these changes as a result of effects on cell membrane phospholipids.

Cytochalasin B

This agent (2 \( \gamma/\text{ml} \)) disrupts microfilaments in many cell types including the AM.\(^2\) It does not impair microtubular morphology. Quantitative bacteriologic methods demonstrate diminished uptake of live \textit{Staphylococcus aureus} from shaking bacteria-AM suspensions in the presence of cytochalasin B. These effects are associated with striking diminution of \(^{14}\text{CO}_2\) production from \(^{14}\text{C}-1\)-glucose and \(^{14}\text{C}-6\)-glucose (77 percent and 42 percent respectively in AM exposed to killed \textit{Staphylococcus epidermidis}). Cytochalasin B did not affect \(^{14}\text{CO}_2\) production from \(^{14}\text{C}-1\)-pyruvate, \(^{14}\text{C}-1\)-acetate or \(^{14}\text{C}-1\)-4 succinate, nor impair the activities of glucose-6-phosphate dehydrogenase and 6-phosphogluconic acid dehydrogenase. Further, the effects are reversible by washing out the cytochalasin B. The association of diminished bacterial ingestion and disruption of the microfilaments suggests that the latter serve as actin-like contractile particles in the ingestion process. The diminution of \(\text{CO}_2\) formation from labelled glucose may possibly arise from a combination of diminished ingestion and impaired glucose transport. The latter possibility is suggested by preliminary evidence indicating that the uptake by AM of the transportable but non-metabolized glucose analogue, 2-deoxyglucose is inhibited by 2 \(\gamma/\text{ml}\) of cytochalasin B.

Drugs Mediated by Cyclic AMP

Agents presumed to elevate intracellular cyclic AMP, such as theophylline (10\(^{-4}\) \text{M}), prostaglandin \(\text{E}_1(10^{-4}\text{M})\), the cyclic AMP analogue, dibutyryl cyclic AMP (10\(^{-4}\) \text{M}) and also dibutyryl cyclic 3', 5' guanosine-monophosphate all produce concentration dependent diminution of \(^{14}\text{CO}_2\) production from both \(^{14}\text{C}-1\)-glucose and \(^{14}\text{C}-6\)-glucose in both resting and phagocytosing AM. These agents did not impair bacterial uptake. Isoproterenol (up to 10\(^{-3}\) \text{M}), epinephrine (10\(^{-3}\) \text{M}) and sublethal concentrations of propranolol had no effects on either glucose conversion to \(\text{CO}_2\) or bacterial uptake. In the absence of measurements of cyclic AMP, it is not possible to make definite statements, but it appears likely that cyclic AMP regulates either glucose transport or glucose metabolism without effects on particle entry.

Conclusion

These studies are examples of the use of pharmacologic agents to analyze some mechanisms of phagocytosis in an important pulmonary defense cell. They suggest that: 1) the metabolic features of phagocytosis may result from modification of cell membrane phospholipids, 2) AM phagocytosis depends on contractile microfilaments, and 3) cyclic AMP regulates glucose metabolism in the AM.

References


Retarded Clearance of Macroaggregated Albumin from the Lung of Asthmatic Patients*

W. Busse, M.D.; C. E. Reed, M.D.; I. Tyson, M.D.; and M. Birnbaum, M.D.

During the course of study of an asthmatic patient who had more than ten episodes of atelectasis of the left lower lobe from mucous plugs, a lung scan with macroaggregated albumin \(^{131}\text{I} \) (MAA-\(^{131}\text{I}\)) was performed. The scan (not the injection of isotope) was repeated daily. Radioactivity appeared normally in the lung, but unexpectedly remained there for five days. Radioactivity is normally cleared from the lung with a half-time of 4.5 to 10 hours.\(^1,2\)

Lung scans were performed in 14 asthmatic patients, ranging in age from 18 to 49 years old, and in severity ranging from mild to very severe. Half the patients required either daily or alternate day prednisone. There was prolonged retention of radioactivity in the lungs of the asthmatics with median radioactivity half-time of 17.5 hours. Normal values at our institution are 8-10 hours (Fig 1). The degree of retention of radioactivity was not dependent upon the severity of the asthma or the use of corticosteroids.

Swiss-Webster mice were given 10\(^9\) \textit{Bordetella pertussis} organisms intraperitoneally. The intraperitoneal or intravenous injection of \textit{B pertussis} can

*From the University of Wisconsin Medical School, Madison.

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create in the mouse a situation which in many respects resembles the atopic state in humans. Four days later, the pertussis-treated and the control mice were given MAA 131I intravenously. Animals from each group were sacrificed at 5 minutes and 2, 4, 6, and 24 hours after the injection. The lungs, liver and spleen were removed and counted in a gamma counter. Radioautographs were made from sections of fixed lungs. Lungs from mice given pertussis retained a greater percentage of radioactivity than the control mice (p = 0.02) (Fig 2).

Radioautographs from the two groups were similar at the above mentioned times. There was no obvious evidence of cellular response at the site of microemboli in either the normal or pertussis-treated animals.

The mechanism by which the radioactive microemboli from MAA 131I is retained in the lungs of asthmatic patients and mice given B pertussis is not established. From examination of the radioautographs, the defect leading to retention of the MAA 131I particle does not appear to reside in a cellular response of lungs. The retention is probably secondary to clearance of the radioactive microemboli by the circulation. The abnormality would therefore appear to be present in the blood, ie plasma or leukocytes.

REFERENCES