vided the molecules have a density equal to that of most proteins, i.e., 1.33 gm./cc. This value of the molecular weight is about one-third of that secured from the diffusion constant alone as previously measured by the method of Anson and Northrop. The difference in the results from the two methods is not unexpected and has been found for other proteins.

The molecular weight may, of course, be computed from the sedimentation constant alone, without use of the diffusion coefficient, provided it is assumed that the molecules are spherical. Applying Stokes's law, the radius of the molecule may be calculated, and if the density is assumed to be 1.33 as before, the molecular weight becomes 200,000. This represents a minimum value, since the spherical form is most favorable for rapid sedimentation. The fair agreement between the two values secured from the sedimentation constant with and without the diffusion constant indicates a shape for the visual purple molecule which is probably not greatly different from that of a slightly oval particle.

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5 Dr. Aurin M. Chase kindly made these extractions for us.

BIOLOGICAL DIFFERENCES IN THE ACTION OF SYNTHETIC MALE HORMONES ON THE DIFFERENTIATION OF SEX IN THE CHICK EMBRYO

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In a former investigation it was shown that male hormone preparations obtained from male human urine and bull testis act differently upon the developing gonads and gonoducts of the chick embryo. The urinary preparations brought about a feminization of the genetic males just as oestrone and oestriol did. Also they had a masculinizing effect as was shown by (1) the hypertrophy of the potential vasa deferentia (Wolffian ducts) in embryos of both sexes and (2) the inhibition of the oviducts in
genetic females. The bull testis preparations, on the contrary, in the concentrations used produced no changes except an hypertrophy of the Wolffian ducts in both sexes. These biological differences in action were ascribed tentatively to the presence of androsterone and dehydroandrosterone in the urinary preparation and of testosterone in the bull testis preparation.

The purpose of the present paper is to analyze the effects of the synthetic male sex hormones giving particular attention to the biological differences in their action. Either propylene glycol or sesame oil solutions of androsterone, dehydroandrosterone, androstenedione and testosterone propionate were introduced into eggs incubated from 43 to 72 hours, stages either prior to or during the early formation of the gonad primordium. The dosage was single and ranged from 0.02 to 2.4 mgs. Development was then continued until the 16th, 17th or 18th day. The hormones were administered to 300 eggs. Of those treated with androsterone and dehydroandrosterone 34% survived, whereas with testosterone propionate 74% survived, thus indicating a considerable difference in the toxicity of the androgenic substances used. The sex ratio of the surviving embryos is 54 ♀ ♂ : 64 ♂ ♂ , showing no differential effect. All survivors were examined for changes in the gross anatomy of the gonads and gonoducts. The histology of the gonads and portions of the gonoducts was studied in 76 cases. By using F₁ embryos of the cross Barred Rock ♀ × Rhode Island Red ♂ , the original sex was readily ascertained by differences in sex-linked plumage characters.

Genetic Females.—Each of the hormones, except androstenedione which is ineffective in the concentration used (0.09–0.66 mg.), brings about a modification in the form and structure of the gonads and gonoducts of the genetic females (Figs. 2, 4 and 5). Usually with concentrations less than 1.0 mg. the right ovary enlarges by the hypertrophy of the medullary tissue and tends to assume a testis-like shape. The left ovary, on the contrary, remains normal in form and histology. The oviducts are usually typical and the Wolffian ducts are hypertrophied only slightly or not at all. Generally when the dosage exceeds 1.0 mg. both the right ovary and the medulla of the left ovary undergo hypertrophy and the cortex of the left shows changes of a degenerative nature. Both ovaries now assume a testis-like form, the right more so than the left (Fig. 4). The 23 embryos histologically examined may be classified into three grades of effects: (1) Those in which the ovarian cortex of the left gonad is generally thinner than normal, and sterile sex cords (presumably of cortical origin) are adjacent to the medulla. The oviducts are more or less rudimentary and the Wolffian ducts distended with fluid. (2) Embryos in which the ovarian cortex of the left gonad is somewhat degenerate and underlain with sterile sex cords. At the hilus of the gonad the medullary tissue has transformed into solid cords containing germ cells (potential testicular
FIGURE 1
Urinogenital system of a 17-day genetic male embryo treated with 1.2 mgs. of dehydroandrosterone. Both right (ro) and left (lo) oviducts well developed; Wolffian ducts (w) moderately swollen; left gonad (g) ovary-like in form, histologically an ovotestis. b, left Wolffian body; c, cloaca. × 3.7.

