ing good and relatively specific binding to the receptor protein in solution, block conduction in the squid axon in concentrations surprisingly close to those previously observed on the synaptic junctions of electroplax.

Conclusion

The dramatic developments of biochemistry in the last few decades have greatly promoted our understanding of cellular function in terms of physics and chemistry, and we are reaching, in some fields, molecular levels. The few examples discussed in this article illustrate the approach to the analysis of the chemical factors that control nerve activity and the recent advances achieved (*40*).

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Science and the News

The Kefauver Hearings: The Drug Industry Finally Has Its Day and Does Quite Well

Last week the Kefauver committee entered its third, and presumably final, year of investigation of the drug industry. The hearings began in December 1959. Kefauver hopes to wind them up in the first few weeks of the new congressional session. What has taken so long is that Kefauver used most of the first two years for an intermittent but what must have been for the industry an excruciatingly prolonged exposé of what he saw as the industry's failure to properly serve the public interest.

Early last summer Kefauver produced a bill intended to reform the industry, and since then the hearings have been, technically at least, devoted to soliciting the views of interested parties on his "Drug industry antitrust bill." This "legislative" (as opposed to investigative) phase of the hearings began with the testimony of the American Medical Association in July, and reached a critical point last week with the testimony of the Pharmaceutical Manufacturers Association. Sandwiched in between was the testimony in September of Welfare Secretary Abraham Ribicoff, presenting the Administration's views. One of the curious aspects of all this testimony was that the drug industry's position turned out to be closer to the Administration's view than to that of its ally, the AMA.

Kefauver is asking for two quite different types of reform. The first half of his bill is concerned with amendments to the laws governing the Food and Drug Administration. In general approach, although not in detail, these amendments followed the recommendations of HEW, which are about the same now, under Ribicoff, as they were before the change in Administration. They would give FDA a stronger hand against makers of substandard drugs, require proof of efficacy as well as the presently required proof of safety before a new drug is allowed on the market, require the drug companies to provide wider distribution of information about new drugs, particularly regarding unfavorable side affects; and give the government authority over the choice of generic names for drugs.

Conflict

The AMA opposed all of these proposals, except the first, on which it took no position. Ribicoff supported, and the industry accepted, all of them, although not in the precise form Kefauver has suggested.

On generic names, for example, the AMA flatly opposed giving authority to the government, on the grounds that

a newly formed nongovernmental committee would serve to correct the abuse that is claimed to exist: a tendency of drug manufacturers to give drugs an unwieldy generic name and a catchy brand name, so encouraging the physician to prescribe by brand name instead of generic name. Ribicoff gave, as a horrible example of this, the case of a drug sold at $7 under the brand name Cortate. The same drug could be bought for $1 if the physician, instead of writing "Cortate" on his prescription blank, wrote "desoxycorticosterone acetate." But Ribicoff said he saw no need for his department to decide all generic names; he asked, instead, for standby authority for the government to step in only when the private committee, which includes representatives of the industry, could not agree on a reasonably simple name. The industry took the same position, and Kefauver appeared ready to accept this change.

Efficacy

On requiring proof of the efficacy as well as of the safety of a new drug, the AMA, again, was in flat opposition. It argued that FDA might interpret this to mean the right to pass on *relative* efficacy, and keep a drug off the market not on the grounds that it would not work, but on the grounds that it would not work as well as other products already on the market. No one has argued that FDA should have this power, partly because, unless a drug is exceptionally effective, it is impossible to reach a firm judgment on just how good it is until after it has been widely used, partly because even if one drug is better for most patients, a second drug is often better for some patients. FDA is already judging efficacy in most cases, on the grounds that if a drug has side effects, as almost all do, or if a drug is going to be used in connection with a life-threatening disease, a judgment on efficacy is a necessary part of judging safety.

The AMA therefore argued that the efficacy provision would be of no real value since it would only extend FDA's authority to harmless drugs to be used for non-life-threatening diseases, and very few of these drugs would be prescription drugs, which are the only kind affected by Kefauver's bill. This small advantage, in the AMA's view, was not worth the risk, however small, of the provision giving FDA power to judge relative efficacy.

