sion of fishable waters have stimulated great interest not only in maintaining fish yields in inland waters but also in projects designed to raise the yields to maximum carrying capacities. For more than half a century, the standard method of aiding fish production was the stocking of lakes and streams with hatchery-reared young fish. In general little or no attention was given to the environmental conditions that obtained in the waters that were stocked until recent years. More and more consideration has been given to various factors that have some influence on fish production in natural waters during the past decade. Up to the present time, such factors as shelter and breeding conditions have been emphasized.

The senior author of this bulletin has been chiefly responsible for the development of devices designed to improve environmental conditions in these respects; he is also responsible for trying these devices out on a large number of Michigan lakes. These experiments and the broad ichthyological knowledge of the authors constitute the fundamental background of the book.

Lake improvement is defined as the creation and maintenance in lakes of conditions which favor the propagation, growth and yield of inland lake fish. The general requirements for the successful production of fish are considered first; these include the physics and chemistry of the water, such as temperature, dissolved oxygen, hardness, depth, spawning conditions, suitable shelter and food supplies. All these subjects are more or less fully discussed, especially with reference to their general bearing on fish production under optimal conditions. The spawning habits of the different species of fish vary widely, for example, and successful reproduction, therefore, depends upon meeting the diverse requirements either naturally or artificially. Food is also a vital factor, so that fish production is substantially proportional to the food supply in the various types of water.

The second, or main, section of the book (pp. 49–201) deals with the construction of brush, log and other artificial structures designed to serve as shelters for fish and their installation in suitable locations. Also the planting of large aquatic plants, which will furnish natural shelters and feeding grounds, is discussed, as well as devices for bettering the spawning conditions. The use of fertilizers is recommended in certain types of lakes for the purpose of increasing the food supply. Methods of aerating the waters of shallow lakes in winter where there is frequently a heavy winter-kill due to the lack of dissolved oxygen are included in this section as well as the control of fish movements, the handling of fish populations showing stunted growth, the removal of excess rough fish, controlling predators and the treatment and prevention of diseases. The final chapter deals with the practicability of lake improvement and its place in fish management. This is followed by an annotated bibliography of 18 pages. The book is a valuable contribution to that phase of aquiculture which is concerned with the production of fish, and it fills a great need in this important field of water utilization.

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STATISTICAL TABLES

Statistical Tables for Biological, Agricultural and Medical Research. By R. A. FISHER and F. YATES. London and Edinburgh: Oliver and Boyd. 1938. viii + 90 pp. 12s. 6d net.

THESE tables will be of great value to research workers in the fields indicated and also in several others. Some of them are important for economic and sociological statisticians. The volume will have a wide appeal not only because of the eminence of the authors and the adequacy of the tables for an extensive range of work, but because the paper, type and arrangement have been well chosen to minimize time and eye-strain. The tables presented are:

I. The normal distribution. (Abscissae in terms of areas.) II. Ordinates of the normal distribution. III. Distribution of t. IV. Distribution of χ^2. V. Distribution of z and the variance ratio. VI. The correlation coefficient—values for different levels of significance. VII. The correlation coefficient—transformation of r to z. VIII. Tests of significance for a 2×2 contingency table. IX. Probits—transformation of the sigmoid dosage mortality curve to a straight line. X. Probits—simple quantiles of the normal distribution. XI. Probits—weighting coefficients and probit values to be used in adjustments of special accuracy. XII–XIV. The angular transformation. XV. Latin squares. XVI. Complete sets of orthogonal Latin squares. XVII–XIX. Balanced incomplete blocks. XX. Scores for ordinal (or ranked) data. XXI. Sums of squares of these scores. XXII. Initial differences of powers of natural numbers. XXIII. Orthogonal polynomials. XXIV. Calculation of integrals from equally spaced ordinates. XXV. Logarithms. XXVI. Natural logarithms. XXVII. Squares. XXVIII. Square roots. XXIX. Reciprocals. XXX. Factorials. XXXI. Natural sines. XXXII. Natural tangents. XXXIII. Random numbers. XXXIV. Constants, weights and measures, etc.

There is an excellent introduction describing the use of the tables, including some ingenious new uses of old tables, such as that of the χ^2 and variance ratio distributions for obtaining partial sums of the Poisson and binomial series, respectively. Other fruits of the authors' remarkable ingenuity include the work on Latin squares and balanced incomplete blocks in biological experiments, as well as other statistical methods

now better known. The section on interpolation at the end of the introduction must be read in order to use the tables efficiently; the methods of interpolation with reference to which several of the tables have been arranged will be novel to most statisticians.

