retrospective study and systematically assessed (1) the relationship between Pa\textsubscript{O\textsubscript{2}}, Sa\textsubscript{O\textsubscript{2}}, and WBC count and (2) the agreement between Sa\textsubscript{O\textsubscript{2}} and Sp\textsubscript{O\textsubscript{2}} in cooled and quickly analyzed ABG.

## Methods

This retrospective study was approved by the Pennsylvania State University College of Medicine Institutional Review Board (IRB number 00000374), and informed consent was waived.

### Subjects

The charts of all subjects admitted to our institution with a newly diagnosed acute leukemia between January 2003 and July 2014 were screened, and all subjects with at least one ABG performed with a concomitant hyperleukocytosis (WBC count > 50 × 10\textsuperscript{9}/L) were included for further analysis.

### Data Collected

Baseline demographic data, significant comorbidities, type of acute leukemia, the use of invasive or noninvasive mechanical ventilation during admission, and 28-d and 6-month survival were collected. Whenever an ABG and a complete blood count were performed simultaneously, we collected Pa\textsubscript{O\textsubscript{2}}, Sa\textsubscript{O\textsubscript{2}}, and WBC count, along with Sp\textsubscript{O\textsubscript{2}} recorded at the same time, when available. Mean arterial pressure, heart rate, and vasopressor requirements (yes/no) at the time of ABG were also recorded. As per hospital policy, ABGs were collected in plastic syringes, stored in ice, and immediately sent (via pneumatic tube system) and processed in the laboratory, in agreement with published recommendations.\[^12\] The type of oxygen or ventilatory support was recorded as follows: no oxygen requirement, oxygen on nasal cannula, high-flow oxygen device (high-flow nasal cannula, Venturi mask), noninvasive mechanical ventilation, invasive mechanical ventilation.

### Statistical Analysis

All results were reported as mean ± SD (SPSS 20, SPSS, Chicago, Illinois). To assess the agreement between Sa\textsubscript{O\textsubscript{2}} and Sp\textsubscript{O\textsubscript{2}}, we used the method described by Bland and Altman,\[^13\] calculating the mean difference (bias, d) and the SD of the differences (precision, s) between Sp\textsubscript{O\textsubscript{2}} and Sa\textsubscript{O\textsubscript{2}}, and the 95% CIs for limits of agreement between Sp\textsubscript{O\textsubscript{2}} and Sa\textsubscript{O\textsubscript{2}} (d ± 2s). We used the 2-tailed Student t test to compare the bias, mean arterial pressure, and heart rate between samples with a WBC count below versus above 100 × 10\textsuperscript{9}/L. A 2-tailed Fisher exact test was used to compare the proportion of cases with hypoxemia (Pa\textsubscript{O\textsubscript{2}} < 55 mm Hg) and vasopressor requirements between samples with WBC below or above 100 × 10\textsuperscript{9}/L, respectively. Analysis of variance for repeated measures was used to assess the effect of leukapheresis on (Sp\textsubscript{O\textsubscript{2}} - Sa\textsubscript{O\textsubscript{2}}) differences. P < .05 was considered statistically significant.

### Results

### Subjects

Of 874 patients admitted during the 11½ year period with a newly diagnosed acute leukemia, 45 subjects were...
included in this analysis. In total, these subjects had 146 simultaneous complete blood counts and ABGs performed. All subjects had acute myeloid leukemia, and 6 had the acute promyelocytic leukemia subtype. None of the 63 patients with hyperleukocytic acute lymphoblastic leukemia had an ABG performed. Baseline demographic, clinical, and biological data as well as survival are detailed in Table 1. ABGs were performed while subjects were breathing room air ($n$ = 110), receiving oxygen on nasal cannula ($n$ = 23) or high-flow device ($n$ = 23), or supported by noninvasive ($n$ = 4) or invasive ($n$ = 93) mechanical ventilation.

