#### SUMMARY

The absorption of phenolsulphonephthalein and of strychnine by deeply anæsthetized dogs has been studied under three experimental conditions: ( $\mathbf{I}$ ) normal dogs in which the injections were made into the anterior abdominal wall; (2) dogs with a traumatized extremity in which the injection was made into the anterior abdominal wall; and (3) dogs with a traumatized extremity in which the injection was made into the injured muscle. There was not a great deal of difference in the absorption of the solutions that were injected into the anterior abdominal wall of normal dogs and of dogs with a traumatized extremity except for a slight delay in the latter group. On the other hand, the absorption of the phenolsulphonephthalein and of the strychnine that was injected into the traumatized area itself was greatly retarded.

#### REFERENCE

 UNDERHILL, F. P., KAPSINOW, R. and FISK, M. E. Studies in the mechanism of water exchange in the animal organism. II. Changes in capillary permeability induced by a superficial burn. Am. J. Physiol., 1930, xcv, 315.

# THE CONCEPTION PERIOD IN NORMAL ADULT WOMEN

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THE epoch making work of Aschheim and Zondek has definitely shown that hormonal secretions play a prominent rôle in pregnancy. These hormones are derived from the ovary and the pituitary gland, and bear a direct relationship to ovulation, fecundation, and menstruation. Recent investigation indicates that there are seven distinct hormonal effects from the pituitary gland and two from the ovary. The effects from the pituitary gland are:

1. The anterior lobe.

a. An effect causing ripening of the graafian follicle with the production of folliculin and egg cell (1).

b. An effect which causes growth of the corpus luteum after ovulation (2).

c. An effect which in conjunction with the corpus luteum causes hypertrophy of the mammary glands (3, 5, 11, 13, 18, 24).

2. The posterior lobe.

a. An effect causing uterus stimulation (12, 13, 18).

b. An effect causing expansion of melanophores (35).

c. An effect causing antidiuresis or water retention (32).

d. An effect causing increased blood pressure (9). The effects from the ovary are:

a. Folliculin which causes hyperæmia of the uterus and tubes in preparation for the egg cell (7).

b. Corpus luteum which produces further growth of uterus and hypertrophy of mammary glands (6, 8).

Ripening of the graafian follicles with the production of folliculin and ovum is brought about by an anterior pituitary hormone. Folliculin causes hyperæmia of the uterus and tubes. When the follicle bursts the corpus luteum spurium is formed and this body in turn causes further growth of the uterus and hypertrophy of the mammary glands. If the egg cell is not fertilized the corpus luteum withers and dies and menstruation takes place. If the fertilized egg is implanted the corpus luteum spurium develops into the corpus luteum gravitatis, which maintains pregnancy and when it begins to wither the posterior lobe hormones re-assert causing rhythmic contractions of the uterus and labor. These reactions are shown by Figures 1 and 2 (13, 14, 15, 30).

Different scientists have shown that the life of the human egg cell is 1 day (18, 24, 34) and that of the sperm cell is 2 to 3 days (18, 24, 36). Also that in a normal regularly menstruating woman with a cycle of 28 to 30 days, ovulation occurs between the fourteenth and sixteenth days (18, 24), and that 10 days are required for the passage of the egg cell through the fallopian tube (18).

Henle has definitely shown that spermatozoa are able to travel a distance of 1 centimeter in 3 minutes (37). That human spermatozoa may reach the fallopian tube in a very short time after being deposited in the female genitalia, there can be no doubt, as shown by the following case, which we observed:

Mrs. B. M., age 25, i-para; diagnosis, dyspareunia, prolapsed uterus. In this case the last coitus was 65 days previous. Examination of vaginal and cervical secretions did not show the presence of spermatozoa. Copulation was had at 8 a.m.; 2 hours later at laparotomy examination of fallopian tubes revealed the presence of numerous spermatozoa.

If the duration of life of the egg and sperm cell is known, as well as the rate of sperm cell motion, the next question which confronts us is: When is the egg cell liberated?

