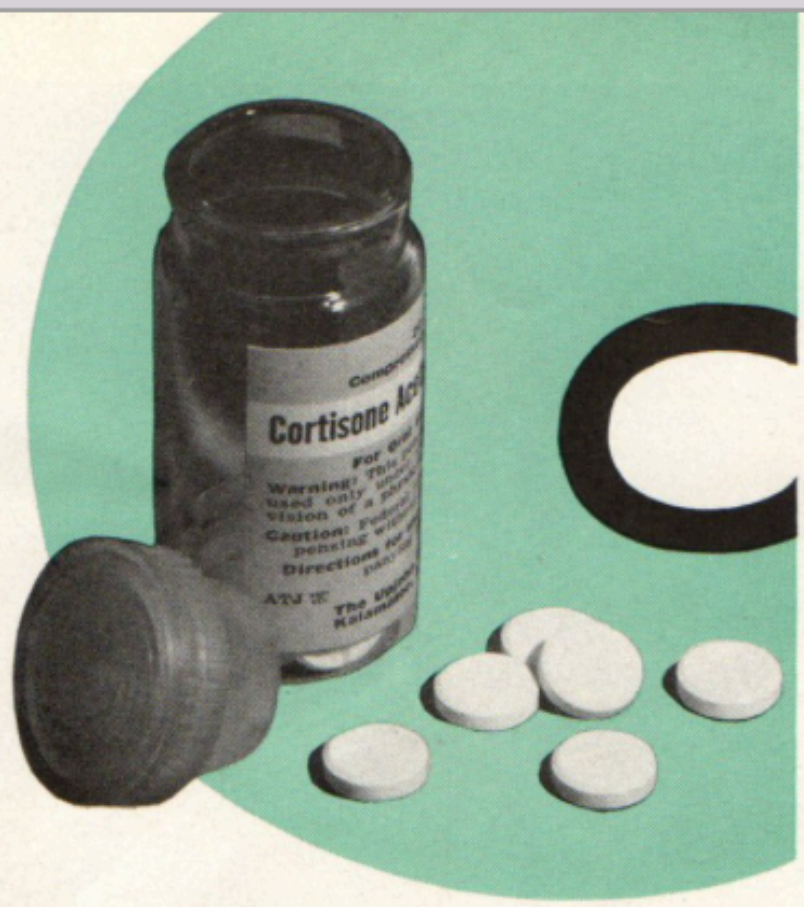


THE STORY ABOUT OUR NEW PRODUCT

CORTISONE

In a two-fold way, the June 9 announcement of Upjohn Cortisone is just the beginning—for the sales picture remains to be seen and the vast new area of hormone therapy is just starting to unfold. Yet it is also the realization of a hard-won goal.

Probably few of us fully appreciate the intense effort that Upjohn expended trying to find a shorter method of producing Cortisone; the all-day meetings, the labs where people literally worked in day-and-night relays, seven days a week. As that phase progressed, the work and enthusiasm spread in ever-widening circles until virtually every department was involved. With the contributions of all these groups falling into place in the over-all plan, Upjohn's Cortisone went to market.

Newspapers, magazines, trade papers, newsreel film, the radio and TV have been telling our story since June. In fact, it's estimated that some 850 articles had appeared and that TV announcements were carried by 26 stations by June 26.

These discussions, for the most part, dealt largely with our unique fermentation process. This in no way means that other operations are less important. Procedures for every step had to be efficiently developed and carried out. But the new process is a key one. It enables us to use plentiful and cheap starting materials like soybeans, yeast, and Mexican yams instead of cattle bile. It simplifies one of the most complicated chemical processes in the pharmaceutical field. It should permit lower prices as production increases. And it's ramifications in the whole field of steroid production are important for the process already has been found adaptable to production of hydrocortisone and corticosterone.

Target for the fermentation-process research was an obstinate oxygen atom.

One of numerous research activities was the screening of microorganisms to determine effectiveness in our hoped-for bio-conversion process. Marian Leigh is the chemist.

In a Cortisone huddle are some of the research team of microbiologists, biochemists, and organic chemists who developed key fermentation step in Upjohn process: Lester Reineke, Bob Levin, Durey Peterson, Marian Leigh, Adolph Weintraub, Herb Murray, and Peter Meister.

