The ability of sera to opsonize yeast particles was examined in sera from 49 patients with sarcoidosis and from 44 healthy control subjects. A modification of the assessment of serum opsonization of yeast phagocytosis by normal polymorphonuclear leukocytes was used, with Coulter counting of the free, unphagocytosed particles (Levinsky, Harvey & Paleja, 1978, *Journal of Immunological Methods*, 24, 251–250).

Defective opsonization was found in 11 patients with sarcoidosis, but in only two controls ($P < 0.01$, Fisher's exact test).

Nine of the 11 patients with defective yeast opsonization had circulating immune complexes ($P < 0.05$). None of them had active disease, but there was no correlation with stage or activity of disease.

### 71. The Ventilatory Effects of Doxapram in Hypoxia and Hypercapnia in Normal Man

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Doxapram is a potent respiratory stimulant, which potentiates the ventilatory response to acute hypoxia in man without increasing resting oxygen consumption (Calverley, Robson, Wraith, Flenley & Prescott, 1978, *Clinical Science and Molecular Medicine*, 55, 23). We now describe the effects of doxapram on the interaction between acute experimental hypoxia and hypercapnia as ventilatory stimulants in normal man.

We have studied six normal men (aged 25–45 years) before and during infusion of doxapram to produce a constant venous plasma concentration of 2.0 $\mu$g/ml. Each subject was seated and the heart rate, tidal volume ($V_t$), respiratory rate ($f_R$) and ‘instantaneous minute volume’ ($V'_{E instantaneous}$) were measured at each breath. The end-tidal oxygen ($PeO_2$) and end-tidal carbon dioxide ($PeCO_2$) tensions were measured by a mass spectrometer linked on-line to a computer, and the ear oxygen saturation ($SaO_2$) was measured non-invasively by a Hewlett Packard 47201A ear oximeter. After the subject became acclimatized to the equipment the ventilatory response to progressive isocapnic hypoxia was measured at each subject’s own stable $PeCO_2$ when breathing air (range 4.5–5.6 kPa) as previously described (Calverley et al., 1978). Carbon dioxide was then added to raise the $PeCO_2$ by 0.5 ± 0.1 kPa and the ventilatory response to progressive hypoxia was again measured at this value of $PeCO_2$. Doxapram infusion was then started and the progressive hypoxic studies were repeated at the same two levels of $PeCO_2$.

The resting normoxic minute ventilation at the lower $CO_2$ tension varied within the group (range 4.7–3.03 litres/min), but rose in all when $CO_2$ was added (13.4–26.1 litres/min), and again when doxapram was infused (11.6–37.9 litres/min) as we have previously reported. In four of the six subjects there was an increase in the slope of the linear relationship between $SaO_2$ and $V'_{E instantaneous}$ at the higher level of $PeCO_2$. The change in the slope of this $V'_{E}/SaO_2$ relationship during doxapram infusion was the same as that produced by raising the $PeCO_2$ in five of these six subjects. The minute ventilation rose further when the high $PeCO_2$ and doxapram were combined in normoxia (26.3–56.5 litres/min) and the slope of the $V'_{E}/SaO_2$ relationship was also increased by combining doxapram and raised $PeCO_2$ in four of the six subjects. We have also measured the ventilatory effects of $CO_2$ rebreathing in hypoxia and of transient hypoxia during exercise in these subjects, with and without doxapram infusion, and our preliminary results suggest that doxapram enhances the ventilatory response to $CO_2$.

These results suggest that the response to doxapram varies with the sensitivity of the individual to other respiratory stimulants, particularly $CO_2$. However, there was no relationship between the plasma concentrations of the drug and the