

pyridine was given preliminary to the morphine treatment. The symptoms then were more pronounced and lasted for a longer time.

The increased toxicity of morphine when preceded by sulfapyridine medication may be seen from Table II (Morphine Exp.). Fifteen mice (group D) which received 300 mg/kg of morphine sulfate after sulfapyridine, without having been tested for their reaction to morphine alone, had convulsions and 13 out of 15 died. The same amount given to 21 mice receiving no sulfapyridine resulted in only 3 fatalities. After a rest period 7 of these mice (group F) received sulfapyridine prior to the morphine injection; all had convulsions and 5 of them died.

Summary. The results reported are similar to those demonstrated for papaverine; the effect of both codeine and morphine being enhanced by sulfapyridine. The increased activity of the drugs after sulfapyridine becomes evident not only in the prolongation of their action but also in the intensity of their effects and in the increase of their toxicity.

Appreciation is expressed to Merck and Co. for supplying sulfapyridine and to Miss Bessie Zirin for her technical assistance.

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Attempt to Recover Sodium Pregnanediol Glucuronidate from Chimpanzee Pregnancy Urine.*

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Using the technic developed by Browne and Venning^{1, 2, 3, 4} for

*The assistance of the Committee for Research in Problems of Sex, National Research Council, is acknowledged.

The writer wishes to thank Doctor Edgar Allen of Yale University for his assistance in promoting the investigation. Considerable time was saved as a result of practical suggestions and aid from Doctors P. E. Smith, E. T. Engle, and their laboratory associates and technicians. Thanks are also due to Doctors S. R. Norris and A. F. Caraway of Jacksonville, Florida, for their generous coöperation in obtaining clinical material for the experiment.

¹ Venning, E. M. and Browne, J. S. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 792.

² Venning, E. M., Henry, J. S., and Browne, J. S. L., *Can. Med. Assn. J.*, 1937, **36**, 83, 297.

³ Venning, E. H., *J. Biol. Chem.*, 1937, **119**, 473.

⁴ Venning, E. H., *J. Biol. Chem.*, 1938, **126**, 595.

the recovery of sodium pregnandiol glucuronidate from pregnancy urine, a number of investigators have shown that gradually increasing quantities of this material may be recovered throughout human pregnancy. Appreciable amounts have also been obtained during the luteal phase of the menstrual cycle.⁶⁻⁸ Attempts to recover pregnandiol from pregnant rabbits, cats, and monkeys have shown negative results.⁹ Marker and Hartman¹⁰ found no trace of any of the pregnandiols in pregnancy urine of rhesus monkeys.

It has been found that some physiological and reproductive processes of the chimpanzee bear a closer resemblance to those of man than of monkey. Because of this fact it seemed desirable to determine whether pregnandiol could be recovered from the urine of chimpanzees. It was also hoped that in the event of positive findings an additional criterion of ovarian activity would be available. A series of tests representing various stages of pregnancy was made with two subjects. As a check on the application of the procedure, clinical specimens were extracted from time to time during the series. The procedure was exactly the same in all cases except for the method of collecting the urine specimens. With the animal subjects this was accomplished with the urine collection cage used regularly in obtaining specimens for pregnancy tests.¹¹ Collections

TABLE I.
Amounts of Pregnanndiol Recovered from Urine of Chimpanzee and Human Subjects.

Subject	Date (1939)	Total quantity Pregnanndiol		per liter (mg)	Melting point	Remarks
		cc	hr			
A	4/24	4000	24	19	255	261st day pregnancy
Soda	4/27	4500	"	0		160th " "
A	5/1	3750	"	23	257	268th " "
Soda	5/6	650	7	0		169th " "
Alpha	5/11	800	20	0		77th " "
"	5/13	900	20	0		79th " "
B	6/8	1900	8	0		25th " cycle
C	8/9	3200	24	21	268	Early labor
Alpha	8/10	1800	24	0		168th day pregnancy
D	8/16	2000	24	40	271	Early labor
E	8/16	1100	24	32	263	7½ mo. pregnancy
Alpha	8/18	870	24	0		176th day "

⁵ Venning, E. H., and Browne, J. S. L., *Endocrinology*, 1937, **21**, 711.

⁶ Stover, R. F., and Pratt, J. P., *Endocrinology*, 1939, **24**, 29.

⁷ Wilson, R. B., Randall, L. M., and Osterberg, A. E., *Am. J. Obstet. and Gynecol.*, 1939, **37**, 59.

⁸ Hamblen, E. C., Ashley, C., and Baptist, M., *Endocrinology*, 1939, **24**, 1.

⁹ Westphal, U., and Buxton, C. L., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 749.

¹⁰ Marker, R. E., and Hartman, C. G., *J. Biol. Chem.*, 1940, **133**, 529.

¹¹ Elder, J. H., and Bruhn, J. M., *Yale J. Biol. and Med.*, 1939, **12**, 155.

were made frequently from this cage and placed in a refrigerator until a quantity sufficient for extraction was secured. Since all specimens were used promptly after collection, only refrigeration was used for preservation.

Table I shows the results of extractions of chimpanzee urine and clinical specimens. All letters refer to the clinical cases. The practice of occasional alternation of tests with chimpanzee and clinical samples was considered necessary in order to eliminate the possibility that negative findings might be due to chance variations or inadequacies of technic. This control was indicated especially by the fact that the method was being used for the first time in these laboratories.

Pregnandiol was recovered from all of the human specimens except that from Subject B, a menstrual cycle specimen. It was never found in chimpanzee urine. The amount of final residue from the chimpanzee urines was negligible in every instance.

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Neutralization (*in vitro*) of Bacteriostatic Activity of Sulfonamides by P-Aminobenzoic Acid.

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Many theories have been advanced to explain the bacteriostatic activity of sulfanilamide and related compounds, but few have convincing evidence in their support. Among the more recent theories advanced is that of Fildes,¹ who proposes that inhibitors of bacterial growth are effective as a result of interference with an "essential metabolite", a substance which has an essential part in the chain of synthesis necessary for bacterial growth. The interference in the case of sulfanilamide as has been demonstrated by Woods,² consists in the competition for an enzyme associated with the essential metabolite and the inhibition occurs in this way because of a chemical similarity to the essential metabolite.

Woods and Fildes^{2, 3} prepared a number of compounds in which

¹ Fildes, P., *Lancet*, 1940, **1**, 955.

² Woods, D. D., *Brit. J. Exp. Path.*, 1940, **21**, 74.

³ Woods, D. D., and Fildes, P., *Chem. Ind.*, 1940, **59**, 133.