Both the industry and Ribicoff, though, backed the efficacy provision, which is, by far, the most widely accepted of all the reforms urged by Kefauver. Ribicoff argued that it would not only close the small gap in the present law but would give the FDA power to prevent unfounded claims for a drug. As things are now, he said, FDA must approve a drug for sale so long as its good effects appear to outweigh its harmful effects; but since FDA has no direct authority to require proof of efficacy, it has no power to disapprove a drug merely because there is a lack of evidence to show that it is as good as its manufacturer claims it is. Ribicoff said that under the present law, FDA must occasionally approve a new drug application with the knowledge that the manufacturer is going to promote it with unsubstantiated claims. FDA must wait for the drug to go on the market and then bring a court action in which the burden of proof is on the government to show that the drug will not do as much as its manufacturer claims, rather than on the manufacturer to show that it will do what is claimed. The industry, in contrast to the AMA, accepted the efficacy provision, insisting only that it be understood that the manufacturer need show only "substantial" rather than definitive proof of his claims. Kefauver said this was all the law would require.

The discussion of other points in the first half of the law was similarly cordial. Neither side was giving in on anything on which it stood any significant chance of winning anyway. The drug industry, for example, had no occasion to follow the lead of the AMA and oppose the wider dissemination of detailed information on drugs since the FDA had already settled the question by putting through a set of new regulations, under its already existing powers, which made Kefauver's provisions superfluous. The AMA had argued that its own newly reorganized information program (a department in the *AMA Journal* and an expanded yearbook) would give the doctor all the information he needs, and that the Kefauver proposal would just fill up the doctor's wastebasket. On proof of efficacy as well as safety, the industry's choice of position, again, was not too difficult to reach: there was not only a great deal of support for this within the medical profession, despite the AMA position, but as a practical matter it is hard to explain to the public or to a congressman why it is unreasonable to expect a manufacturer to have reasonable proof that a drug will do what it is claimed to do. The AMA had not been able to offer an explanation of how the provision could be interpreted to give FDA power to keep a useful drug off the market merely because it seemed not as useful as another drug. The AMA's reasoning, apart from a disinclination to give the government any greater control than it now has over the medical profession, appeared to be that even a comparatively worthless drug sold through exaggerated claims might turn out to be surprisingly valuable and that it would, therefore, be best, providing the drug met the safety test, to allow wide latitude. But if the AMA's information program was going to be as effective as it was promised to be, it would be difficult to see how a drug promoted through unsupported claims would get the wide use that would turn up its surprising value.

Patents

Where the industry and Kefauver sharply parted company was on the second half of the bill, which was aimed at restricting patent rights in the drug industry. This was the part of the bill that was closest to Kefauver's heart, but he clearly took a beating, and at the end of the hearing he in effect conceded what had already become obvious: that the patent law changes he was asking stood no chance of getting through Congress.

The first half of the bill contained reforms which had been urged for years. In 1950, for example, the AMA's own council on drugs had recommended that the efficacy test be added to the law. The reforms have very little to do with the antitrust and monopoly problems that the Kefauver committee was authorized to study. If he had cared to, Senator Hill, chairman of the Labor and Welfare committee, could have claimed jurisdiction and kept Kefauver from dealing with these reforms at all. Kefauver's special interest and his own ideas appear in the patent section of the bill, where he proposed to bring down the price of drugs by removing much of the perfectly legal monopoly powers which the major companies hold through their patents. Curiously, the reason this approach was so promising was the very fact that the drug industry is one of the least monopolistic of large industries. Twenty-two companies are classed as major, 140 are substantial enough to belong to

the Pharmaceutical Manufacturer's Association, and there are more than a thousand lesser companies. Kefauver proposed that a drug manufacturer be required to license any of his competitors to produce a patented drug after three years. He also wanted to bar patents for molecular modifications—minor changes in a known drug which will produce a patentable variation—unless the variation were proved superior to its predecessor.

In this way, Kefauver felt, the high profit margins the manufacturers were enjoying on many drugs would be forced down by the loss of the patent monopoly. He argued that the three years of normal patent protection plus royalties on all sales of the drug for the remaining 14 years of the patent protection, when compulsory licensing would be in effect, would give the companies all they needed to enable them to recover the heavy investment in research and testing usually needed before a useful new drug was produced. He argued that the second patent provision, prohibiting protection for minor variations of known drugs, would complete the job by removing the incentive for the industry to aim much of its research at producing patentable variations of known drugs at the expense of concentrating fully on producing new drugs of the most benefit to the public. As a result, he believed, even though the first provision might lead to less spending on research, the second would offset this loss by assuring that the money that was spent would be spent in a more productive way.

