only when the compound capable of tautomerization is in the liquid phase, or in solution. And that is just the case with the free radicals under consideration.

6. The two radicals, α -naphthyl-diphenylmethyl and α -naphthyl-xanthyl, were found to give a molecular weight less than that calculated for the monomolecular phase. Schlenk and Renning's¹¹ results show that α -naphthyl-biphenyl-phenylmethyl exhibits the same unusual behavior. We have good reasons to believe that our results are not due to experimental errors, and we took pains to verify them repeatedly. The cause of this unexpected result may possibly lie in a still further dissociation of the triarylmethyl itself, $R R' R'' C \rightleftharpoons R R' C + R''$.

¹ Gomberg, *Berlin, Ber. D. Chem. Ges.*, **40**, 1907, (1860); **42**, 1909, (406); Gomberg and Cone, *Liebigs Ann. Chem. Leipzig*, **370**, 1909, (190); **376**, 1910, (208).

² Gomberg, *Berlin, Ber. D. Chem. Ges.* (406); **46**, 1913, (228).

³ Compare G. N. Lewis, these PROCEEDINGS, **2**, 1916, (588).

⁴ Gomberg and Cone, *Berlin, Ber. D. Chem. Ges.*, **37**, 1904, (2037).

⁵ Schlenk and Mair, *Liebigs Ann. Chem., Leipzig*, **394**, 1912, (179).

⁶ Schmidlin, *Das Triphenylmethyl*, Stuttgart, 1914, (94).

⁷ Piccard, *Liebigs Ann. Chem., Leipzig*, **381**, 1911, (347).

⁸ Schlenk, *Ibid.*, **372**, 1909, (4); **394**, 1912, (186); *Berlin, Ber. D. chem. Ges.*, **43**, 1910, (1756); Schmidlin and Garcia-Banus, *Ibid.*, **45**, 1912, (3176).

⁹ Schlenk and Renning, *Liebigs Ann. Chem., Leipzig*, **394**, 1912, (189).

¹⁰ Schlenk, Herzenstein and Weickel, *Berlin, Ber. D. chem. Ges.*, **43**, 1910, (1754).

¹¹ Schlenk and Renning, *Liebigs Ann. Chem., Leipzig*, **394**, 1912, (195).

SEX-DETERMINATION AND SEX-DIFFERENTIATION IN MAMMALS

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The principle of zygotic sex-determination is generally regarded as established for mammals as for other animal groups. The reasons for this are (1) the identity of sex of all individuals derived from a single zygote: e.g., identical twins, quadruplets of armadillos, etc.; (2) the facts of sex-linked inheritance, which demonstrate the inheritance of certain sex factors in a Mendelian way; (3) the dimorphism of spermatozoa in mammals as in other groups with zygotic determination of sex. We must therefore regard sex as *determined*, in the usual sense of the word, at the time of union of the gametes.

The question, however, arises, whether sex-determination involves an irreversible tendency to the corresponding sex-differentiation, or

whether such differentiation is more or less controllable, or even completely reversible?

Up to a certain stage in the development of mammals there are no morphological evidences of the determined sex. Prior to this stage sex-characters are identical in both kinds of zygotes; the gonad first enters on a phase of male differentiation in both sexes, which subsequently changes to the female direction in the female zygotes only; both male and female sex-ducts arise in each kind of zygote, and by subsequent corelative progressive and retrogressive differentiation the conditions of the appropriate sex are produced; external parts also appear similarly at first in both sexes. The possibilities for complete reversal of the indicated sex-differentiation would therefore seem to lie within this so-called sexually indifferent stage, and to diminish progressively as differentiation proceeds.

There are many indications that each zygote, whether determined as male or female, has both tendencies, both sets of sex-factors; in other words that the reactions for male or for female differentiation are both possible for each zygote; but that they are to a considerable extent mutually exclusive in bisexual animals. The initial sex-determination is, therefore, a condition in which there is a quantitative superiority of one or the other tendency or set of factors. The advance of development progressively limits the possible operations of the inferior set of factors, so that, by both positive and negative limitations, reversal of the initial sex-index becomes increasingly more difficult.

It has long been known that the degree of development of the sex-characters that arise after birth is dependent in mammals upon internal secretions of the sex-glands (sex-hormones) circulating in the blood. This is seen in the well-known effects of castration; and partial reversal of sex-differentiation has been secured by implantation of the sex-gland of the opposite sex following castration.¹ But the more fundamental sex-characters, like other fundamental characters, are differentiated in mammals before birth. Such are the type of sex-gland, whether ovary or testis, the type of sex-ducts, whether vasa deferentia or female reproductive tract, and the type of the external organs of reproduction.

The problem of the extent to which sex-differentiation may be reversible carries us back therefore to the sexually indifferent stage, and the question arises whether the sex-characters that develop before birth are, like those arising after, dependent for the degree of their development upon sex-hormones, and whether, like the latter also, they are more or less reversible by action of the sex-hormones of the opposite sex?

