ditional evidence for the possible interference of hydrogen bonding with enolization was obtained from attempts to synthesize the enol acetate of cholestane-3β,5α-diol-6-one which has been shown to give a doublet in the 3-μ region (*5*). On refluxing this steroid with acetic anhydride and acetyl chloride, only the 3,5-diacetate was isolated in excellent yield (*8*).

Although variations in the carbonyl absorption did not occur, it is believed that a hydroxyl-ketone type bonding was prevalent. This was indicated by examination of the spectrum of 7-ketocholestanol which had only one absorption band in the 3-μ region (*4*) and suggested that the double bond in the unsaturated analog afforded a more rigid structure that favored bonding of the carbonyl group. As expected, the infrared spectrum of 7-ketocholesteryl acetate gave no absorption bands in the hydroxyl region, confirming that the 3β-hydroxyl group also was involved in the hydrogen bonding. Furthermore, spectroscopic examination of 7β-hydroxycholestenone (*9*) disclosed only one hydroxyl band and fortified the interpretation that 7-ketocholesterol had a more favorable steric arrangement for hydrogen bonding than compounds that have similar functional groups at other positions.

It is suggested that difficulty in synthesizing enol acetates be examined on the basis of the possibility and intensity of hydrogen bonding.

References and Notes

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Communications

Big Business and Research

Although I am loath to engage in public controversy, Philip Reichert's communication [*Science* **120**, 434 (1954)] requires an answer. Reichert emphasizes that the university professor has as his first function education rather than the performance of research. This definition is one with which others might disagree, since there is considerable support in the history of universities for their function as centers of learning in which education of disciples and free investigation of ideas or objective observations have equal importance.

The application of business methods to research has resulted in "a flood of immediately practical therapy" without any doubt. However, the great advance in basic knowledge upon which the practical applications must be based have rarely resulted from business methods in research. Business is fundamentally interested in profit, and therefore it is axiomatic that the research must be directed toward a profitable end. Even the "basic research" supported by business is of limited scope and usually is directed toward the solution of some project that has business interest. To any scientist who has dealt with the research performed in business organizations, or who has attempted to find money for basic research in grants from business organizations, the truth of my statements must be obvious. I base them upon my own experiences in this regard.

"The widespread distribution of information on new medical products" is a plague of the medical profession. The information is never unbiased (well, hardly ever!). Motivation need not be questioned. The results are evident in the pounds of "continuing postgraduate courses" that cross my desk daily. Several examples lie before me as I write, published by "ethical pharmaceutical" concerns, in which recommendations are made as though they were based upon incontrovertible fact, whereas these recommendations, in truth, either are directly contrary to the majority opinion among responsible investigators or are the subject of raging controversy.

"From the point of view of the patient—the average citizen—," he had better depend on physicians who form their opinions independently, from sources of information that are divorced from the immediate pressure of financial interest.

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In so far as R. W. Lippman's conclusions are based upon his own experiences, his conclusions are naturally valid for him. As a researcher who has crossed to the other side of the desk, I have during the last 10 years assisted in distributing many thousands of dollars in grants to approximately 20 first-line investigators. None of these men seem to be hampered by the fact that they are working for organizations that have a profit motive.

The difference between business research and university research is largely the pressure of the time element, and this usually means that the grants are

generous so that time can be saved and additional help provided for the investigator.

One point that needs careful consideration is the traditional attitude of suspicion and derogation which Lippman shares with the medical profession generally —that "profit motive" is synonymous with bias and dishonesty. To begin with, the profit motive is psychologically the most powerful incentive to any activity, and let us agree that the profit motive and the free enterprise system under which we live have not done too badly for us.

If I may use my own direct experience, as Lippman uses his, I should like to go back to 1946 when I was intimately connected with the promotional drive behind penicillin, a new drug then, and in fact a new concept in medicine. I remember that 100,000 units of the amorphous material sold for $20, when it could be obtained at all. Competition at that time was very strong, and research into methods of production, control, and packaging bordered on the hysterical. Today, 1 million units of crystalline penicillin can be purchased in any drug store in the United States for about 40 ct.