FIGURE 2
Urinogenital system of a 17-day genetic female given 0.75 mg. of androsterone. Both right and left (o) ovaries have assumed a testis-like form; left oviduct (lo) greatly inhibited—posterior half missing; both Wolffian ducts (w) much distended with fluid. b, right Wolffian body; c, cloaca. × 3.7.

FIGURE 3
Urinogenital system of a 17-day genetic male treated with 1.0 mg. testosterone propionate. Testes (t) small but normal in form. Wolffian bodies (b) and ducts (w) swollen. c, cloaca. × 3.7.

FIGURE 4
Urinogenital system of a 17-day genetic female treated with 2.0 mgs. of testosterone propionate. Ovaries (o) decidedly testicular in form; oviducts, particularly the left (lo), have undergone extreme retrogression; ro, right oviduct; Wolffian bodies (b) and especially the ducts (w) greatly hypertrophied. c, cloaca. × 3.7.
cords). The left oviduct is quite rudimentary, the right either typical or longer than usual. The Wolfian ducts are usually much distended with fluid. (3) Embryos in which cortex of the left gonad is generally more degenerate (even absent over anterior portion) than in the preceding grade. Sterile cords (cortical) are usually present in the outer surface of the medulla and a region of distinct testicular cords with germ cells is seen at the hilus (Fig. 5). Testicular cords likewise appear in the hypertrophied medullary tissue of the right ovary. The left oviduct is generally reduced to a short rudimentary ostial portion containing a lumen, the remainder consisting of oviducal ligaments only; the right, on the contrary, is usually increased in length. The Wolfian ducts and many of the mesonephric tubules become enormously swollen. See figure 4. In general embryos exhibiting this grade of effect occur with a higher frequency when the dosage approaches 2.0 mgs. Finally it should be noted for the embryos of these grades, that the posterior end of the left ovary often exhibits a higher degree of modification in the male direction than the anterior end.

**Genetic Males.**—The Wolfian ducts and certain mesonephric tubules of the male embryos hypertrophy as they do in the genetic females. The gonads and oviducts, however, respond quite differently to the different hormones. With testosterone propionate the testes are reduced in size but show no essential change in form or structure (Fig. 3). The oviducts never persist. With androsterone and dehydroandrosterone, however, a strong feminizing action is seen which is very similar to that of oestriol and oestriol (Willier, et al.³). The left testis changes into a flattened ovary-like body consisting of ovarian and testicular tissues (ovotestis). The right testis remains histologically unchanged until the left testis is strongly feminized whereupon it becomes reduced in size, assumes an ovarian shape and develops some ovarian medullary tissue. The oviducts persist throughout their length and may even hypertrophy. The male thus comes to resemble closely a normal female (Fig. 1).

**Degree and Order of Sex Transformation of the Females.**—Although a histological study reveals considerable variation in the degree of intersexuality attained in the genetic female embryos for a given dosage, in general it is roughly proportional to the quantity of male hormone administered. The hormones, except testosterone propionate when larger doses are required, are nearly equally effective in producing a given grade of intersexuality. The minimum effective dose of androsterone and dehydroandrosterone is found to be about 0.19 mg. Although this was not ascertained for testosterone propionate a higher dose is indicated since doses between 0.25 and 0.40 mg. were found to be ineffective in nine embryos examined. Furthermore doses of 2.4 mgs. do not bring about any greater effect in the ovary at least than 1.0 mg. of androsterone and de-
hydroandrosterone. The male hormones bring about only a partial sex reversal of the genetic females even though administered in doses as high as 2.0 mgs. and more. This large quantity contrasts strikingly with the action of oestrone and oestriol which in doses of much less than 1.0 mg. may completely feminize a genetic male.

