REVIEW OF REVIEWS[1]

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With pharmacological information, as with all knowledge, blowing out spheroidally, it becomes increasingly necessary, as well as interesting, to explore the chronological development of the expansion. The history of pharmacology may well become a major factor in holding the discipline together.

In the light of this consideration, pharmacologists may welcome Holmstedt & Liljestrand's *Readings in Pharmacology* (58). It is a helpfully illustrated, biobibliographical account with quoted selections of major contributions to pharmacology from antiquity to the present. It is, thus, the first satisfactory attempt to review the development of the science, from the slow accumulation of empirical lore, to the emergence of significant explanatory concepts. The review is comprehensive, but it is conventionally oriented. It might have been wiser for the authors to have restricted their selection to contributors who are no longer with us than to have risked criticism by featuring the living.

Mostly, the otherwise excellent volume can be criticized for giving no more than passing mention of some early, significant contributors to pharmacology. These would include such figures as Nicander, the earliest toxicologist; the 12th century Nicolaus of Salerno; Leonhart Fuchs (1501–1566); P. J. Pelletier (1788–1842); J. B. Caventou (1795–1877); B. W. Richardson (1828–1896); James Blake (1815–1893) who first investigated the relationships between chemical constitution and biological activity; E. Fourneau (1872–1949), the great detective-pharmacologist and pioneer drug designer; and Gordon Alles (1901–1963) who developed the amphetamines. Indeed, reference to such a standard authority as Garrison & Morton's *Medical Bibliography* (45a) would readily indicate the extent of significant omissions. These omissions are unfortunate, in an otherwise extremely informative and stimulating volume.

A very readable and interesting review of the long search for plant remedies and their active principles that may be used in medicine is skillfully given by Kreig (71a), the dashing ex-Marine. Her *Green Medicine* is a highly entertaining blend of biography, exploration, and basic pharmacological research, and although it is popularly designed, it may be of considerable interest and value to pharmacologists.

There are two recent trends in pharmacology which show some of the characteristics of fadishness. One is an increasing preoccupation with molecular pharmacology. A considerable review of a molecular basis for drug action

[1] This review covers pertinent publications to July 1, 1964.

is given by Ariens (4) and is extended by Ariens & Simonis (6). The latter review deals more specifically with the interaction of one or more drugs with different receptors. Ariens (5) has edited a relatively large volume dealing with molecular pharmacology, with special reference to the mode of action of biologically active compounds. In this symposium, there is a consideration of the concept of receptors and discussions on drug distribution, drug metabolism, stimulus-effect relations, and the interaction of drug molecules with receptors. Baker (8) analyzed factors in designing active site-directed irreversible inhibitors.

The second current fad deals with clinical pharmacology. This is becoming increasingly popular and is oriented toward drug therapy in human disorders. Claims are made for the necessity of special training in this field, and a rather naive attempt is being made to invest this aspect of pharmacology with an aura of superiority. It represents a sort of a triumph of anthropocentric conventionalities among certain pharmacologists. One might have a bit more respect for the effort if it were not so regressively stereotyped in its emphasis on therapeutics. Why not include consideration of the use of drugs for diagnosis of disease or for prevention of disease?

An important aspect of clinical pharmacology is the continued concern over drug safety. This has been promoted effectively in response to pressures upon the United States Food and Drug Administration, and by popular indignation as a result of the widely publicized disasters resulting from the extensive use of certain new drugs. All of us seem to forget that some toxicity is to be expected from every chemical agent, and there is no such thing as absolute drug safety. Even common drinking water or ordinary table salt, in excess, may be toxic. We simply must learn that there is a certain risk to be taken by everyone in taking any drug whatsoever. We have accustomed ourselves effectively to the risks of automobiles, and it would seem that we might be able to learn to become equally accustomed to the risk of drugs.