### Table 1. Demographic, Clinical, Biological, and Survival Data for the 45 Subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60.0 ± 12.9</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>25/20</td>
</tr>
<tr>
<td>Comorbidities, $n$</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>5</td>
</tr>
<tr>
<td>COPD</td>
<td>3</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>0</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1</td>
</tr>
<tr>
<td>Previous cancer</td>
<td>6</td>
</tr>
<tr>
<td>Smoking history</td>
<td>15</td>
</tr>
<tr>
<td>Biological data on admission</td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.54 ± 0.71</td>
</tr>
<tr>
<td>Bilirubin, mg/dL</td>
<td>0.98 ± 0.47</td>
</tr>
<tr>
<td>LDH, units/L</td>
<td>4132 ± 3510</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>8.4 ± 1.5</td>
</tr>
<tr>
<td>INR</td>
<td>1.99 ± 2.05</td>
</tr>
<tr>
<td>Platelets, $\times 10^9$/L</td>
<td>53 ± 73</td>
</tr>
<tr>
<td>WBC count, $\times 10^9$/L</td>
<td>133.87 ± 93.52</td>
</tr>
<tr>
<td>$P_{\text{aO}_2}$, mm Hg</td>
<td>58.3 ± 18.7</td>
</tr>
<tr>
<td>$P_{\text{aCO}_2}$, mm Hg</td>
<td>37.8 ± 11.3</td>
</tr>
<tr>
<td>$S_{\text{aO}_2}$, %</td>
<td>90.3 ± 7.8</td>
</tr>
<tr>
<td>$S_{\text{aCO}_2}$, %</td>
<td>95.3 ± 2.9</td>
</tr>
<tr>
<td>Clinical data</td>
<td></td>
</tr>
<tr>
<td>Mean arterial pressure on admission, mm Hg</td>
<td>93 ± 17</td>
</tr>
<tr>
<td>Heart rate on admission, beats/min</td>
<td>103 ± 20</td>
</tr>
<tr>
<td>Subjects requiring vasopressors within 24 h, $n$</td>
<td>8/45</td>
</tr>
<tr>
<td>Subjects requiring invasive mechanical ventilation during admission, $n$</td>
<td>27/45</td>
</tr>
<tr>
<td>Duration of mechanical ventilation, d</td>
<td>7.3 ± 5.8</td>
</tr>
<tr>
<td>Day 28 survival, $n$</td>
<td>19/45</td>
</tr>
<tr>
<td>6-mo survival, $n$</td>
<td>8/45</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.

LDH = lactate dehydrogenase  
INR = international normalized ratio  
WBC = white blood cell

### Agreement and Correlation Between $S_{\text{aO}_2}$ and $S_{\text{PO}_2}$

Among the 146 ABGs performed in 45 subjects, we were able to collect simultaneous $S_{\text{aO}_2}$ and $S_{\text{PO}_2}$, and performed Bland and Altman analyses for 57 samples in 18 subjects. The mean ($S_{\text{PO}_2} - S_{\text{aO}_2}$) was 2.5%, and the 95% CI for limits of agreement between $S_{\text{PO}_2}$ and $S_{\text{aO}_2}$ were ($-10.1,15.1$)% (Fig. 1). Plotting $S_{\text{PO}_2}$ versus $S_{\text{aO}_2}$ (Fig. 2), we observed a poor correlation with a coefficient of determination ($r^2$) of 0.19.

### Effect of WBC Count on $P_{\text{aO}_2}$ and on the Agreement Between $S_{\text{PO}_2}$ and $S_{\text{aO}_2}$

Figures 3 and 4 represent the distributions of $P_{\text{aO}_2}$ and ($S_{\text{PO}_2} - S_{\text{aO}_2}$) versus WBC count, respectively. The coefficient of determination for the correlation between ($S_{\text{PO}_2} - S_{\text{aO}_2}$) and WBC count was 0.44; thus, 44% of the ($S_{\text{PO}_2} - S_{\text{aO}_2}$) variations were explained by WBC count.
S\textsubscript{aO\textsubscript{2}}) variance was accounted for by variations in WBC count. Figure 5 displays the effect of WBC count on the agreement between S\textsubscript{pO\textsubscript{2}} and S\textsubscript{aO\textsubscript{2}}. The correlation equation is S\textsubscript{pO\textsubscript{2}} − S\textsubscript{aO\textsubscript{2}} = 0.05 × white blood cell count − 4.0 (r\textsuperscript{2} = 0.44).

