covery of penicillin, This happened when Fleming's attention was drawn to a staphylococcus culture undergoing lysis around a contaminating colony of a green *Penicillium*. The dictum of Pasteur that "chance favors only the prepared mind" has not been applied with greater accuracy than to this observation of Fleming's. This story has been told many times and need not be dwelt upon here. It is important to mention, however, that it was Fleming who subcultured the *Penicillium* and tested the effect of the broth upon different bacteria. He demonstrated the formation of a diffusible antibacterial substance (penicillin) that possessed a selective action against bacteria. Fleming also made the first comparisons of various mold cultures for their ability to produce penicillin and found this ability to be characteristic of only one particular group of molds.

Fleming further established that penicillin had no injurious effect on leucocytes and was not toxic to animals. This led him to suggest that penicillin might find application in the treatment of diseases caused by sensitive organisms. In fact, he used the active broth for the treatment of septic wounds. This led him to predict that "penicillin would one day come into its own as a therapeutic agent."

True, Roberts in 1874, Tyndall in 1876, Duchesne in 1897, Gratia in 1925, and many others in those intervening years had observed that green molds belonging to the *Penicillium* group were able to produce chemical substances that could prevent bacterial growth and even dissolve bacterial cells. But most of these observers did not have the background to appreciate the significance of these phenomena. None labored so arduously or understood so well the natural defenses of the body as did Fleming. None was so well prepared to take advantage of this observation as was Fleming by his previous studies on lysozyme.

Unfortunately, Fleming did not have at his disposal the necessary chemical assistance or the help of a large group of collaborators. It remained, therefore, for the team of Florey and Chain, 10 years later, to bring about the isolation and purification of penicillin and to demonstrate its potentialities as a chemotherapeutic agent. It is generally conceded that the Nobel Prize Committee reached a fair decision in linking the names of Florey and Chain with that of Fleming in making its award in 1945. A certain degree of credit for the development of penicillin should also be given to several American Government and university laboratories as well as to the pharmaceutical industry, with its excellent teams of chemists and bacteriologists, pharmacologists, and engineers.

As one of his biographers emphasized, Fleming possessed curiosity, insight, ingenuity, and persistence. He had the natural curiosity of a scientist, the insight required for successful experimentation, the ingenuity needed to enable him to develop the methods necessary to solve a problem, and the persistence to carry his study through to a successful conclusion.

In spite of the adulation of the public and the honors constantly showered upon him, Fleming remained modest in his claims; he was just "a simple bacteriologist," as he put it. Asking nothing in return, he gave to the world one of the greatest discoveries that has ever fallen to the hand of man to bestow. Because of his discovery, the world has become a better and healthier place in which to live.

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New Adrenal Cortical Steroid

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IT has long been known that extracts of the adrenal cortex possessed activity that, in some respects, far exceeded that of the known adrenal steroids. Although attempts to isolate the substance(s) responsible for this activity were unsuccessful for more than 20 years, much was learned of the properties of the "amorphous fraction" in which it remained (*1*) after the six known biologically active steroids had been removed.

This fraction had little effect on carbohydrate metabolism or on prolonged muscle work performance and did not produce appreciable atrophy of the adrenal cortex or involution of the thymus (*2, 3*). It was highly active, however, in tests of survival and of maintenance of the growth and well-being of adrenalectomized animals. The weight, the clinical state, and the serum electrolytes of adrenalectomized dogs could be maintained with daily doses of 1 to 2 μg/kg. Although it thus resembled desoxycorticosterone (DOC) in its properties, it differed from DOC in possessing far greater activity by weight and in its failure to depress the serum potassium even when given in large doses (*3*).

In 1951 Tait, Simpson, and Grundy (4) subjected adrenal cortical extract to paper chromatography and assayed the material eluted from serial sections of the paper for its activity in depressing the Na^{24}/K^{42} ratio in the urine of suitably prepared adrenalectomized rats. They found that the region occupied by cortisone possessed a high degree of activity that was clearly not caused by the cortisone itself.