Knaus, by means of a manometer noted that there was increased uterine pressure following the injection of posterior lobe pituitrin due to uterine contractions and that when corpus luteum was present the uterus did not respond by contractions (36). In this manner he was able to determine the time of ovulation. This he found to be in the 28 day cycle of menstruation on the fourteenth to the sixteenth days before the next menstruation (18, 24). From these facts it is evident that in a 28 day cycle the corpus luteum spurium functions for about 14 days, when implantation of a fertilized egg occurs the corpus luteum spurium is changed to corpus luteum gravitatis, or if fertilization and implantation do not occur it withers and dies and menstruation is brought about. On this view pregnancy is not a hit and miss affair, but is regulated by the meeting of the egg and sperm cell before one or the other has withered and died (18, 36).

Ogino, of Japan, studied this question by examining the coitus in relation to ovulation and noting its ability to fecundate. He arrived at the following conclusions:

1. For women regularly menstruating every 28 days the period of time the human sperm cell was able to impregnate the ovum was the 8 day period lying between the twelfth and the nineteenth day before the next menstruation or in other words, between the tenth and the seventeenth day after menstruation had started, other days being physiologically sterile.

2. If the cycle is longer or shorter than 28 days the period of conception is moved so many days ahead or behind.

3. For those women who do not have a greater variation in the menstrual cycle than 10 days a formula for the period of conception could be stated as follows:

Beginning of conception is 10 plus cycle of minimum days—28.

End of conception period is 17 plus cycle of maximum days—28.

4. In computing the period of conception of any woman 12 menstrual cycles should be known, noting the maximum and minimum length of time of each. If the menstrual cycle should vary more than 10 days, then the formula is still theoretically correct, but of not much practical value (31).

Knaus, of Austria, working independently, arrived at similar conclusions, but elaborated them more fully as follows:

1. For women with a regular menstrual cycle of 26 days, conception possibilities are limited to the time from the ninth to the thirteenth days, inclusive.

2. For women with a regular menstrual cycle of 27 days, conception possibilities are limited to the time from the tenth to the four-teenth days, inclusive.

3. For women with a regular menstrual cycle of 28 days, conception possibilities are limited to the time from the eleventh to the fifteenth days, inclusive.

4. For women with a regular menstrual cycle of 30 days, conception possibilities are limited to the time from the thirteenth to the seventeenth days, inclusive.

5. For women with a regular menstrual cycle of 34 days, conception possibilities are limited to the time from the seventeenth to the twenty-first days, inclusive.

6. For women with a regular menstrual cycle of 28 to 30 days, conception possibilities are limited to the time from the eleventh to the seventeenth days, inclusive, with the maximum of same at the fourteenth to the sixteenth days.



7. For women with a regular menstrual cycle of 26 to 30 days, conception possibilities are limited to the time from the ninth to the seventeenth days, inclusive, of the menstrual cycle.

For menstrual cycles of other variations, the conception period may be computed in the same manner as stated above. These calculations being true only for normal, healthy women with regular variations in the cycle as stated above (16, 19 to 29).

Ogino established the time of ovulation in an empirical manner during the course of laparotomies on women. He has a 5 day ovulation period in a constant menstrual cycle.

Knaus determined the time of ovulation by measuring the uterine contractions by means of a manometer. He has a 2 day ovulation period in a constant menstrual cycle. It seems to us that Knaus' method is more definite and precise; therefore, we follow the doctrine of Knaus.

Based upon this initial research we decided to study this question by examining the coitus at various times to determine its ability to fecundate. Our material was chosen from 87 apparently normal couples including 8 nationalities and 725 copulations. Where pregnancy was thought to have occurred it was checked by the modified Aschheim-Zondek test on rabbits.

Our observations are as follows:

CASE I. E. B., aged 36 years. Menstruation commenced at the age of 13, was of regular cycle, 28 to 30 days; duration 4 to 5 days. Patient was married at the age of 16 on the thirteenth day after previous menstruation; result pregnancy. For 5 years after birth of child, not desiring more children, various contraceptive methods as suppositories, douche powders, and pessaries were used. During the fifth year, while wearing a pessary, she became pregnant and aborted at the second month. At this time she was informed by a friend to abstain from coitus between



the tenth and twentieth day of her menstrual cycle. This she practiced successfully for 13 years without the use of any contraceptive measures whatever, except accurately noting the dates on the calendar as well as duration of each cycle as the months went by. At the beginning of her fourteenth year of this procedure, she was informed that she must not figure from the first day of menstruation, but from the last. She accordingly changed her system. The next and only coitus occurred on the fourteenth day from the beginning of the last menstrual period. Result: amenorrhœa, of 2 months. On the third day after the second missed cycle, the Aschheim-Zondek test revealed pregnancy. Ten days later, by self-induced means, she aborted a 2 months fetus. In this case the cohabitation date lies within the period of conception for her.