S\textsubscript{aO\textsubscript{2}} was > 88%, the proportion being only 4 of 36 samples for WBC count < 100 × 10\textsuperscript{9}/L (P = .003). Similarly, 11 of 19 samples with WBC count > 150 × 10\textsuperscript{9}/L had P\textsubscript{aO\textsubscript{2}} < 55 mm Hg, whereas S\textsubscript{pO\textsubscript{2}} was > 94%, the proportion being only 5 of 62 samples for WBC count < 150 × 10\textsuperscript{9}/L (P < .001). The lowest P\textsubscript{aO\textsubscript{2}} observed was 22 mm Hg in a subject with a WBC count of 365 × 10\textsuperscript{9}/L, breathing O\textsubscript{2} 4 L/min via nasal cannula with a S\textsubscript{pO\textsubscript{2}} of 96% and no clinical sign of respiratory distress.

**Comparison of (S\textsubscript{pO\textsubscript{2}} − S\textsubscript{aO\textsubscript{2}}) Differences Before/After Leukapheresis**

Six subjects who underwent leukapheresis to quickly decrease their WBC count had ABGs performed before and after the procedure. (S\textsubscript{pO\textsubscript{2}} − S\textsubscript{aO\textsubscript{2}}) was 9.4 ± 9.2% before leukapheresis versus 0.5 ± 3.8% afterward (P = .055). Three subjects with very high WBC count (> 150 × 10\textsuperscript{9}/L) all exhibited large S\textsubscript{pO\textsubscript{2}} to S\textsubscript{aO\textsubscript{2}} differences (10–20%) before leukapheresis, which decreased to < 5% after the procedure (Fig. 6).
Hypoxemia During Extreme Hyperleukocytosis

The main findings of this study are the large bias and limits of agreement and the poor correlation between $S_{aO_2}$ and $S_{pO_2}$ in hyperleukocytic acute myeloid leukemia. This poor agreement seems directly related to the severity of hyperleukocytosis, as it worsened with increasing WBC count and disappeared after leukapheresis in some subjects. It is clinically relevant especially for very high WBC count and disappeared after leukapheresis in some sub-
jects. It is clinically relevant especially for very high WBC count and disappeared after leukapheresis in some subjects. It is clinically relevant especially for very high WBC count and disappeared after leukapheresis in some subjects.

Spurious hypoxemia (or leukocyte larceny) was first described in 1979,5,14 and a few small series have been published since, mostly in subjects with chronic myeloid or lymphocytic leukemias6,7,9,14,15 and severe hyperleukocy-
tosis, but no study thus far had investigated the magnitude and clinical relevance of this phenomenon. The pathophysiology of spurious hypoxemia has been thought to involve oxygen consumption by increased numbers of leukocytes inside the syringes (leukocyte larceny) before analysis.5 This hypothesis was supported by an in vitro study using continuous $P_{O_2}$ measurement in blood samples from 5 hyperleukocytic leukemia subjects and also from granulocyte donors, where authors observed a progressive decrease in $P_{O_2}$ in hyperleukocytic samples, reaching values as low as 20 mm Hg within 10 min.16 This progressive decline was grossly proportional to WBC count and was not subsequently observed in the same subjects after cytoreductive therapy or in whole blood from the granulo-
cyte donors.16 These results are also consistent with the decrease in $P_{O_2}$ expected when applying Henry’s law to hyperleukocytic samples, using known data on in vitro oxygen consumption by leukocytes17; assuming, for in-
stance, that the oxygen consumption of leukocytes is about 0.1 $\mu$O$_2$/10$^9$ cells/h,18 one would expect a drop in $P_{O_2}$ of about 50 mm Hg within 10 min for a WBC count of 100 $\times$ 10$^9$/L at ambient temperature. This $P_{O_2}$ decay could be related not only to the WBC count but also to the type of cells, as immature leukocytes seem to have higher metabolic rates than normal cells.19