In succeeding studies (*5*) the separation of the

active component from cortisone was achieved (*6, 7*), and a substance with the same characteristics was found in adrenal venous blood (*8*). The crystallization of the substance from adrenal extract was achieved almost simultaneously in Switzerland (*9*), England (*10*), and the United States (*6, 11*). Analytical, biological, and clinical work was begun with the small amounts of available material.

A dual structure was demonstrated (*12*), 18-aldo corticosterone (3,20-diketo-11, 21-dihydroxy-Δ^4-pregnene-18-al) and the 11-hemiacetal thereof, and the name aldosterone was suggested.

Preliminary data indicate that aldosterone is about 30 times as active as DOC in producing sodium retention in the adrenalectomized rat (*13*) and about 30 times as active as desoxycorticosterone acetate (DOCA) in maintaining sodium balances and well-being in the adrenalectomized dog (*14*) and the Addisonian patient (*15, 16*). It is about 5 times as active as DOC in increasing potassium excretion (*13*). Assays based on decreases of urinary Na/K ratio in adrenalectomized rats have given figures of 85 to 120 times the activity of DOC and DOCA. Differences in method are doubtless responsible for the lack of consistency in results.

Aldosterone resembles DOC further in having no effect upon the abnormal water excretion in the hypoadrenal state in the doses thus far used and probably no effect (one patient) in rheumatoid arthritis (*15*). It is more active than DOC but less active than cortisone in glycogen deposition (*17*) and eosinophil depression. Its activity resembles that of cortisone in the cold-stress assay (*18*). It is said to raise blood pressure and body sodium to normal in hypoadrenocorticism but not to produce abnormal increases, as does DOC, even in doses several times those required for maintenance, and not to depress the serum potassium (*14, 15*). In one respect its action is thus far unique: it was reported to decrease pigmentation in three Addisonian patients (*15, 16*).

As the evidence accumulates, it thus appears that the presence of adolsterone alone will explain all the known properties of the "amorphous fraction."

As these studies with aldosterone were being conducted, a number of workers were extracting a sodium-retaining substance from urine that appears on physical and chemical grounds to be identical with it (*19, 20, 21*). It appears in the urine of edematous patients with cardiac failure and nephrosis, of patients with cirrhosis with ascites, and of normal subjects on salt restriction; its excretion is not greatly increased by ACTH but may be increased by growth hormone (*20*).

The development of our knowledge of this newly discovered adrenal cortical steroid is an illuminating example of the rapid clarification of an area of medical interest by the coordinated efforts of chemists, physiologists, and clinicians.

Note added in proof. Since this manuscript was submitted, aldosterone has been detected in the peripheral blood of normal men (*22*), and evidence for its presence in placental tissue has been presented (*23*). It has been crystallized from the urine of a nephrotic child (*24*) and from the adrenal cortical adenoma of a patient with Cushing's syndrome (*25*). The diagnosis of "primary aldosteronism" has been applied (*26*) to a patient showing hypertension, hypokalemia, and large quantities of urinary aldosterone-like steroids, who lost all these features upon removal of an adrenal cortical adenoma (*27*). It is of interest that she had no edema. Direct evidence (*28*) also suggests that the potency ratio of aldosterone to DOC based upon potassium loss is comparable to that based on sodium retention.

Aldosterone applied locally has been reported to differ from other cortical steroids in *increasing* granulation tissue in rats (*29*); it did not produce hypertension or blood vessel or kidney damage on chronic administration, as did DOC in dosage 25 times higher (*30*). It did not inhibit the production of ACTH, as implied in its failure to reduce 17-ketosteroids (in 4 days) in a child with the adrenogenital syndrome (*31*) but did appear to inhibit its release upon cold stress in rats (*32*). It was again found ineffective in rheumatoid arthritis (*33*).

