TABLE I. Solubility of N^2O in Human Fetal and Uterine Tissues at 37° and at N^2O Tension of 760 mm Hg.

Tissue	α N^2O (per g tissue)	$\frac{\alpha \text{ Tissue}}{\alpha \text{ Blood}}$
Spleen	.589	1.430
Skel. muscle	.473	1.148
Skin	.458	1.112
Liver	.377	.915
Brain	.439	1.065
Heart	.496	1.204
Lung	.432	1.048
Scalp	.327	.798
Placenta	.331	.803
Umbilical cord	.333	.808
Uterine muscle	.472	1.145
Mean	.430	1.043

with N^2O, and its Bunsen solubility coefficient (α) was calculated according to the technic of Kety *et al.*(1). From 5 to 8 determinations of Bunsen coefficient were made for each type of tissue. Variations from one determination to another did not exceed 1% ($\pm$.003).

Results. Table I lists Bunsen solubility coefficients (α) of all fetal tissues studied and of uterine tissue. Placenta, umbilical cord and scalp had the lowest solubility coefficient for N^2O while the spleen had the highest. Average value for solubility coefficients of all the fetal tissues and of uterine muscle was 0.430. There was no significant difference between values obtained from the immature, premature and full term fetuses.

The tissue-blood partition coefficient for N^2O (S factor) varied from 0.798 for the scalp to 1.430 for the spleen, average 1.043.

Discussion. The present data indicate that the N^2O solubility coefficient varies considerably from one fetal tissue to another, but is the same whether the fetus is immature or at full term. It has been stated that N^2O solubility depends a great deal on the fat content of a given tissue(1). Whether the difference observed in the present studies was due to a difference in fat content of the various fetal tissues cannot be stated. At any rate, in considering the pregnant uterus as a whole, and for the purpose of applying the N^2O technic for uterine blood flow measurement, the mean for all the tissues involved is the most important. This mean was 0.430 which gave a partition coefficient for pregnant uterus and blood of 1.043. These figures are very close to those obtained from homogenates of a whole fetus and myometrium, and also close to the value of unity given to factor (S) in study of uterine blood flow. Therefore, the error due to this factor in the previous data (2) is insignificant.

Summary and conclusion. 1) N^2O solubility in fetal tissues was studied in one immature, one premature and one full term fetus. 2) Bunsen coefficient varied from one tissue to another. The mean for all tissues including placenta, cord and myometrium was 0.430. These figures give a N^2O partition coefficient between whole pregnant uterus and blood of 1.043.

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Effect of Sudden Time Displacement by Air Travel on Synchronization of Adrenal Function. (24674)

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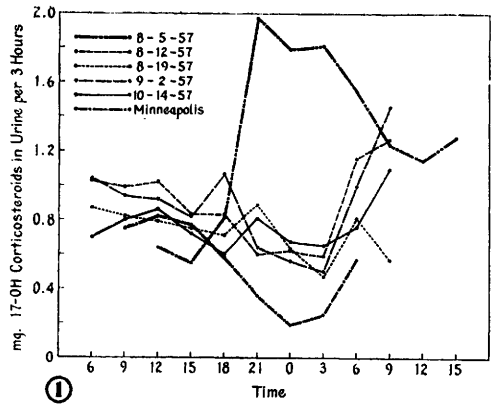
Very few data are available on the effect of sudden change in geographic position on periodicity of physiological functions. Therefore, a study was undertaken on the effect of an airplane trip from Minneapolis, Minn. to Tokyo, Japan, and to Seoul, Korea, with a prolonged stay in Seoul.

Materials and methods. Departure from



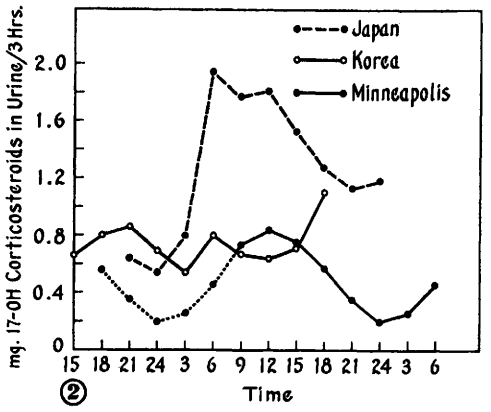


FIG. 1. Times are recorded according to local time. Japan time is displaced 9 hr so peak excretion (21 to 24 hr Japan time) corresponds to 6 to 9 hr Central Standard Time. Korean time is displaced 9½ hr, but excretion is now synchronized with Korean time. Time line indicates time of starting each collection, *e.g.* 6 indicates the period 6:00-9:00, etc.