Although scattered case reports or small series of spu-
rious hypoxemia have been published,5-8 our study is the first to systematically investigate the magnitude of spuri-
ous hypoxemia in a large population of acute leukemia subjects with hyperleukocytosis. Other authors have chal-

gened the magnitude of spurious hypoxemia and sug-
gested that part of the observed hypoxemia might actually be real and related to either unrecognized leukostasis or increased methemoglobinemia.19 Indeed, increased methemoglobinemia described during acute leukemia20 is associated with false $S_{pO_2}$ readings and was also proposed to account for low $S_{aO_2}$ in hyperleukocytic subjects.19 How-

ever, methemoglobinemia is unlikely to explain spurious hypoxemia, as it is associated with normal $P_{aO_2}$21 and could not account for the extremely low $P_{aO_2}$ observed in the present study and others.5,9,22,23

Overall, we described a poor correlation between $S_{aO_2}$ and $S_{pO_2}$ in the presence of a WBC count $> 50 \times 10^9$/L, as attested by the low coefficient of determination ($r^2 = 0.19$) observed when plotting $S_{pO_2}$ versus $S_{aO_2}$. Although correlation analysis may not be the best approach to compare $S_{aO_2}$ and $S_{pO_2}$, a large meta-analysis of 74 studies reported an $r^2$ of 0.8 between $S_{aO_2}$ and $S_{pO_2}$,24 much higher than the $r^2$ of 0.19 that we observed for subjects with WBC count $> 50 \times 10^9$/L. The bias and 95% CI for limits of agreement in our whole population (2.5% and ($-10.1,15.1$)% were also larger than those reported by most studies in non-hyperleukocytic subjects24-26 but were probably negatively affected by samples with extreme WBC count. Indeed, the bias and 95% CI for limits of agreement that we observed in subjects with WBC count $< 100 \times 10^9$/L (0.4% and ($-7.9,8.6$)% are similar to those reported in studies in critically ill27 and COPD28 populations. Conversely, the bias and 95% CI for limits of agreement were 3.8% and ($-10.3,18.0$)% for WBC count $> 100 \times 10^9$/L, whereas one of the largest studies on 102 general ICU subjects reported a bias of only 0.02% with 95% CI for limits of agreement of ($-4.2,4.2$)%29. Although peripheral vasoconstric-
tion can cause false $S_{aO_2}$ readings,28 the large ($S_{aO_2}$ - $S_{pO_2}$) differences for WBC count $> 100 \times 10^9$/L are unlikely to be explained by a worse hemodynamic status associated with hyperleukocytosis, as we found no difference in heart rate or vasopressor requirements between the 2 groups, and if anything, mean arterial pressure was higher for those with WBC count $> 100 \times 10^9$/L. As expected, bias and 95% CI for limits of agreement were even poorer for WBC count $> 200 \times 10^9$/L (11.0% and ($-2.4,24.5$)%,

Fig. 6. Effect of leukapheresis on white blood cell count and ($S_{aO_2}$ - $S_{pO_2}$) in 6 subjects who had arterial blood gas analysis performed before (shapes on the right) and after (shapes on the left) leukapheresis. For the 3 subjects with large $S_{aO_2}$ to $S_{pO_2}$ differences (10–20%) before leukapheresis, ($S_{pO_2}$ - $S_{aO_2}$) decreased to below 5% after the procedure. The 6 different shapes represent the 6 individual subjects.
Hypoxemia During Extreme Hyperleukocytosis

Acute myeloid leukemia. The most probable explanations for the lineage specificity of this observation are: (1) acute myeloid leukemia is the most frequent acute leukemia in adults and (2) symptomatic pulmonary leukostasis is more frequent in acute myeloid leukemia subjects, who are therefore more likely to have ABGs performed. Indeed, among 874 patients admitted for acute leukemia in the present study, only 63 had acute lymphoblastic leukemia, and none of them had ABGs performed during their admission.