Freerksen (41) edited an important colloquium on kinetic aspects of drug action in particular relation to dosage of medicaments. This explored the relation of drug dosage to various kinetic factors in the onset, duration, and disappearance of action.

A considerable symposium on drug safety was opened by Beyer (13). Crocker & Vandam (22) reviewed untoward reactions to radiodiagnostic contrast media, giving 47 references. Meyler's (80) systematic survey of the side effects of drugs has gone into its fourth edition, and a fifth edition is planned for early publication. Herrick & Cattell (55) edited a volume on methodology in the clinical testing of new drugs, with emphasis on toxicity and side effects. Peck (91) has given a short survey of the preclinical evaluation of drugs for evidence of teratogenic activity.

The appalling mass of publications on drugs is emphasized by the survey made by Sewell (101) on behalf of the National Library of Medicine and Senator Humphrey. These surveys indicate the nature and magnitude of the current situation.

Names are important, and with drugs, names have economic significance. In a short note on drug names, Cutting (23) indicates that drugs may have code names, nicknames, exact chemical names, public names, and trademarked names. It is, of course, the trademarked names which have the economic significance and to which drug manufacturers are so devoted. One would think that any quality assurance which results from a trademarked name could just as well be made by the use of the public name of the drug, followed by the name of the company which manufactures it; thus, the manufacturer could be presumed to guarantee quality. This labeling might result in at least some reduction in the current, ridiculous confusion caused by the unnecessary multiplication of different names for an identical chemical agent.

Meier (78) has inaugurated the systematic investigation of experimental pharmacogenetics. His important volume, on the physiopathology of heredity and pharmacological responses, covers considerations of factors influencing drug metabolism, and hereditary operants of pharmacological significance in mice, rats, hamsters, rabbits, guinea pigs, dogs, and cats. He considers specific inherited traits in experimental and farm animals which may have potential pharmacological interest. He further gives considerable discussion to the comparative aspects of blood coagulation. In an appendix, he gives advice on the procurement of animals for research.

In pharmacological experimentation, the care of experimental animals remains an important consideration. Cohen (21) has edited another important symposium on research and animal housing. This includes discussion of appropriate facilities for experiments involving infectious disease and radioactive isotopes. The volume includes comments on lighting, ventilation, waste disposal, cage washing, operating rooms, and diagnostic control.

ENZYMES

Enzyme multiplicity and function in regulating metabolic pathways was reviewed by Kaplin, Stattman & Gorin (63). The structural aspects of enzymes and related compounds were considered in an extensive symposium opened by Fraser (39). This included considerations of the relation between protein structure to function in acetylcholinesterase, chymotrypsin, adenylosuccinase, glutamic dehydrogenase, cytochrome *c*, and hemoglobin. The specificities of lipases were reviewed by Desnuelle & Savory (26), Paoletti (86) edited a considerable volume on lipid pharmacology, in which enzyme action plays a major role.

ABSORPTION, METABOLISM, AND EXCRETION OF DRUGS

An excellent review of the absorption and distribution of drugs has been edited by T. B. Binns (14). This includes considerations of alimentary absorption, physical-chemical factors, the kinetics of absorption, brain and placental barriers, particle size, and includes specific reference to the absorption and distribution of steroids, antihypertensives, salicylates, hematinics, and

amebacides. Although the separate chapters in the book vary in style and value, the effort as a whole offers the most important recent summary of helpful information on the absorption and distribution of drugs.

With respect to membranes, in regard to absorption of drugs, a general discussion on the structure and function of membranes and surfaces of cells, edited by Bell & Grant (10), is important. This reviews significant aspects of membranes and cell surfaces in regard to passage of various types of ions. Wasserman (109) has edited a special monograph on the transfer of calcium and strontium across biological membranes. This contains a great deal of detailed information with critical analysis.