Professor Fisher sends the following erratum. The formula for the range at the top of p. 8 should be

$$1/2PQ = 2/(1-R^2).$$

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SPECIAL ARTICLES

THE TOXICITY AND ABSORPTION OF 2-SULFANILAMIDOPYRIDINE AND ITS SOLUBLE SODIUM SALT[1]

THE discovery of the chemotherapeutic activity of 2-sulfanilamidopyridine in experimental pneumococcus as well as streptococcus infections in mice[2] has led to a trial of the drug in human pneumococcus infections, as well as in various other bacterial diseases. The clinical use of 2-sulfanilamidopyridine was undertaken before a chemical description or any adequate pharmacological and toxicological study of the drug was reported. The only study of the toxicity of the drug is that reported by Wien,[3] who concluded "that this substance has a big advantage over sulfanilamide in being much less toxic," having "about one fourth the toxicity of sulfanilamide."

The above conclusion of Wien has been widely quoted. However, since all Wien's toxicity data were obtained by oral administration of an acacia suspension of the drug and since 2-sulfanilamidopyridine is a rather insoluble substance and is poorly absorbed, considerable doubt exists as to the validity of his conclusion. It has been shown that many sulfanilamide derivatives of low solubility owe their lack of toxicity to poor absorption from the gastro-intestinal tract, and it has been pointed out that determinations of the toxicity of such compounds administered by the oral route may be misleading because of low absorption when large doses are given.[4, 5, 6] Our finding, that when 2-sulfanilamidopyridine is given as its very soluble sodium salt, both the toxicity and the absorption are quite different from that of 2-sulfanilamidopyridine itself, would appear to justify the publication of this preliminary note.

The sodium salt of 2-sulfanilamidopyridine[7] was prepared as follows. One part of sulfanilamidopyridine was suspended in 20 volumes of boiling 95 per cent. alcohol, and 1.5 moles of 1.3 M alcoholic sodium hydroxide were added per mole of sulfanilamidopyridine. The solution was chilled 2 hours in ice, and the white crystalline precipitate filtered, washed with cold alcohol and dried at 110°. Yield, 80 per cent. Titration with standard acid and methyl red showed 98.9 per cent. purity; colorimetric analysis[8] indicated 100.1 per cent. purity. These values were essentially unchanged by recrystallization from 95 per cent. alcohol. In this colorimetric analysis, it is important to note that unless the solution of the sodium salt is treated with the strong trichloroacetic acid solution before dilution, considerably lower (about 8–10 per cent.) results are obtained. On this account, further work was done with the sodium salt to establish its purity. One gram of sodium salt was titrated with standard acid to neutrality using methyl red, the precipitate was filtered off, washed with a small amount of cold water, and dried at 110° for a few minutes and drying completed in a vacuum desiccator. A 97.1 per cent. recovery of the sulfanilamidopyridine resulted, m. p. 190.4–190.9°, unchanged by admixture with a carefully purified sample of the original material. The sodium salt was prepared also by adding sufficient alcohol to completely dissolve the sulfanilamidopyridine, adding alcoholic sodium hydroxide to the solution and immediately cooling. Yield, 71 per cent. A third preparation of the sodium salt was made without the use of alcohol, by dissolving the sulfanilamidopyridine in 1.5 moles of warm 3 M aqueous sodium hydroxide and chilling. Yield, 60 per cent. (A further 20 per cent. yield may be obtained by adding 20 parts of absolute alcohol to the mother liquor). The sodium salts prepared by all three methods appeared to be identical. We have no explanation to offer for the low results which are obtained by the usual colorimetric method.

The sodium salt is a white product, crystallizing from 95 per cent. alcohol in clusters of radiating thin rods. It melts with decomposition at 316.5–317°. Its solubility in the non-aqueous solvents is low, as would be expected of an organic sodium salt. It dissolves in water to the extent of approximately 63 grams per 100 cc (25°). The pH of a 1 per cent. aqueous solution is 10.4; that of a 10 per cent. solution, 11.0.

Acetylsulfanilamidopyridine was prepared by treatment of a warm aqueous solution of the hydrochloride

[1] This investigation has been aided by a grant from The John and Mary R. Markle Foundation.

[2] Whitby, *Lancet*, 1: 1210, 1938.

[3] Wien, *Quart. Jour. Pharmacy and Pharmacology*, 11: 217, 1938.

[4] Marshall, Cutting and Emerson, *Jour. Am. Med. Assn.*, 110: 252, 1938.

[5] Marshall, Cutting and Cover, *Bulletin Johns Hopkins Hosp.*, 63: 318, 1938.

[6] Finestone, Bliss, Ott and Long, *Bulletin Johns Hopkins Hosp.*, 62: 565, 1938.

[7] The 2-sulfanilamidopyridine was kindly furnished by Merck and Company and by the Calco Chemical Company.

[8] Sulfanilamidopyridine can be estimated by the same procedure as used for sulfanilamide.[9, 10]