CASE 2. F. E., aged 28 years. Menstruation began at the age of 14 years, was occurring every 26 to 28 days, duration 4 days. She was married at the age of 21, the date being about halfway between two menstruations. Result, pregnancy. Following birth of child she developed a painful right ovary. Menstruation became profuse, 5 to 6 days in duration, varying from 26 to 34 days. She was advised by her physician that another pregnancy might result in an operation being necessary so she used various contraceptive measures for 6 years. At this time, feeling that her procedure was correct, she adopted a son. Later she was advised that contraceptives were injurious and unnecessary, if she would abstain from intercourse between the eleventh to the seventeenth days of menstrual cycle. The previous 4 periods were as follows: 26, 30, 28, and 32 days in duration. The only cohabitation during the month was on the nineteenth day after the beginning of the last menstruation. Result: amenorrhœa. The Aschheim-Zondek test proved the existence of pregnancy. This day lies within the dates of conception possibilities for her.

CASE 3. A. A., aged 25 years. Menstrual cycle varied from 29 to 33 days, duration 4 days. Last 4 menstruations were as follows: January 27, 1932, February 29, 1932, March 29, 1932, April 30, 1932. Only cohabitation on May 16, 1932, then amenorrhcea. The Aschheim-Zondek test on June 12, 1932, proved the existence of pregnancy. The cohabita-

M. Days	I	3	5		7	9		II		13		15		17	19		21		23		25		27	29	31	
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6-1										1111	<				 	$\boxtimes$				$\boxtimes$						
6-29						÷				1111		>	1111		 		$\boxtimes$			$\boxtimes$				 		
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8-23				$\boxtimes$					1111	>					 										·	
9-19			$\boxtimes$			Connector Connec		<							 										 	
10-14			$\boxtimes$		$\boxtimes$					>					 				_							
II-IO									<						 	$\boxtimes$										
12-6												>			 	$\boxtimes$		$\boxtimes$			$\boxtimes$					
I-4										Contrast of Contra	/											_				
2-I										/																
2-28				$\boxtimes$		Constant Con			/																	

TABLE I.—CASE I, A. F.

■ Menstruation. IIII Period of conception. /< Maximum period of conception. ⊠ Cohabitation.

tion date in this case falls within the conception period for this woman.

CASE 4. A. R., aged 26 years. Menstrual cycle was 27 to 33 days, duration, 4 days. The last 5 menstruations are as follows: January 2, 1932, February 3, 1932, March 1, 1932, April 3, 1932, and May 4, 1932. Only cohabitation was on May 18, 1932. The next menstruation due to occur during the first week in June failed to materialize by June 16, on which date the Aschheim-Zondek test proved the existence of pregnancy. The cohabitation here is within the period of conception possibilities for this cycle.

CASE 5. A. N., aged 42 years, vi-para; 3 abortions. Menstrual cycle was 30 to 31 days. Last two menstruations were as follows: January 10, 1932, and February 10, 1932. The only coitus was on February 25, 1932. The following day her husband left home to seek work in a distant state and was gone for 4 months. This woman did not menstruate during the next 3 months. Being in ill health and believing that she was entering upon the climacteric she consulted a physician. The Aschheim-Zondek test proved pregnancy was the cause of amenorrhœa.

CASE 6. W. E., aged 22 years, regular 26 to 28 day cycle menstruation. Confined on August 14, 1931. First menstruation postpartum was December 25, 1931. Next four as follows: January 22, 1932, February 17, 1932, March 16, 1932, and April 14, 1932. One coitus occurred on April 30, 1932. On May 14, 1932, Aschheim-Zondek test was positive for pregnancy.

CASE 7. E. A., aged 21 years. Regular menstrual cycle 26 to 30 days. Last menstruation was on April 6, 1932. Cohabitation was on April 22, 1932. On June 11, 1932, Aschheim-Zondek test was positive for pregnancy.

CASE 8. A. B., aged 40 years, viii-para; menstruation every 26 to 27 days; duration 2 to 3 days. Last menstruation on August 10, 1931; cohabitation on August 21, 1931. On September 18, 1931, Aschheim-Zondek test was positive for pregnancy. In her case the conception date lies on the second day of the period of conception for her.