The doses thus far used in man (10 to 1000 μg a day) have never approached the doses of cortisone and hydrocortisone (10 to 200 mg a day) known to be clinically effective.

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News and Notes

Survey of Biological Abstracting

Perhaps no problem facing the individual scientist today is more defeating than the effort to cope with the flood of published scientific research, even within one's own narrow specialty. The situation offers a grave threat to the international character of science and the integration of scientific knowledge. Much more efficient and universal indexing and abstracting systems become daily more essential; yet instead we have only a multiplicity of such systems operating without coordination of plan, overlapping in great measure and at the same time leaving great areas of the literature scarcely covered at all.

In order to provide a clear conception of the present situation and to indicate the directions in which planning should proceed, a survey of biological abstracting, supported by funds from the National Science Foundation and other agencies, was conducted under a contract with *Biological Abstracts* during the period between August 1952 and January 1954. An advisory committee helped to plan the survey, and a staff of 12 persons was employed for part-time work. I served as director. In order to balance general opinion against evidence, it was decided to undertake a program of two parts: (i) a statistical analysis of the current effectiveness of biological abstracting services, and in particular of *Biological Abstracts*; and (ii) a sampling of opinion among American and foreign biologists with regard to the use, merits, defects, and desired changes in the over-all abstracting program.

The full report of the Survey of Biological Abstracting runs to 63 mimeographed pages. It is hoped that it can be reproduced in full for distribution to all who may need the detailed information. Such persons should write to the office of the American Institute of Biological Sciences, 2000 P St., NW, Washington 6, D.C. A condensed, but still much fuller report than the present notice, will appear in two installments of the *AIBS Bulletin* in the issues of January and April 1955. Inasmuch as many biologists who do not hold membership in AIBS were sent the questionnaire regarding the use of abstracting services and were asked their opinions regarding present service and desired improvements, and yet many of these persons do not see the *Bulletin,* it seems desirable to present here a brief summary of the findings and conclusions and to direct interested persons to the fuller reports.

In order to determine the actual state of current abstracting and indexing—proportion of coverage of the literature, delay in publication of abstracts and indexes, overlapping between services, and so forth—four statistical analyses were conducted. They were intended to answer the following questions: (i) What proportion of the world's biological literature is now being abstracted? (ii) In those journals stated to be covered (by a particular service), what proportion of articles published is actually abstracted, and how long is the average lag between publication of article and publication of abstract? (iii) What is the extent of overlapping between abstracting services—specifically, between *Biological Abstracts* and other individual services? (iv) What is the completeness of coverage of particular subjects by *Biological Abstracts,* in comparison with available, supposedly complete bibliographies?

From the data of the present survey, a general evaluation of the abstracting program of *Biological Abstracts,* chiefly as it was conducted in the years 1947–49, may be made. There were estimated to be about 22,000 current biological and partly biological research and review journals in the world, of which the *Abstracts* covers approximately 10 percent. Of the articles published in this 10 percent of journals, the percentage of biological articles actually abstracted varies from nearly 100 percent in some journals to as low as 30 percent in others. The proportion abstracted does not depend on the importance of the periodical in a scientific sense but instead mainly upon the American, rather than foreign, origin of the periodical and especially upon the provision to *Biological Abstracts* of authors' abstracts. The interval between publication of article and publication of abstract averages two-thirds to nine-tenths of a year for United States periodicals, depending upon whether or not authors' abstracts are supplied. For the foreign journals, it ranges from two-thirds of a year for author-abstracted British journals up to an average of nearly 1½ years for European foreign-language journals. Thus, although the lag in publication of abstracts might be somewhat reduced, the present showing is not bad, in contrast to the very poor showing made in regard to the coverage of articles.

When *Biological Abstracts* is compared with other abstracting services that cover in part the same subjects, the comparison is not unfavorable. *Chemical Abstracts* is often praised as a model abstracting service, yet the survey shows that its coverage of subjects