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**COVER:** One half of a computer microprocessor on one silicon chip. Made by RCA, the integrated circuit uses the latest complementary metal-oxide-semiconductor (CMOS) technology and was designed for use in such microcomputer applications as automotive controls, electronic cash registers and military devices. The chip (magnified  $\times 20$ ) contains some 3,000 transistors. Such miniaturization has been instrumental in developing the latest generation of computers. See story page 154. (Photo: RCA)

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## The role of lungs expanding: Air sacs to endocrine glands

The lungs were thought, for centuries, to be hollow air sacs that inflate and deflate with every breath. Anatomists and physiologists have found that lungs are, instead, incredibly complex gas exchange factories. Adult human lungs contain about 300 million tiny air spaces called alveoli, each of which is equipped with 1,000 capillaries. These carry blood cells to within one micrometer of the life-giving air. These capillaries, if stretched end to end, would reach from San Francisco to Denver. The surface area inside the lung for exchanging oxygen and carbon dioxide is about 80 square meters, the size of a backyard swimming pool. The lungs are, all in all, far from being hollow air sacs.

Recent discoveries are leading the way to another shift in thinking about the lungs. They might be considered, it now seems, to be the equivalent of huge glands; in other words, to have endocrine functions in addition to their role as the organs of gas exchange for the blood. An endocrine gland is one that secretes hormones into the blood. The lungs, instead, actually modify existing hormones, but the regulating and controlling effects are much the same.

A session exploring the metabolism of two blood hormones in the lungs was held at the annual meeting of the American Chemical Society last week in Chicago. One conclusion from the discussions was that the lungs may be a major regulator of blood pressure.

Y.S. Bakhle of the Royal College of Surgeons in London reviewed what is understood about the processing of the two hormones, bradykinin and angiotensin, by the lungs. Bradykinin is a circulating hormone which acts as one of the most potent substances for lowering the blood pressure. Angiotensin I, a pro-hormone, converts to angiotensin II to become the most potent substance known for raising the blood pressure. Medical researchers have, in the past few years, found that as bradykinin passes through the lungs in the blood, it is inactivated, and that as angiotensin I passes through, it is converted to angiotensin II. The lungs, therefore, eliminate a hormone that lowers blood pressure and create a hormone that raises the blood pressure. Further study has shown that one enzyme, called "converting enzyme," is responsible for both conversions.

Finding the site of this enzyme in the lungs has become a major objective in several laboratories. James W. Ryan and Una S. Ryan of the Papanicolaou Cancer

Research Institute in Miami, leaders in this search, reported their techniques for finding what is almost certainly that site in the lungs. They hypothesized that converting enzyme would be found connected somehow to the capillary endothelial cells. These "unremarkable looking cells," James Ryan says, line the miles and miles of capillaries inside the alveoli. Because the lungs are situated between the right and left sides of the heart and receive, each minute, the body's complete blood flow, these capillary linings would have access to all of the blood. They would, therefore, be a logical site for a blood-pressure-controlling enzyme. That is exactly what the Ryans are finding.

The most difficult problem, Ryan says, was to isolate this ephemeral single-celled layer from the inside of a minute capillary so that tests could be made to search for the enzyme. They were able to isolate some of the endothelial cells from the larger pulmonary artery, and have tested them (although, Ryan says, definitive proof of their hypothesis will await isolation of the capillary endothelium). The Ryans then, in collaboration with colleagues from the Cleveland Veterans Hospital, were able to biochemically mark the converting enzymes with an electron dense substance and view the complexes with electron microscopy.

Locating this enzyme is important for several reasons, Ryan says. There has been no previous description of circulating hormones in the blood that are processed by an enzyme attached to one site, so this information describes an entirely new "endocrine-type" system. Also, he says, knowing that the enzyme is located on the capillary surfaces will give pharmacologists greater latitude in designing drugs to control blood pressure by activating or inactivating this converting enzyme. And of far-reaching significance is the basic knowledge that the lung has endocrine functions. Besides illuminating the physiology of the body, this knowledge may have important and immediate applications. When a patient, for example, is placed on a heart-lung machine, Ryan says, he receives oxygenated blood but "is often much sicker after perfusion than he should be." This might be because the heart-lung machine does not regulate bradykinin and angiotensin as do the normal lungs. It might be possible, Ryan says, to attach converting enzyme to the silicon-stainless steel mesh inside the machine so that the patient receives a more nearly normal blood supply. □