The main limitation of this study is its retrospective design and the inherent concern about the reliability of the data collected. Pulse oximetry is subject to plethysmographic artifacts, and we were not able to account for some factors affecting its reliability (methemoglobinemia); thus, S\textsubscript{pO2} recorded in the charts could be false. We tried to minimize this bias by ensuring that consistent S\textsubscript{pO2} values were recorded around the time of ABG, but we cannot rule out, despite all of our precautions, the possibility of false S\textsubscript{pO2} readings. However, extreme hyperleukocytosis in acute leukemia is so infrequent that a study prospectively recording S\textsubscript{pO2} and S\textsubscript{aO2} would be difficult to perform. Although our hospital policy requires all ABGs to be stored on ice and immediately processed, we could not control for the exact time elaps between ABG collection and analysis. Because of the irreducible time required for transport to the laboratory, receipt, labeling, and accessioning of the samples, we estimate this delay at about 10 –15 min. As discussed above, however, even a few minutes may be enough to cause P\textsubscript{aO2} decay, and the only way to prevent that delay would be to use portable gas analyzers at bedside. Another limitation is the lack of a control group with normal WBC count; however, the bias and 95% CI for limits of agreement that we observed for WBC count between 50 and 100 \times 10\textsuperscript{9}/L were similar to those reported in general ICU subjects, so that the poor agreement observed for WBC count > 100 \times 10\textsuperscript{9}/L can probably be ascribed to hyperleukocytosis. Our choice to include subjects with WBC count > 50 \times 10\textsuperscript{9}/L is also arguable, but it was based on a study reporting a rapid decay in P\textsubscript{aO2} in blood samples with a WBC count of 55 \times 10\textsuperscript{9}/L. Although these results were obtained by in vitro studies using tonometry in a few samples, our data actually suggest that spurious hypoxemia is clinically unacceptable for WBC count > 100 \times 10\textsuperscript{9}/L. Finally, oxygen supplementation may have altered the relationship between P\textsubscript{aO2} and WBC count, as presented in Figure 3. We were not able to present data with uniform F\textsubscript{IO2} (due to the small number of subjects for a given F\textsubscript{IO2}) or P\textsubscript{aO2}/F\textsubscript{IO2} ratios, as accurate computation of F\textsubscript{IO2} is challenging for patients receiving oxygen via nasal cannula or face mask. Notwithstanding this limitation, the relationship between P\textsubscript{aO2} and WBC count as depicted in Figure 3 remains convincing. Indeed, one would expect the subjects with higher WBC count to have lower P\textsubscript{aO2} and higher \textsuperscript{5,8,10}
have presented more severe respiratory symptoms and to have received more oxygen, which could have artificially increased their $P_{aO_2}$ as compared with subjects with lower WBC count. The fact that we observed, on the contrary, extremely low $P_{aO_2}$ in subjects with higher WBC count suggests that supplemental oxygen did not distort the overall relationship between $P_{aO_2}$ and WBC count and, if anything, strengthens our results.

Conclusions

In acute leukemia subjects with hyperleukocytosis, even cooled and quickly analyzed ABGs exhibited unacceptably poor agreement and correlation between $S_{aO_2}$ and $S_{aO_2}$ for WBC count $> 100 \times 10^9/L$. This spurious hypoxemia seems grossly proportional to WBC count and may lead to significant misinterpretation of the subject's oxygenation status. The clinical practice guidelines for immediate cooling and analysis of ABG for very high WBC count are reinforced but may not be sufficient to prevent spurious hypoxemia.

REFERENCES


