research which gives the field a kind of unity and which fully justifies this interesting monograph by one of the leading "explorers" of our day. Because of the variety of observations which are now carried on below one hundred degrees absolute it has been impossible in a small book to do more than pick out and describe briefly a few of the more striking examples in each line of work. As stated in the preface: "Though this book may be of some use to the specialist, we have had in mind as prospective readers rather physicists specializing in other fields . . ." For this purpose the material is admirably selected.

The book is divided into four parts, the first and longest being entitled "Phase Equilibrium" and dealing with the history and recent developments in liquefaction, measurements of low temperatures and phase diagram studies. The early work of Pictet, Dewar and Linde is graphically described with many quotations from original letters and papers. Unfortunately, the date of Kammerlingh Onnes' death is given as 1924 instead of 1926. The second part deals with the "Solid State," x-ray methods, thermal energy, the "Third Law of Thermodynamics." The third part covers "Orbit and Spin," the production of temperatures of the order of one hundredth of a degree by the Giauque method. The fourth part, "The 'Free' Electron," deals with superconductivity. There is an excellent bibliography covering the literature up to May, 1937.

The work described undoubtedly constitutes one of the most exciting chapters in modern science and the authors have presented the material in a vigorous and interesting manner. As a reference book, it could have been made much more valuable by the more careful labelling of equations and figures with units.

DONALD H. ANDREWS
THE JOHNS HOPKINS UNIVERSITY

SOUND WAVES, THEIR SHAPE AND SPEED

Sound Waves, Their Shape and Speed. By DAYTON C. MILLER. The Macmillan Company. 1937.

PROFESSOR MILLER in this small book gives us an account of certain work which he has done some time ago and never before fully reported. The first research here treated included the development of his phonodeik, the instrument with which he obtained by purely mechanical means most satisfactory photographic records of the form of sound waves. The second major item deals with a series of experiments in which apparatus somewhat like the phonodeik was used to measure the velocity of sound from high-power guns, the form of their sound-waves, and the pressures produced by them at various distances. In addition, there is an important chapter on spark-photography of sound waves, and of bullets in flight, and one on the velocity of sound in air.

The account which Professor Miller gives of these studies is a model of clarity, and the research itself is a model of thoroughness and scientific accuracy. Every student of physics should read this book for the interest in the subject-matter and for the example it sets in proper research methods and in the presentation of results.

F. A. SAUNDERS
HARVARD UNIVERSITY

SPECIAL ARTICLES

EXPERIMENTAL INTERSEXUALITY: THE PRODUCTION OF FEMINIZED MALE RATS BY ANTENATAL TREATMENT WITH ESTROGENS[1]

THE production of masculinized female rats by antenatal administration of androgens has been reported.[2,3,4] Until very recently attempts to produce feminized male rats by the antenatal administration of estrogenic substances (estrone, estradiol and estradiol benzoate) have been unsuccessful. Dosages that would conceivably cause feminization of the genetic male fetuses, when administered to pregnant rats, caused resorptions of the pregnancies. However, one full-term litter which showed slight changes in sexual development was obtained. The mother of this litter had been given 0.8 mg estradiol in divided doses from the thirteenth day to the twentieth day of pregnancy. Two new-born males of this litter were serially sectioned, and it was noted that there had been definite inhibition of development of the prostatic diverticula and of the seminal vesicles.

A generous amount of estradiol dipropionate has been made available to us through the courtesy of Dr. Ernst Oppenheimer, of Ciba Pharmaceutical Products, Inc. This compound is very slowly absorbed and consequently has a very prolonged estrogenic effect. Thirty-two pregnant rats have been injected with this compound, usually in single doses of 0.375 mg to 4.0 mg on the thirteenth, fourteenth or fifteenth day of pregnancy. Nineteen of these animals have carried to term and 24 males have been obtained from these litters. Fourteen of these males, the mothers of which had received 2.0 to 4.0 mg of estradiol dipropionate, had grossly visible nipples at birth and were hypospadiac. Normally nipples are not present in the males rats of our colony. Normal new-born males

[1] This work has been supported in part by a grant from the Josiah Macy, Jr., Foundation.

[2] R. R. Greene and A. C. Ivy, SCIENCE, 86: 200, 1937.

[3] R. R. Greene, M. W. Burrill and A. C. Ivy, *Proc. Soc. Exp. Biol. and Med.*, 38: 1, 1938.