The investigation of a remarkable phenomenon in twins of cattle furnishes a positive answer to this question so far as the female is concerned.

The female of two-sexed twins in cattle, commonly known as the free-martin, has long been known to be absolutely sterile as a general rule; however a small percentage of such females is perfectly normal. I have found by a study of the embryonic development that the phenomenon of sterility is due to fusion of the embryonic membranes of the twins, and an anastomosis of the arteries and veins of the female and male associates, but more especially of the arteries, so that there is literal community of blood during foetal life.² If the anastomosis of the blood-vessels does not take place, the female is perfectly normal as is usual in the twins or multiple births of all other mammals. In cattle again if the twins be of the same sex both are perfectly normal.

Nature has thus performed here a perfectly controlled experiment, which shows that blood community of foetal life between embryos of different sex causes sterility of the female. This fact can be explained only on the assumption that the foetal blood carries specific sex-hormones, because the only system of the female that is affected is the reproductive system. The male, on the other hand, is normal in all its parts, and this finds explanation in the fact that the sexual differentiation of the male antedates by a little that of the female, and the development of female sex-hormones is probably inhibited from the start.

The time at which the anastomosis of the blood vessels occurs is a question of fundamental importance. Sex-differentiation begins in cattle when the embryo is about 25 mm. long. The evidence at my command indicates strongly that fusion of the embryonic membranes begins at about this time or a little earlier; in a pair of twins 15 mm. long the membranes overlapped but were not yet fused; in another pair, of which one member was 35 mm. and the other 40 mm. in length, the membranes were perfectly fused so that the place of union could no longer be detected. The vascular areas of the two sides overlapped, but the larger vessels did not anastomose; a capillary connection at least between the two sides certainly existed. In another pair 50 mm. long the fusion was perfect and the anastomosis of the blood-vessels also. Study of normal embryos also shows that the conditions precedent to fusion are fully established before the 20 mm. stage; and study of the gonads of the free-martin shows that the development of the ovarian cortex is probably inhibited from the beginning, i.e., from about the 25 mm. stage. There can be no doubt that the blood community dates from about the time of the sexually indifferent stage, but it certainly varies more or less

both with reference to the time of origin and the extent of the vascular anastomosis.

We have hitherto noted only that the free-martin is sterile whenever blood-community with its male twin exists during foetal life, i.e., in about seven-eighths of all cases, and that otherwise it is normal. What is the nature of this sterility? Observers from the time of John Hunter³ (1786), who have studied the anatomy of free-martins, have all noted the intersexual character of its reproductive system—the internal organs of reproduction are largely male in type, the external female—and the later students of the free-martin have generally regarded it as a modified male on account of the character of the internal organs and for other reasons (Spiegelberg,⁴ D. Berry Hart,⁵ Bateson,⁶ Cole⁷). The gonad is sometimes absent or exceedingly rudimentary, but when well developed it never exhibits any trace of ovarian cortex, and its structure is testis-like, though germ-cells are not formed. The sexual ducts show reduction or absence of the female parts and a graded series of development of the vas deferens. The external parts are usually typically female. We have on the one hand, therefore, failure of development of the internal female reproductive organs, and, on the other hand, the male parts, which usually degenerate, undergo development. Anatomically the free-martin is definitely intersexual, to a variable extent as will be seen.

The writer has studied the anatomy of 22 foetal free-martins ranging in size from 7.5 to 28 cm. The striking results of this examination were (1) The gonads remain rudimentary in size during this period; (2) the female ducts fail to develop; they frequently remain in part as undeveloped rudiments, but in other cases disappear as completely as in the male. (3) The male ducts develop in varying degrees, always more than in the normal female, though rarely to the same extent as in the male. (4) Gubernacula invariably developed in the free-martins and formed peritoneal evaginations exactly as in males. (5) In one of the oldest foetuses the gonads had entered the saccus vaginalis as in the male. (6) In my material the external organs were always typically female.

Miss Chapin⁸ made a histological investigation of the gonads of the foetal free-martin under my direction and determined that the ovarian cortex never forms, but that a quite typical albuginea develops over the surface as in the testis of the male. The medullary cords, homologue of the seminiferous tubules of the male, also underwent unusually great development.

A seven weeks old free-martin examined by the writer possessed testes

and vasa deferentia, but no trace of uterus or vagina. The testes had descended and lay beneath the skin in the region of the groin. No scrotum was formed and the external parts were typically female. A free-martin described by Numan in 1844 was even farther transformed in the male direction, and the external parts were also modified.

The various cases can be arranged in a series of increasing male-likeness, but the transformation of the female zygote owing to action of the male sex-hormones does not in the case of the free-martin, in the material at our command, proceed all the way to the normal male condition. It is perhaps worth noting that, if it ever did, we would be unable to detect it, except on a basis of much larger statistics than we possess. But the rarity of the more extreme detectable cases makes it seem very improbable that other cases jump all the way across the gap to the normal male.