Doubts

There is little doubt that Kefauver's patent limitations would indeed force down the price of drugs. Where Kefauver ran into serious difficulty was on the question of what else they might do. All of Kefauver's proposals are intended to have an effect on the price of drugs. The provision in the first part of the bill giving FDA a stronger hand against the makers of sub-standard drugs, for example, will, Kefauver hopes, make physicians more willing to prescribe by generic name instead of trade name. More active FDA supervision of manufacturers, Kefauver believes, will tend to lessen the feeling among physicians that in order to assure that their patients get first-quality drugs it is best to specify the trade name of a manufacturer of known reputation. In fact, the effect may be just the opposite, for although the great majority of unbranded prescriptions are just as good as those sold under well-known trade names, the more active FDA is in taking action against substandard drugs, the more often physicians will be reminded that there is at least a slightly greater chance that their patients will get a substandard product if they fail to specify a known trade name. It is perfectly possible that the effect of this reform will be both to make it even safer than it is now to prescribe by generic name and at the same time to make physicians even more wary of doing so.

This typifies the difference between the proposals in the two parts of the bill: in the first half, you have widely supported, long-discussed reforms which may or may not have a significant effect regarding Kefauver's special interest in lowering the cost of drugs. In the second half of the bill, you have provisions which will have a direct effect on drug prices, but which may or may not have good effects on the overall performance of the industry. In the first instance, pressure is on those who oppose the reforms to show what is wrong with them; in the second instance, those who oppose the reforms have only to raise a reasonable doubt about the wisdom of the proposal and they will have assured that the most Congress will do will be to say, "Let's look into this thing more carefully before rushing ahead." This is what the industry did very well.

Kefauver, for example, had assembled a good deal of data on the discovery of important new drugs in countries with varying degrees of patent protection. He interpreted the data to show that his proposals would not lead to a reduction in the number of important new discoveries even though they were likely to reduce the total overall number of new discoveries. The industry was able to offer an alternate interpretation of the same data which suggested just the opposite. This was all the industry had to do. Its interpretation was not convincing enough to thoroughly refute Kefauver, but it was convincing enough to raise doubts that Kefauver was right. On point after point, the industry was able to raise similar doubts, and sometimes quite convincing ones. Kefauver had not been proved wrong but as for his immediate chances of getting his patent proposals enacted into law, he might as well have been proved wrong.—H.M.

Population Boom: Administration Presents a Policy Statement That Is Ingeniously Confusing

In a speech that received surprisingly little attention, the Administration recently set forth its policy on the "population explosion" in lesser-developed countries.

The speech contained the Administration's first comprehensive statement on this politically sensitive subject. As is the style in virtually all official pronouncements that touch on birth control, bones were available for the watchdogs of all partisans. Behind the cautious verbiage and qualifications, however, was an acknowledgment that the Kennedy Administration desires to come to grips with the population problem.

Since the attitude of its predecessor was strict aloofness, the distance traveled to date by the Administration is relatively considerable. It has publicly exhumed the subject and has deemed it respectable for public discussion by government officials. It publicly acknowledges, in addition, that it has gone to the extent of helping some lesser-developed nations survey their population problems. Such surveys must inevitably precede any attempt to develop a population control program. And some officials say privately that in a few countries, U.S. assistance has gone beyond the census-taking stage.

Assistance Offered

The speech setting forth the U.S. position on population control was delivered 30 November in Washington by William T. Nunley, special assistant to Under Secretary of State George W. Ball. Nunley spoke at the National Conference for International Economic and Social Development, which comprises several hundred organizations and individuals supporting U.S. foreign aid efforts. He described his speech as an officially approved statement.

Sentiments favorable to U.S. assistance for population control predominated in his audience, and what Nunley had to offer was denounced as evasive by several persons present. In many respects it unquestionably was evasive, but strewn here and there through its five pages were some of the most remarkably frank public statements ever issued by a U.S. official on the subject of population control.

Nunley pointed out in the course of