As a rule the first noticeable effect produced in the genetic females is a hypertrophy of the right ovary and of the Wolffian ducts. The left ovary and left oviduct are generally unaffected. Higher doses are necessary to bring about changes in the left ovary and left oviduct. In such cases the ovarian cortex and left oviduct are more or less inhibited and accompanied by structural changes in the ovarian medulla and a distention of both Wolffian ducts with fluid. In low grade modifications the medulla of the left ovary merely hypertrophies but in the higher grades where cortex is more strongly inhibited, the medullary tissue in the hilar region develops into testicular cords (Fig. 5); and many scattered testicular cords likewise develop in the medullary tissue of the right ovary. The formation of testicular cords in the medulla of the left ovary farthermost from the ovarian cortex may be indicative of a diminution in the extent of the inhibitory influence which the latter, from ovariotomy studies in the fowl, is known to have upon the ovarian medulla. On theoretical grounds it would be expected that as the ovarian cortex is inhibited more and more by the male hormones the transformation of medulla into testicular cords would spread from the hilus toward the surface. It is interesting to point out that when a testis is converted into an ovary by the action of oestrone or oestriol the order is reversed. That is, the transformation of testicular cords into ovarian medulla proceeds in the direction from the superimposed cortex inward toward the hilus, the cords there retaining their male form last.

Dual Physiological Action.—From the results it is seen that androsterone and dehydroandrosterone have both masculinizing and feminizing effects, whereas testosterone propionate has a masculinizing effect only upon the differentiating gonads and gonoducts. The possibility that testosterone propionate in the concentrations used may have a feminizing effect also upon embryos of other breeds must be recognized since Wolff and Wolff⁵⁴ have shown that acetate of testosterone is quantitatively less effective in producing both intersexual males and females of embryos of the Leghorn breed than in F₁ embryos of the cross Light Sussex females X Rhode Island Red males. Except for a more pronounced hypertrophy on the Wolffian ducts, androsterone is equally as effective as dehydroandrosterone in producing masculinizing and feminizing changes. Testosterone propionate is not greatly different from the other two male sex hormones, except for quantitative differences already noted, in producing masculinizing effects.
The difference in action of androsterone and dehydroandrosterone on the female components of genetic males and females is quite puzzling. As has been noted, these androgens bring about the development of ovarian
cortex and the persistence of the oviducts in genetic males. In genetic females, on the contrary, they have an inhibitory action on these components. That is, the action of these substances in genetic females is wholly masculinizing in nature, whereas in genetic males both feminizing

**FIGURE 5**

Ovotestis of a genetic female treated with 2.0 mgs. of testosterone propionate. Note mass of testicular cords in hilar portion of medulla, i.e., adjacent to adrenal (lower-most tissue in figure). Ovarian cortex thinner than normal. × 210.
and masculinizing effects are seen, the former being greater than the latter. The significance of these findings remains for future study.\textsuperscript{5}


\textsuperscript{3} Wolff, E., and Wolff, Em., \textit{C. R. Soc. Biol.}, 123, 1191–1193.


\textsuperscript{5} The principal conclusions presented in this paper were communicated to the National Academy of Science in October, 1937 (\textit{Science}, 86, 409).

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\textbf{THE GENERALIZED CLEBSCH-GORDAN FORMULA}

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The formula of Clebsch-Gordan which furnishes the analysis of the Kronecker product of any two irreducible representations of the two-dimensional unimodular linear group is one of the most important results of group theory in regard to the application of this theory to quantum mechanics; indeed Weyl, in his book on Group Theory and Quantum Mechanics (English edition pp. 128–129) affirms that "it may justly be considered as the fundamental mathematical formula for the classification of atomic spectra and for the theory of the valence bond." We point out here that it is but a special case of a general formula giving the analysis of the Kronecker product of any two irreducible rational, integral representations of the full $n$-dimensional linear group \textit{which depend on a single label}; the typical rational integral representation $\Gamma_{(\lambda)}$ of the full $n$-dimensional linear group depends on $j$ labels $(\lambda_1, \ldots, \lambda_j)$, $j = 1, 2, \ldots, n$ and the generalized Clebsch-Gordan formula has reference to those particular representations for which $j = 1$.

There is also a Clebsch-Gordan formula which furnishes the analysis of the Kronecker product of any two irreducible representations of the $3$-dimensional rotation group. We point out here that this is but a special instance of a general formula which furnishes the analysis of the Kronecker product of any two irreducible representations of the full $n$-dimensional real orthogonal group \textit{which depend on a single label}; the typical irreducible representation $\Gamma_{(\lambda)}$ of the full $n$-dimensional real orthogonal group depends on $j$ labels $(\lambda_1, \ldots, \lambda_j)$, $j = 1, \ldots, k$, where $k = \frac{n}{2}$ or $\frac{n-1}{2}$ according as $n$ is even or odd and the generalized Clebsch-Gordan formula has reference to those representations for which $j = 1$. The $n$-dimensional rotation