CASE 9. H. L., aged 35 years, no children; regular menstrual cycle of 30 days, duration 5 days. Last period was February 29, 1932, cohabitation March 13, 1932. Result, pregnancy.

CASE 10. H. C., aged 21 years, on August 27, 1925 was confined. This woman believed that as long as she was nursing a child and did not menstruate that she could not become pregnant. Feeling secure in this belief no contraceptive measures were used. Eight months after her confinement, no menstruation having appeared as yet on October 12, 1926, she consulted a physician and pregnancy was diagnosed. She was again confined. In this case no menstruation occurred between the birth of the first child and the birth of the second child.

# COHABITATIONS REGULATED BY TIME WHICH DID NOT RESULT IN PREGNANCY

CASE I. A. F., aged 27 years, i-para. This woman used the premenstrual and postmenstrual period of sterility for cohabitation. The details are shown in Table I.

In this case there were 48 cohabitations which did not result in pregnancy.

Eighty-seven cases consisting of 12 different menstrual cycles and 8 nationalities were studied for the period of physiological sterility. The details of this study are shown in Tables II and III.

Cohabitations before and after menstruations total 725 and not a single cohabitation of these two groups resulted in pregnancy.

# SURGERY, GYNECOLOGY AND OBSTETRICS

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Cases	Cycle	Months		Days before next menses														
	Cycic	MOITIN	I3	I2	II	10	9	8	7	6	5	4	3	2	I.	LOLAI		
. 3	26-27	4							2	3	2	I	6	6	4	24		
5	26-28	6						I	2	7		16		9	14	49		
9	· 26–30	3							6	9	I2			14	8	49		
3	26-34	4								2	4	I	5	3	7	22		
6	27-33	5								3	9	4	6	20	5	47		
23	28-30	2			4			6			9		8		12	39		
. I .	28-34	5											2	I		3		
2	28-36	2									8	4	r	5	6	24		
7	29-33	3								8		7	5		9	29		
r	29-30	5			I	2		I	3	2		I	2	v	I	I3		
I2	30	2			2		4		2			7		3	4	22		
I5	30-31	2			7		IO		4	7	I		9		I2	50		
87					14	2	14	8	19	41	45	41	44	бі	82	371		

## TABLE III

Cases	Cvcle	Months	ths Days after menstruation														
			I	2	3	4	5	6	7	8	9	10	II	I2	Total		
3	26-27	4 ·	4	I	3	4									12		
5	26–28	6	8	7	18	14									47		
9	26–30	3	14	8	<b>I</b> 4	12									48		
3	26-34	4	II	2	6	5									24		
б .	27-33	5	IO	8	I2	IO									40		
23	28–30	2	38	4	12	IO	7								71		
I	28-34	5	2		3		4	I							IO		
2	28–36	2	I		2	2									5		
I	29-30	5	3		I		I	I							6		
7	29-33	3	3	12	I	9	6								31		
I2	30	. 2	. 10	3		12	4				5.				29		
I5	30-31	2	I2	3		12	4								31		
87			116	48	72	90	26	2							354		

### SUMMARY

The anterior lobe secretion motivates the ovary. The corpus luteum inhibits the posterior lobe secretion and maintains pregnancy. When the corpus luteum withers the oxytoxic principle of the posterior lobe secretion asserts itself and labor is brought about. Fecundation is only possible when the sperm cell is properly timed to meet the egg cell.

### CONCLUSIONS

1. Hormones play a major rôle in pregnancy. 2. The sperm and egg cells detached from their respective breeding places have a very limited time to live. For the egg cell it is not longer than 1 day. For the sperm cell it is 2 to 3 days.

3. Every normal regularly menstruating woman has a definite ovulation period.

4. Every normal regularly menstruating woman has a definite period of physiological sterility and a definite period of fertility in each cycle.