A review of much contemporary interest, covering 236 references, has been made by Moya & Thorndike (82) on the effects on the fetus and newborn of drugs used in labor. This includes a critical analysis of factors involved in placental transfer and distribution, as well as in regard to the excretion of such drugs as skeletal muscle relaxants, volatile anesthetics, barbiturates, tranquilizers, narcotics, and belladonna alkaloids.

Sisodia & Stone (102) have surveyed mechanisms of drug secretion into bovine milk. This survey is comprehensive and useful.

An interesting symposium on the metabolism of herbicides was introduced by Freed (40). This symposium dealt primarily with the metabolism of various herbicides in plants, especially in relation to triazine compounds. It also included consideration of the mammalian metabolism of various herbicides, such as propyl-butyl-ethyl-thiocarbonate in rats and dichloro-phenoxy-acetic acid in sheep.

Various substances which inhibit iodide transport were analyzed by Wolff (117). He classifies them as metabolic inhibitors, e.g., SH-compounds and quinones; transport inhibitors, e.g., cardiac glycosides, phloridzin, acetazolamide, and quinidine; and competitive anions, e.g., halides and SCN. Naturally, this review is chiefly concerned with the transport of iodine and other anions in the thyroid gland.

CHEMOTHERAPY

Reviving interest in chemotherapeutic problems is reflected in an increase in significant reviews of various aspects of chemotherapy. These reviews range from such general considerations as that of Feingold (36) on the action and toxicity of antimicrobial chemotherapeutic agents, to detailed considerations of various aspects of cancer chemotherapy. In special chemotherapy, Gray (51) edited an important symposium on listeric infection, which is not to be confused with infectious mononucleosis. In listeric infection, the consensus is that tetracycline is the antibiotic of choice. Steigman & Skloes (105) reviewed the treatment of amebiasis, merely repeating what has been well-discussed for many years.

Among the antibiotics, Kirby & Bulger (69) reviewed new penicillins and cephalosporins. Of particular importance is the analysis of Gale (45) of the mechanisms of antibiotic action, surveying 240 references. The actions are

classified as (*a*) against bacterial cell walls, as with the penicillins; (*b*) against protoplast membranes, as with tyrocidin, gramicidin S, and polymyxin; (*c*) against protein or nucleic acid synthesis, as with chloramphenicol, tetracyclines, and streptomycin, and (*d*) inhibiting nucleic acid synthesis, as with the case of actinomycin.

Cancer chemotherapy continues to attract great interest. Hawkins, Owen & Danielli (54) give a short, succinct review of the toxicity and antitumor action of some alkylating sulphonamides. Much interest has been aroused by the discovery of oncolytic action in vinca alkaloids from the common periwinkles. Johnson and associates (61) well reviewed the antitumor action of these compounds. Segaloff (100) has well summarized the effects of steroids in cancer chemotherapy.

An important symposium on cancer chemotherapy, arranged by the American Cancer Society, was opened by Burchenal (19) with the consideration of problems basic to cancer chemotherapy research. Hitchings (56) summarized the role of purine antagonists, and Welch (113) analyzed the activity of pyridimine antagonists. Bertoni (12a) and Nichol (85) reviewed the role of folic acid antagonists in cancer chemotherapy, while Price (93) did the same for alkylating agents. Kessler (68) considered phthalanilide compounds, and Mihich (81) surveyed the status of guanyl hydrazones in treating malignant growth.

The mode of action and toxicity of such radiomimetic drugs as busulfan and chlorambucil are well reviewed by Elson (32). He details, especially, the hematological effects of these compounds in comparison with radiation exposure.

The pharmacology of antimitotic agents was well reviewed by Dustin (30), with reference to 233 publications. He indicated that it is impossible at the present time to make a clear classification of anticancer agents and that the best hope for success lies in mitotic antagonists with specific action on some special tissue. Nevertheless, a tentative classification is given on the basis of spindle poisons such as sulfhydryls, colchicines, vinblastine, podophyllin, griseofulvin, carbamates, and chromosome poisons such as the antimetabolites for folic acid, purine, and pyrimidine. He also indicated the character of antimitotic action on the part of glutamine antagonists, such as azaserine, of antibiotics, of acriflavines, of certain quinones, and of aromatic diamines. He further surveyed the antigrowth action of alkylating agents such as chlorethyl sulfides and amines, as well as epoxides, corticoids, and nucleases.