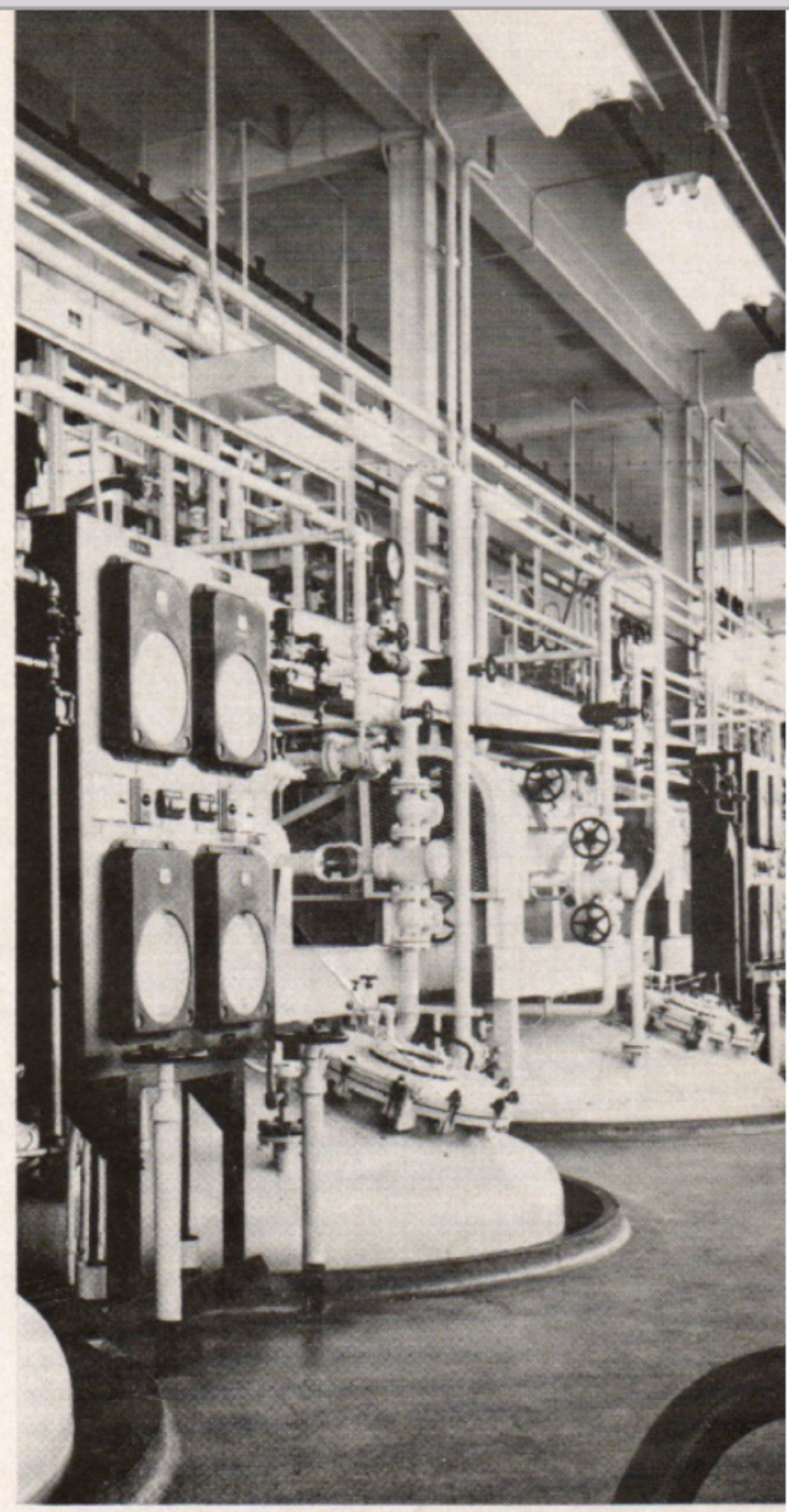
Reference: The Upjohn News, July 1952
source: www.upjohn.net

This atom—when, and *only* when, it is in the number 11 position in the molecule—gives Cortisone its particular qualities. Formerly the steps required to put oxygen in this position were "the most difficult series of steps" in the synthetic production of this adrenal gland secretion. The easier way which we found requires any of several starting materials and mold of the order which includes bread molds. As the starting material ferments (for twenty-four to forty-eight hours) in a special culture to which the mold has been added, it is transformed to an intermediate substance with oxygen in the crucial 11 position. This compound is then converted to Cortisone.

President Gilmore made the decision to "Go ahead—and spare no effort" in Cortisone research about three years ago when early clinical investigations were being acclaimed. Four research groups were set up to investigate the four approaches that had been culled from literally dozens of possibilities. Leaders of the four groups were Dr. John Hogg, Dr. Bob Levin, Dr. Arnold Ott, all of the Department of Chemistry; and Dr. Bill Haines, Department of Endocrinology. Later on, the entirely new microbiological tack, which proved so successful, was taken. Under Assistant Research Director Dr. Harold Kolloff, the Chemistry Department's Dr. Dave Weisblat and Bob Levin assembled a team of people with diverse specialties. In addition to those pictured on page 20, the team included Dr. Sam Eppstein and Dr. Bob Edwards.

Prospects of this new angle were staggering because there were thousands of organisms to be investigated. One of the group's first projects was to devise a new method of paper chromatography. This new assay was very important because it quickly told just which hormones were produced by our fermentation process and how close these were to the eagerly-sought Cortisone. Bob Levin stressed its success when he said "We couldn't have found our present key compounds at all by the old methods."

Clinical investigations into the uses of Cortisone are keeping pace with the fast-moving processing research. Initially, clinical Cortisone research was directed against one of the oldest and most crippling chronic diseases of man, rheumatoid arthritis. While not a cure, Cortisone affords dramatic symptomatic relief and can even prevent crippling in this disease. Now, broadening areas of research have shown the scope of Cortisone's applicability in a wide range of allergic, ocular, skin, and collagen diseases. Both clinic-and-production wise, Cortisone is proving worthy of the enthusiasm and energy it has so far exacted.



Because process is similar to one by which antibiotics are now made, fermenters in that Production department are used to convert starting material to a Cortisone intermediate by action of mold growth.

Some call group to left the "most photographed line in the Company right now." It's the Cortisone line where tablets are compressed, bottled, and capped, and includes Bert Busick, right; Barbara Carr and Unabelle Harris, foreground; and, clockwise but with faces hidden, Eva Underkircher, Janet Baylor, Bernardine Vander Ploeg, June Ballentine, and Eleanor Van Den Berge.