We cannot make a comparison with the $20 price of 1946 because 100,000 units today, which are sold for approximately 10 ct, cannot be compared as a product, since no one today would think of selling the crude amorphous penicillin. It is true that the basic research that produced penicillin was done in a university hospital, but it is also true that it languished on a shelf there for a decade. It was only when the profit motive entered the picture that this kind of progress was possible. The most miraculous drug is of little value until the physician at the bedside has the actual package in his hand, and if it is the "pressure of financial interest" that puts it there, let us at least appreciate the part that it takes in the lifesaving picture.

I referred briefly to "packaging." The 1946 amorphous penicillin was outdated in a matter of weeks. Present-day penicillin may be dated 2 years ahead. The intensive (and expensive) work of the first-class pharmacological and production engineers that went into this one aspect alone is never given a passing thought by the man who is the most benefited by such a detail, the man who opens the package at the bedside.

This is no isolated case. I lived through the same pattern with the synthesis of vitamin C, with the steroid hormones, with the wide spectrum antibiotics, and now with the *Rauwolfia* products.

Lippman's opinion that the "widespread distribution of information on new medical products" is a "plague" is again a traditional attitude that for the sake of American medical progress definitely needs changing. Big business has learned the hard fact that bias does not pay off. The profit motive itself makes for honesty, because the largest profit always goes to the man who best satisfies a human need.

"Recommendations [that] . . . are directly contrary to the majority opinion among responsible investigators" would have an F.D.A. citation so fast that the medical director of the company involved would be looking for another job that same week. I think it important that more physicians know how closely the government agencies scrutinize the labeling and brochures on pharmaceutical products. It is just impossible to make a claim unless it is well supported by investigators of unimpeachable reputation.

I have been increasingly proud of the organizations that have eagerly hunted out the discoveries that showed promise, distributed them to teams of trained investigators under grants, and so reduced the lag between laboratory bench and bedside. This pattern of research is no longer new and untried. It would not work if investigators did not want it to work, since it depends on men as well as on money.

The "talent scouts" of big business are a new profession; they might be called "medical expediters." Big business has learned to rely on, and to pay for, only the best-trained medical specialists. No management wants to risk its reputation and its capital on a gamble with truth, and nothing sells so well as a pharmaceutical product that really lives up to its claims.

The "profit motive" is under attack from many quarters of the world; I wish it were not so fashionable for those of us who live under it and benefit from such an economy thoughtlessly to add fuel to this attack. The attitude of automatically suspecting everything with a profit motive as having inherent bias is completely unrealistic. Let me cite two examples of what I meant by the "continuing postgraduate course."

1) At least twice a month every physician in America receives, at no cost whatever, a number of digest magazines. One of them in particular is edited by one of the best-loved and most impressive figures in American medicine. His list of editorial assistants and consultants reads like a roll call of the most honorable names in our profession. This is a "profit motive" job. Any physician that follows it carefully from month to month will have enough material on which he can form his opinions independently.

2) One of the most useful and informative of educational methods, as well as the most expensive, is the medical motion picture. There is hardly a field in modern medicine in which there does not exist, sponsored by a profit-making company, a competent and interesting motion picture, always produced under the direction of a great name in that specialty. Booking these for a medical meeting is usually free, or there is a very nominal shipping charge.

These are parts of the "continuing postgraduate" education to which I referred. Their integrity and lack of bias are guaranteed by the prominence of the professional names behind them. The entire cost of such projects as these is underwritten by commercial houses; their motivation is not hidden, nor can I see it as evil.

That there is a change from the traditional attitudes of medicine is nowhere better exemplified than in a pamphlet received this very morning from my own county medical society on *Guidance for Medical Co-*

operation with Public Press, TV and Radio. Many of the practices that as recently as 5 years ago would have landed a practitioner before his ethics committee are now not only permitted but encouraged. Programs of the learned societies have speakers and discussants from universities and hospitals side by side with workers from the pharmaceutical companies' research laboratories. Major investigators freely acknowledge by footnote the support of commercial grants.