ANESTHESIA AND ANALGESIA

Renewed interest in the general field of anesthesia and analgesia is apparent from the increasing number of significant reviews in the field. The general problem of control of pain has been well reviewed by Wang (108). An interesting survey of substances producing pain and itch has been made by Keele & Armstrong (65). They analyzed pain production which was caused

by the release of potassium ions, acetylcholine, histamine, 5-hydroxytryptamine, and plasma kinins. They indicated further, the mechanism of pain production by stings, venoms, and vesicants.

Lasagna (72) offers a clinical evaluation of morphine and its substitutes as analgesics. This is a particularly satisfying review since it is based on an application of the most advanced methods of clinical control, particularly those of subjective factors.

General anesthesia.—The uptake and distribution of anesthetic agents is thoroughly reviewed in a volume edited by Papper & Kitz (87). Some of the discussions make use of mathematical models and electrical analogs. The surveys include consideration of physical-chemical factors, respiratory and circulatory conditions, and biotransformations within the body. Pauling (90) offers a short review of his hydrate microcrystal theory of general anesthesia. In a significant short note, Featherstone (35) emphasizes the role of protein binding of small nonhydrogen-bonding molecules, such as those of xenon, ethylene, nitrous oxide, and cyclopropane. His point of view is supported by Lasser, Elizond-Marto & Crankl (73), with respect to pentobarbital.

Of current interest is the evidence of renal toxicity from various analgesics. This matter has been analyzed by Gilman (47) and discussed elsewhere in this volume. The Pappers (88) have also well considered the effects of pre-anesthetic, anesthetic, and post-operative drugs on renal function. They refer to 44 reports on the effects of various analgesic drugs on renal flow and kidney activity. The whole field of the metabolic effects of anesthesia was systematically reviewed by Nagai & Papper (83).

An extensive symposium on anesthetics and endocrine function was opened by Vandam (106). In this symposium, Baez & Orkin (7) gave particular attention to the effects of anesthetic agents on the response of the microcirculation to circulating humors, with reference to 102 reports. Alper, Flacke & Krayer (3) considered the pharmacology of reserpine and its implications for anesthesia, with reference to 186 publications.

Local anesthetics.—Of particular interest, historically, is the publication of an excellent survey account of Carl Koller (1858–1944) and his introduction of cocaine as a local anesthetic. This contribution has particular significance because it is based on Koller's correspondence and relations with Freud (1856–1939), and is so well written by Koller's daughter, Hortense Koller Becker (9). The psychological mechanisms involved in peripheral nerve block by local anesthetics have been reviewed by deJong & Wagman (25). Adriani and associates (1) have surveyed the comparative potency and effectiveness of topical anesthetics in humans, surveying and listing some 40 agents, in order of decreasing effectiveness, tetracaine (1 percent), dibucaine (0.5 percent), cocaine (20 percent), dyclonine (1 percent), and lidocaine (4 percent).

PSYCHOPHARMACOLOGICAL AGENTS

The first of a projected, two-volume survey of psychopharmacological agents has appeared under the editorship of Gordon (50). This is a compre-

hensive and exhaustive survey and covers in great detail the current studies in various types of compounds which alter central nervous system activity. Rossi (98) has given a short review of psychotherapeutic agents and has also reviewed synergism among central nervous system depressants (99). Paton & Lindgren (89) edited the volume on the pharmacological analysis of central nervous system activity which comprises part of the *Proceedings of the 1st International Pharmacology Meeting*. As might be expected, the material in the volume is uneven in quality and in presentation. Brazier (18) has offered a clear analysis of the effect of drugs on human electroencephalograms, giving 139 references. This important review includes psychopharmacologic drugs, anesthetics, convulsants, and anticonvulsants. It also includes a discussion of the significance of electrical silence in the brain.