5. Cohabitation must be properly timed with ovulation if pregnancy is to result.

6. Pregnancy may be brought about or avoided at will by the observation of these two periods of time.

### BIBLIOGRAPHY

- I. ASCHHEIM. Hormon und Schwangerschaft. Med. Klin., 1926, No. 22.
- 2. Aschheimand Zondek. Die Schwangerschaftsdiagnose aus dem Harn durch Nachweis des Hypophysen-vorderlappenhormons. Klin. Wchnschr., 1928, No. 7.
- ASDELL. The growth and function of the corpus luteum. Phys. Rev., 1928, No. 8.
- ATHIAS. Sur le déterminisme de l'hyperplasie de la grande mammaire et de la sécrétion lactée. Compt. rend. Soc. de Biol., 1916, lxxix. 5. Bouin and Ancel. Rôle du corps jaune dans le
- déterminisme expérimental de la sécrétion mam-
- maire. Compt. rend. Soc. de Biol., 1914, lxxiv. FRAENKEL. Die Funktion des Corpus Luteum. Arch.
- f. Gynaek., 1903, No. 68. GERHARDT. Sex Hormones and their therapeutic ap-7.
- plication. J. Am. M. Ass., xcviii, 2033. GLEV. Sur l'inhibition de l'ovulation par le corps jaune. Compt. rend. Soc. de Biol., 1928, xcviii. 8.
- GRAVES. Gynæcology. 2d ed., p. 78.
   HAMMOND. The effect of pituitary extract on the secretion of milk. Quart. J. Exper. Physiol., 1913, vi.
- 11. HARTMANN, DUPRE, and Allen. The effect of follicular and placental hormones upon the mammary glands and genital tract of the opossum. Endo-
- crinology, 1926, No. 10.
  12. KNAUS. The action of pituitary extract upon the pregnant uterus of the rabbit. J. Physiol., 1926, lxi.
  13. Idem. Experimentelle Untersuchungen zur Physiol-
- ogie und Pharmakologie der Uterus-muskulatur in der Schwangerschaft. Arch. f. exper. Path. u. Pharmakol., 1927, cxxiv.

- 14. Idem. Das Verhalten der Uterusmuskulatur in Schwangerschaft und Geburt. Wien. klin. Wchnschr., 1028, xli.
- 15. Idem. Ueber den Mechanismus der Geburtsausloes-Ztschr. f. Geburtsh. u. Gynaek., 1928, No. 94. ung.
- 16. Idem. Arch. f. Gynaek., 1929, cxxxviii. 17. Idem. Muenchen. med. Wchnschr., 1929, No. 28.
- 18. Idem. Ueber den Zeitpunkt der Empfaengnisfachigkeit des Weibes. Allg. deutsche Hebam.-Ztg., 1930, No. 15.
- 10.
- Idem. Arch. f. Gynaek., 1930, cxl, cxli. Idem. Klin. Wchnschr., 1930, No. 21. 20.
- Idem. Zentralbl. f. Gynaek., 1930, No. 8. Idem. Arch. f. Gynaek., 1931, cxlvi. Idem. Mitt. d. oest. Gesundheitsamtes, 1931, No. 10. 21.
- 22.
- 23.
- Idem. Ueber den Zeitpunkt der Konzeptionsfaehigkeit 24. des Weibes. Muenchen. med. Wchnschr., 1931, No. 9. Idem. Progrès méd., 1931, No. 30. Idem. Zentralbl. f. Gynaek., 1931, No. 26.
- 25.
- 26.
- Idem. Aerztl. Kor., 1932, No. 10. Idem. Klin. Wchnschr., 1932, No. 1. 27.
- 28
- Idem. Zentralbl. f. Gynaek., 1932, No. 12. 20.
- KUESTER. Pituitary and eclampsia. Arch. f. Gynaek., 30.
- 30. KUESIER. Huntur, and Compared and Series a
- Gynaek., 1930, No. 8; 1932, No. 12.
   ORDINSKY. Antiduretic activity of pituitary extract. J. Am. M. Ass., xcviii, No. 23, 2034.
   PAPANICOLAOU. A specific inhibitory hormone of the corpus luteum. J. Am. M. Ass., 21, 1923.
   PINCUS Proc. Roc. R. Loc. 2013
- PINCUS. Proc. Roy. Soc. B., 1930, cvii.
- SCHUEBEL. On the separation of the substances of the 35. posterior lobe of the pituitary. Klin. Wchnschr., 1931, No. 10, 1835. WERNER. Wie sind die zeitlichen Zusammenhaenge
- 36. zwischen Menstruation, Ovulation und Befruch-tung?" Wien. klin. Wchnschr., 1931, No. 40.
- 37. WILLIAMS. Obstetrics. 6th ed., p. 100.