It follows from the data that the female zygote must contain factors for both sexes; the primary determination of the female sex must therefore be due to dominance of the female factors over the male. If we think of this as a simple quantitative relation, as Goldschmidt⁹ (1916) has done, we can explain the intersexual condition of the free-martin as due to an acceleration or intensification of the male factors of the female zygote by the male hormones. The degree of the effect which is quite variable, as we have seen, would of course be subject to all quantitative variations of the hormone. Thus the case of the free-martin could come under the same general point of view as that of the intersexes of *Lymantria* according to Goldschmidt with the one exception that the quantitative differences between the male and female factors of the female zygote necessary for the differentiation of female characters, are reduced in the free-martin by internal secretions instead of by variations of potency of the male factors in different varieties as in the intersexual hybrids of *Lymantria*.

The case of the free-martin shows that a gonad with a primary female determination may form a structure which is morphologically a testis, (cf. Chapin 1917) through suppression of the cortex and over development of the medullary cords and urinogenital union under the influence of male sex-hormones. Lesser degrees of transformation are of course possible, so that it is certain that the gonad of a mammalian female zygote is capable of most, at least, of the series of transformations that may exist between an ovary and a testis. Whether the transformation in the male direction may proceed under such conditions to the production of true spermatocytes and spermatozoa is at least doubtful. Such elements have not hitherto been described for free-martins, if we

except D. Berry Hart's statement concerning the gonads of Hunter free-martins, that "in only one are spermatozoa present." More than six words seem necessary to establish so important an exception.

Regarding other parts of the internal reproductive system we have seen that the free-martins exhibit a graded series of inhibition of the female ducts and of development of the male ducts which may obviously correspond to variable time of onset, intensity, and perhaps duration of action, on the male sex-hormones. The series extends nearly to the normal male limit in exceptional cases. There is indicated a rough parallelism at least between the grade of transformation of the gonad and that of the remainder of the internal reproductive system. The external organs of reproduction are the least liable to modification, but they do not escape in all cases, and may even exhibit considerable transformation in the male direction, if we can accept Numan's case.

The fundamental determining factor in these events is undoubtedly the male sex-hormones as has been argued previously, but the entire causal nexus is by no means clear. We do not know what the results of embryonic castration of the female might be in itself, and hence we are unable to assert definitely in just what positive ways the male hormones act on the female zygote, because the earliest determinable result of such action is the suppression of the ovarian cortex, which must be regarded as practically equivalent to castration. This action at least is due to the male hormones; how much of the subsequent events is due to mere absence of ovarian tissue, and how much to positive action of male sex-hormones is more or less problematical. It is well known that spayed females of certain birds and mammals tend to develop male characters; heifers with cystic degeneration of the ovary also develop certain male characteristics (Pearl and Surface, 1915),¹⁰ so that we must admit in principle the possibility that much of the male development in the free-martin is due to the lack of inhibitions normally furnished by the ovary.

It is also probable that the various parts of the reproductive system have other means of correlation, and act and react on one another in various ways. Certain indications of this are seen in lateral variations, as for instance in one of my cases where a large gonad on one side is associated with a large Wolffian duct, and seminal vesicle, and a much smaller one on the other side with a correspondingly smaller duct and vesicle.

When, therefore, we attribute the free-martin condition to the male hormones we only mean to assert that they are the primary cause, and not that they are the decisive factors in each member of the series of events.

The possibility exists, however, that definitely planned experiments may enable us to regulate time and dosage of hormones better than is done in this experiment of nature; the results of such experiments cannot of course be foreseen. Nor can it be predicted in advance what the results of the inverse experiment might prove to be, i.e., treatment of the male zygote from the beginning of six-differentiation with female hormones. Such experiments will be necessary for the full solution of the stated problem. We can, however, state, confidently ¹¹on the basis of the present results that sex-determination in mammals is not irreversible predestination, and that with known methods and principles of physiology we can investigate the possible range of reversibility.¹¹

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¹¹ A full account of the work is in press in *Journal of Experimental Zoology*, 23, No. 2.

THE CRYSTAL STRUCTURE OF MAGNESIUM

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Magnesium is assigned by crystallographers to the holohedral class of the hexagonal system, with axial ratio 1.624. The structure given below agrees with this symmetry. The arrangement of atoms is that of hexagonal close packing, the arrangement which equal hard spheres assume when closely packed, except that the structure is shortened by about one-half of one percent in the direction of the hexagonal axis. This is the fourth type of arrangement of atoms in elementary substances thus far observed, viz.: the diamond type, characteristic of diamond, silicon, bismuth and antimony, where each atom is surrounded by four equidistant nearest neighbors; the centered cubic lattice, characteristic of iron, and probably also of nickel and the alkali metals, where each atom is surrounded by eight equidistant nearest neighbors; the face-centered cubic lattice, or closest-packed cubic arrangement,