Much interest has been recently aroused on the action of hallucinogens as a result of their morbid use for "kicks," especially by psychological misfits, as well as by misguided "sociologists." A special warning on the popular use of hallucinogens has been given by Farnsworth (34). Braceland (17) has broadly considered the use and abuse of central nervous system stimulants and tranquilizing agents. Hollister (57) has analyzed complications from psychotherapeutic drugs, referring to some 50 reports occurring in 1963, of various untoward reactions to phenothiazines, rauwolfia alkaloids, and thioxanthines. McKown, Verhulst & Crotty (77) have analyzed 968 cases of tranquilizer ingestion reported to the National Clearing House for Poison Control Centers. They call attention of physicians to the frequency of central nervous system depression after tranquilizer ingestion and the high incidence of suicide attempts with the less potent tranquilizers. Gittleman, Klein & Pollack (48) reviewed the effects of psychotropic drugs on long-term adjustment.

In connection with specific psychotherapeutic compounds, Feldman (37) opened a symposium on nialamide in childhood depressions. Lingjaerde (75) reviewed tetrabenazine in the treatment of psychoses, comparing its central mode of action with that of reserpine. Friend (42) discussed anti-Parkinsonism drug therapy, giving a concise summary with relative actions and costs of such drugs as benztropine, biperiden, cycrimine, chlorphenoxamine, diphenhydramine, ethopropazine, orphenadrine, procyclidine, scopolamine, and trihexyphenidyl. Forster (38) edited a symposium, evaluating drug therapy in neurological disorders.

Drug addiction is gradually taking its place as part of the increasingly-important consideration of psychopharmacology. Weeks (112) has offered an interesting review of experimental narcotic addiction. Essig (33) surveys, with 61 references, addiction to nonbarbiturate sedative and tranquilizing drugs, referring to meprobamate, glutethimide, ethinamate, ethchlorvynol, methyprylon, and chlordiazepoxide. It is clear, as various mild tranquilizing agents are more extensively used among millions of people, that evidence of some sort of addictive effect will appear among some susceptible individuals. It is particularly difficult to determine whether or not real addiction, in the sense of physical dependence, occurs, or whether the continued use of the

drug is conditioned by psychological factors. One of the most important agents, to give an objective indication of addiction to morphine alkaloids, is nalorphine. The discovery, development, and significance of this interesting drug are well reviewed by Way & Elixir (110).

Isselbacher & Greenberg (60) conclude that factors other than poor nutrition are involved in the pathogenesis of liver disease in alcoholics. They surveyed many metabolic activities under the influence of alcohol, many of which may relate to cirrhosis.

AUTONOMIC DRUGS

Reviews on autonomic drugs are decreasing in number. It is not clear whether this is a reflection of decreased study of autonomic drugs or merely a lack of incentive to furnish more reviews than those which have already appeared on this subject. White (116) has surveyed the relation between cholinergic drugs and EEG activation. Spoelstra (104) has reviewed the caloric effects of epinephrine and norepinephrine. Karlsberg, Elliott & Adams (64) have analyzed the effect of various pharmacologic agents on cerebral arteries, pointing out that serotonin is a constricting agent antagonized by methysergide and that dilation occurs with histamine, papaverine, isosuprine, and 10 percent carbon dioxide. Genest, Marc-Auréle & Mignault (46) opened a general symposium on angiotensin, sodium, and hypertension. An excellent review with 101 references is given by David (24) on new antihypertensive drugs, referring to sedatives, mebutamate, syrosingopine, mono-amine-oxidase inhibitors, veratrum alkaloids, hydralazine, and saluretic hypotensives.