[4] R. R. Greene, M. W. Burrill and A. C. Ivy, SCIENCE, 87: 396, 1938.

have a completely formed penile urethra. In eight animals (all from different litters) the testes were in abnormally high position and in three, the testes were in the typically female position, at the base of the kidney.

Eight of these new-born males (each from a different litter) have been serially sectioned to date. One animal (0.5 mg estradiol dipropionate) showed marked inhibition of the ventral prostatic diverticula and a moderate inhibition of the posterior diverticula. In another animal (1.0 mg estradiol dipropionate) the ventral prostatic diverticula were absent and the posterior diverticula were scanty. In six animals (2.0 to 4.0 mg estradiol dipropionate) the prostatic diverticula were entirely absent. Furthermore, in each of these six animals there was a vagina which was comparable in development to that found in the normal new-born female. In four of these six cases marked inhibition of the right vas deferens was found. The lumen of the vas was absent throughout most of its length and, in some regions, even the epithelial cells had apparently completely degenerated. In all animals the seminal vesicles exhibited some inhibition or departure from normal development in that the cranial flexure which is typical of this organ at this stage was absent. The epididymides also showed evidence of inhibition inasmuch as the convolutions of the ducts were less numerous than in the normal males.

On the basis of the few animals observed, it seems that the amount of development of female structures (vagina and nipples) and inhibition of male structures has a fairly definite relationship to the dosage given.

The females in these litters have not been examined microscopically to date. However, some changes from the normal have been grossly visible. Large nipples have been present in the new born. Normally nipples do not appear in the female rats of our colony until the fifth to tenth day. Usually in the same litter the females had more and better developed nipples than the males. The uteri were grossly enlarged and apparently distended. The development of the ovarian capsule had been inhibited; with the higher dosages no ovarian capsule was present.

CONCLUSIONS

The administration of large amounts of an estrogenic substance to the pregnant rat has so modified sexual development of genetic male fetuses that feminized males or intersexed animals have resulted.

R. R. GREENE
M. W. BURRILL
A. C. IVY

DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY,
NORTHWESTERN UNIVERSITY MEDICAL SCHOOL

XANTHINE OXIDASE: AN ALLOXAZINE PROTEID

A XANTHINE oxidase preparation has been obtained that is 500 times more active per unit dry weight than the whole milk used as a source. The activity has been determined by measuring manometrically the oxygen consumption, usually with hypoxanthine as the substrate, though xanthine and aldehydes may also be employed. Solutions of this enzyme preparation containing 6 mg/cc have a strong golden brown color and possess an absorption spectrum with a band in the visible lying between λ400–500 mμ. This band disappears if hypoxanthine is added to a solution from which air is excluded. The original color can then be rapidly restored by the admission of air. If the spectrum of the reduced enzyme preparation is subtracted from that of the oxidized form, a spectrum is obtained which is similar to that of the "gelbe ferment" in having two bands centered at λ370 mμ and λ465 mμ, respectively. The prosthetic group may be split off from the protein by the addition of acid or alcohol. Such solutions are pure yellow in color, fluoresce strongly and possess the characteristic absorption spectrum of a flavin with two bands centered at λ450 mμ and λ375 mμ. Definite proof of the flavin nature of the prosthetic group is furnished by the fact that it can be quantitatively converted by the method of Warburg and Christian[1] into a lumiflavin, the absorption spectrum of which is identical with that given by these workers. Complete separation of the flavin part from the protein without destruction of the latter has not yet been accomplished. It is, however, possible to obtain a partial separation. The protein part so obtained shows a 3–4 fold increase in activity on the addition of the flavin component. The flavin alone is inactive. If the flavin containing co-ferment of the amino acid oxidase recently isolated by Warburg and Christian[2] or lactoflavin phosphate is substituted no increase in activity is obtained. It therefore appears that xanthine oxidase is to be classified as an alloxazine proteid whose active group is of a different composition from those flavins hitherto known. Further details will be published elsewhere.

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ERIC G. BALL,
Fellow of the John Simon Guggenheim Memorial Foundation
KAISER WILHELM-INSTITUT FÜR ZELLPHYSIOLOGIE,
BERLIN-DAHLEM

[1] O. Warburg and W. Christian, *Biochem. Zeits.*, 266: 377, 1933.
[2] O. Warburg and W. Christian, *Biochem. Zeits.*, 296: 294, 1938.