In brief, if research is dominated by big business with all its great resources, its drive toward the practical, its profit motive, let us realize also that its life blood and success are a sober recognition of the value of top names, top people, top authority, top quality of work. The bigger the business, the more certain can you be that it has grown through the complete realization that honesty pays off! This pattern is completely typical of the pattern of our entire economy and is one of the most potent proofs of its value.

The next time any one of our physician leaders gives an injection of his 40-ct penicillin, I hope he will look at it and visualize the business that made it possible for him to have it. Maybe we should try to throw off the shackles of some of our traditional attitudes and try to examine the activities of big business with the same detached and objective evaluation that we habitually give to our test-tube and laboratory bench work.

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R. W. Lippman is a practicing physician who also is engaged in research; he is a former fellow of the John Simon Guggenheim Memorial Foundation. Philip Reichert, ex-Rockefeller Institute, and still maintaining a consulting practice in cardiology, is currently director in a large advertising agency of a division that prepares promotional material directed to the medical, dental, and auxiliary professions.

Forms for Literature Citations

McCasland's proposed telegraphic system of literature citation [Science **120**, 150 (1954)] would certainly be convenient for compilers of bibliographies. I should like to consider it from the point of view of the users of bibliographies. What does the user want from a reference? Unless he is merely engaged in the reprehensible practice of copying it into a bibliography of his own, he wants to find out more about what the cited paper contains. To do this, he must consult either the original paper or, if this is not possible, an abstracting journal. In the latter case the author's name is essential, and, therefore, since not all libraries receive all journals, McCasland's suggestion of eventually omitting the author's name seems impractical. If the original paper is to be consulted, a minimum reference would seem quite satisfactory.

Here, however, we come up against the fact, well known in communication theory, that a message which is subject to distortion by "noise" must contain an appreciable amount of redundancy if its meaning is to be sure of surviving. When the message is a citation, the noise is furnished by the bibliographer's mistakes, his secretary's errors in transcription, the printer's errors, and even the blunders of well-intentioned editorial assistants. Actual experience in checking thousands of literature citations made by professional mathematicians has shown that these sources of noise are quite serious. The commonest mistake is a one-digit error in a date or a volume number; more baffling problems arise when the author writes, for instance, *Math. Z.* when he intends *Math. Ann.* In such cases redundancy saves the day: it is easy to find out whether the impossible **12** (1936) really means **22** (1936) or **12** (1926). Again, since volume 56 of *Math. Z.* was roughly contemporaneous with volume 125 of *Math. Ann.*, it is easy to decide, given both volume and date, which journal was intended.

A four-letter code for the journal name suffers badly from lack of redundancy. A single garbled letter may make the name unintelligible or even impossible to reconstruct. An abbreviation like *Trans. Am. Math. Soc.* is recognizable even with several bibliographer's or printer's errors, while **AMST** is not. Experience again shows that authors are rather careless in writing abbreviations of journal names. This particular one would probably frequently come out **TAMS:** the transposition would be obvious to an alert reader, but hardly so to an automatic sorting device.

Some apparently redundant items are not really redundant, and are likely to remain indispensable until that millennial day when all editors of journals do just what McCasland recommends. The year does not always determine the series: there are journals that have started series 3 before completing series 2. There are also journals that have appeared several years later than their dates or (more remarkably) before their dates. Since it is sometimes desirable to know in what year a paper actually appeared, it would be helpful if the present citation system were on occasion extended (rather than contracted) to indicate both the official date and the actual date of publication.

I even hope for one other expansion in citations, namely the citing of inclusive pages. This is now customary in mathematical journals, and there are several good reasons for it. One is that if one wants to order a microfilm or photostat copy, one needs to know in advance how long the paper is.

In general, it would seem that citations are already so brief that little space could be saved by shortening them still more, whereas any further compression is against the interests of the people who use the citations and for whose benefit they presumably are intended.

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3 August 1954.