The extraordinary amine-induced hypertensive episodes, noted in patients receiving mono-amine-oxidase inhibitors, and who then may ingest cheese or receive drugs such as imipramine or meperidine, were reviewed by Horwitz and associates (59). These episodes seem to be controllable by phentolamine.

CARDIOVASCULAR

Important reviews on the influence of various physical factors in the analysis of the action of drugs on myocardial contractility, together with the influence of beat interval on heart muscle, have been made by Blinks & Kock-Weser (15). With reference to over 500 publications, they discuss the significance of force-velocity relations and passive elasticity, and problems of cardiac architecture, oxygenation, resistance to shortening, fibre length, length-tension, volume relations, isometric tensions, fibre length in fatigue, anoxia, effects of temperature, and the effects of ions. All drugs with inotropic action studied so far seem to cause symmetrical shifts in curves relating tension to fibre length; i.e., at all fibre lengths, the tension developed is increased by an amount proportional to the initial level. Positive inotropic effects of cardiac glycosides, epinephrine, and norepinephrine, are decreased by cooling. The influence of physical factors in the heart must be taken into

account in the design and interpretation of experiments involving inotropic actions of drugs.

In a further extension of this review, Kock-Weser and Blinks (70), with 324 references, surveyed interval-strength relations in various kinds of heart muscle, with an analysis of species characteristics, and go on to a consideration of the relation of inotropic action of drugs to interval-strength relations. They considered cardiac glycosides, sympathomimetic amines, acetylcholine, and metabolic inhibitors, noting changes in inactivation due to electrolytes. Cardiac glycosides, in concentrations causing positive inotropic effects, need not cause a net loss of potassium from the heart, and, conversely, potassium loss under the influence of other substances need not be associated with a positive inotropic effect. Studies of drug action on interval-strength relations, as indicated by Bowditch (1840–1910) in 1871, may help in understanding mechanisms by which drugs alter myocardial contractility. The general effect of electrolytes on smooth muscle contraction has been reviewed by Bohr (16). Bellet (11) made a brief, rather uncritical resumé of the drug treatment of complete heart block, referring to many diverse compounds from ephedrine, quinidine, and digitalis to molar sodium lactate.

DIURETICS

A critical evaluation of diuretics, with a consideration of their chemistry and pharmacology, has been offered by deStevens (27). This reviews the physiology of the kidney and the chemistry of diuretic compounds as a background for the evaluation of diuretics. Clinical data are included. Detailed information is given on the action of xanthines and pyrimidines, triazines, organomercurial compounds, sulfonamides, thiazides and hydrothiazides, aldosterone and its antagonism, and miscellaneous diuretics such as inhibitors of the antidiuretic hormone, and unsaturated ketones. There is a review of the therapeutic use of diuretics in the treatment of hypertension. A useful appendix compares the mode of action of various diuretics and gives public and trade names. A special review of thiazide diuretics has been made by Earley & Orloff (31).

ENDOCRINES

Way & Sutherland (111), with reference to 144 reports, pharmacologically consider brain substances and their relation to endocrine effects. The proceedings of a conference on thyrotropin were edited by Werner (114). Prout (94) has reviewed the chemical structure of insulin in relation to its biological activity and antigenicity. Riddle (96), referring to 255 reports, has surveyed prolactin in vertebrate function and organization, as a releaser of parental instinct, showing that it dominates the reproductive cycle and is a basic metabolic hormone.

The current status of human pituitary growth hormone was reviewed by Li & Liu (74). Clayton (20) has surveyed the utilization of sterols by insects. Berczeller, Young & Kupperman (12) have reviewed, with reference to 57

reports, the therapeutic use of progestational steroids. They conclude that the matter is still experimental even in cases of habitual abortion. They indicate that the wise use of these compounds may remove adverse reactions in the menstrual cycle and relieve endometrosis. Their social value as contraceptives remains controversial. Duncan, Lyster & Clark (29) opened a symposium on "Provest" (an estrogen-progesterone combination) with a consideration of its biological activities, especially in relation to fertility.

