

lessly expose patients to highly toxic drugs and encourage physicians to avoid the laboratory diagnosis necessary to pick the proper drug for the most successful treatment. These experts maintain that whenever two or more antibiotics are needed to overcome an infection, good medical practice demands carefully adjusting the dosages of each ingredient to the individual patient's requirements; fixed combinations do not permit such flexibility, although proponents claim the proportions are calculated properly for most patients. Furthermore, the critics say, indiscriminate use of antibiotic combinations results in the emergence of dangerous bacterial strains that are resistant to all drugs.

"The only defense I can see for a combination is that the physician says, 'I don't know, I'm guessing.' Would you want to be treated that way?" demands Dr. Robert Wise of Jefferson Medical College in Philadelphia.

ANOTHER CRITIC

There is "very little rationale that we can see in these antibiotic combinations," says Dr. Calvin M. Kunin, of the University of Virginia, who is scheduled to testify at the Senate hearings. Dr. Kunin headed a group of advisers from the National Academy of Sciences who urged the FDA to remove the drugs from the market because of lack of efficacy.

The drug companies will defend the combinations as vigorously as they can. "Clinical reports show that our combination of tetracycline and novobiocin has retained its clinical efficacy after 11 years," insists R. T. Parfet Jr., Upjohn president.

Combinations of all kinds have important advantages, industry medical men say. Among their claims: The mixtures may be more effective than single drugs, attacking a wider variety of infections treating several medical problems simultaneously such as depression and anxiety or incorporating different attacks on a single ailment. Combinations can be safer minimizing the amount of a toxic ingredient by including other less harmful agents. They can offer added convenience by reducing the number of pills to be taken and easing the risk of medication mistakes by patients particularly the aged. Finally the products can save the public money by curtailing the need for extra prescriptions.

Drug industry men also contend the antibiotic combinations may be a practical necessity for many small-town doctors, who don't have sophisticated laboratory facilities and must treat many patients without careful diagnosis. "When a busy physician doesn't have time to see what bacteria is causing infection, it probably makes good sense to give as wide a spectrum antibiotic as you can," insists a spokesman for the Pharmaceutical Manufacturers Association. The motive behind most mixtures, of course, is to combine antibiotics that are effective against a variety of bacteria.

But if the Nelson hearings follow their past pattern, the companies will have little chance to present their rebuttal. The committee is interested in spotlighting the industry's mistakes, not in giving it a platform for self-defense, spokesmen for drug manufacturers assert.

In any case, the drug firms may be somewhat vulnerable on the issue of the antibiotic combinations. Privately, some of their own experts express doubts about the value of many mixtures. With the development of highly effective new drugs, such as the synthetic penicillins, and with the growth of knowledge about bacterial infections, the touch-all-bases theory behind some of the combinations has become harder to defend. Medical men outside the industry almost universally condemn them; these critics claim that although there may have been some medical justification for these products years ago, profit-making has now become the prime purpose in selling them.

The companies will counterattack, however, by demanding Administrative hearings and a chance to argue their case before the FDA. That could temporarily stay most agency orders to withdraw their products from the market. The first confrontation will probably come this year over Upjohn's Panalba. E. R. Squibb & Sons, the Lederle Laboratories division of American Cyanamid Co., Chas. Pfizer & Co. and other companies may join the fray later.

But the FDA has the authority to take immediate action, particularly if it finds hazards exist. Thus, one type of antibiotic mixture—combinations of penicillin and streptomycin—may be barred from sale without the formality of a hearing. The reason: Streptomycin's known risk of causing deafness by damaging the auditory nerve. Though the penicillin and streptomycin combinations are small-volume items, they are sold by many companies, including Squibb, Upjohn, Pfizer and Eli Lilly & Co.