MISCELLANEOUS

An interesting summary of the role of magnesium in biological processes has been made by Aikawa (2). Hartigan (52) reviewed the use of lithium salts in affective disorders.

The important matter of the pharmacological action of bacterial toxins was reviewed by Raskova & Vanecek (95). West (115), with reference to 287 reports, surveyed the mechanism of anaphylaxis, as a possible basis for a pharmacologic approach to allergy. This includes reference to histamine, 5-hydroxytryptamine, and mast cells, together with the influence of stress and cortico-steroids.

Nahas (84) made a review of the clinical pharmacology of THAM (tris-hydroxy-methyl-amino methane), with reference to 125 reports. Its high buffer capacity and its low toxicity and rapid elimination made it useful to correct acute acidosis or to be used as a gastric antacid and systemic alkalinizer. Haunz (53) edited a concise symposium on diabetes mellitus, including a discussion on the mode of action of insulin, the treatment of acute diabetic acidosis, oral hypoglycemic agents, and the management of juvenile diabetes. Glass (49) offered a monumental analysis of the gastric intrinsic factor which had been postulated by Castle (19a) in 1928. Glass surveyed its function in relation to cyanocobalamin, with reference to 1311 reports. Perlman (92) edited an extensive symposium on the vitamin B_{12} coenzymes. This included discussions on the chemistry and synthesis of cobamide coenzymes and on B_{12} coenzymes both in micro-organisms and animals. Robins (97) reviewed phosphatadyl ethanolamines and their relation to enzymes. Soine (103) surveyed naturally occurring coumarins and related compounds.

Vigran (107) opened a considerable discussion on anticoagulant therapy, discussing coumarins in particular.

In spite of the joking about scientists first getting scientific news from some of our popular weekly publications, and at the risk of violating the conventional tabu of referring—in a supposedly serious scientific discussion—to a bit of popular reporting, this Review of pharmacological reviews would not really be satisfactory without mentioning Kerr's (67) popularized (and undocumented) survey of DMSO (dimethyl sulfoxide). This amazing, distributive solvent, now readily obtainable from lumber by-products, seems to have remarkable analgesic and even water-balancing powers of its own. It is certain to get intensive clinical pharmacological study.

TOXICOLOGY

Gabriel (44) edited a symposium on veterinary toxicology, with reference to plant poisons, selenium, lead, thallium, fluorine, nitrate, arsenic, various herbicides, fungicides, insecticides, and radionuclides. Frost (43) opened a short symposium on food additives and the significance of their residues in animal tissues.

The 6th Annual Air Pollution Medical Research Conference Report was opened by Merrill (79) and included an extended discussion of the body burden of pollutants from the air. Kotin & Falk (71) reviewed atmosphere pollutants and indicated the extent of carcinogens. Kehoe (66) opened a symposium on lead poisoning, with a consideration of the dangers from tetraethyl lead in automobile exhaust gases.

The chronic toxicity of ethylene oxide was reviewed by Joyner (62). Marki & Witkop (76) reviewed the venom of the Columbian arrow-poison frog, *Phyllobates bicolor*. Salicylate toxicity was stressed in a symposium by Dixon (28). The report that salicylates depress protein-bound iodine levels in blood was interesting.

IN PROSPECT

Reviews of pharmacological material seem to be getting more diverse as the field of pharmacology extends. It is to be anticipated that there will be an increasing number of reviews on pharmacological topics of widely diverse character. It may well be that reviews in pharmacology will continue to offer the best means whereby the discipline can retain some semblance of unity. *Annual Review of Pharmacology* seems to offer the best way by which interested scientists may keep currently abreast of significant developments in the ever-expanding area of pharmacology and toxicology.

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