FIG. 2. Times are recorded according to Central Standard Time. Minneapolis curve has been extended by dotted line to show relationship to Korean and Japanese curves. Korean curve is the one dated Oct. 14 in Fig. 1.

Minneapolis occurred Aug. 1, 1957, from Seattle, Wash. Aug. 3, 1957. Arrival in Tokyo, Japan was Aug. 5, 1957 (Aug. 4 Central Standard Time). Urine collections every 3 hours were started immediately and continued 30 hours. Dates of subsequent collections in Seoul, Korea began Aug. 12, Aug. 19, Sept. 2, and Oct. 14. Urine volumes were measured for each 3 hour period day and night and a portion placed in a test tube with a few drops of toluene as preservative. Three meals composed of usual American foods were eaten at usual meal times. Fluid was not restricted. In a previous study in Minneapolis, however, equal feedings were eaten every 3 hours for 24 hours(1). Specimens were sent to Minneapolis by airmail and analyzed for sodium and potassium by flame photometry and for total 17-hydroxycorticosteroids by the method of Silber and Porter using glucuronidase hydrolysis(2).

Results. Results of 17-hydroxycorticosteroid excretion are recorded in Fig. 1. Potassium and sodium data are recorded in Tables I and II. It is clear that steroid excretion was greatly altered the first 24 hours after leaving United States. The time displacement in Japan is 9 hours and in Korea 9½ hours. Peak excretion occurred at night instead of the day and corresponds quite well with the expected peak for Central Standard Time (CST) (USA). When time is 6:00 in Minneapolis it is 21:00 in Tokyo and 20:30 in Korea. Peak excretion in Japan occurred at 21:00 to 24:00 period which corresponds to 6:00 to 9:00 CST. Lowest excretion in Japan occurred at 15:00 to 18:00 (24:00 to 3:00 CST). Curves in Fig. 2 are plotted so that they all referred to CST instead of local time. Then the excretion curve of 17-hydroxycorticosteroids in Japan superimposes on that in Minneapolis but a representative curve from the Korean study is displaced by 9 hours. The peak was exaggerated though, perhaps because of excitement and anxiety. Subjective symptoms on day of arrival in Japan included extreme sleepiness from 15:00 to 22:00 o'clock even though sleep had been adequate on the plane, and wakefulness from midnight to 6:00. During adjustment period in Korea wakefulness at night and sleepiness in afternoons persisted for about 3 weeks. This was not a daily phenomenon after the first few days and gradually disappeared.

Potassium excretion (Table I) follows the peaks of 17-hydroxycorticosteroid excretion reasonably well. Note the very high excretion during the night of the first 24 hours in Tokyo. The excretion pattern which most closely mimics that in Minneapolis is the one on Oct. 14, 1957. The variation in potassium excretion cannot be accounted for by the fact that food was eaten only during the day. A very

TABLE I. Potassium Excretion, meq/3 Hr.

Date	6–9	9–12	12–15	15–18	18–21	21–24	0–3	3–6	6–9	9–12
8- 5			13.4	15.0	5.8	11.4	21.8	17.0	14.9	6.5
			5.1	3.5						
12	4.7	5.7	3.6	5.1	5.1	6.7	3.9	4.1	4.2	8.0
19	8.7	7.9	9.3	10.4	8.5	4.4	10.8	4.6	3.7	5.8
9- 2	9.1	11.5	13.8	12.3	9.2	4.3	5.4	3.9	4.3	9.5
10-14	6.0	12.6	12.3	12.3	7.5	4.6	4.5	7.4	7.7	12.7
Minneapolis		15.8	23.6	6.5	8.8	5.7	3.1	3.1	3.7	

Time is recorded as local time.

TABLE II. Sodium Excretion, meq/3 Hr.

Date	6–9	9–12	12–15	15–18	18–21	21–24	0–3	3–6	6–9	9–12
8- 5			18.4	31.8	20.8	22.0	37.1	35.8	27.6	13.0
			7.2	9.0						
12	12.6	23.0	27.0	25.8	42.1	39.9	25.9	14.4	17.5	13.5
19	13.7	17.8	23.8	21.3	28.4	18.3	25.5	14.9	11.3	33.1
9- 2	4.9	20.4	26.2	25.5	38.8	23.0	22.4	18.6	11.9	23.2
10-14	15.4	34.2	21.7	21.9	24.9	24.9	8.1	21.2	10.3	20.3
Minneapolis	12.2	12.3	11.2	6.6	11.0	16.2	11.0	14.2		

Time is recorded as local time.

large excretion occurred during the night in Tokyo and excretion of potassium in Korea followed quite closely the steroid excretion and was not greatest at the time following largest or evening meal. This becomes even more significant when compared with the excretion study in Minneapolis during which time equal feedings were eaten every 3 hours throughout the 24 hour period. Sodium excretion (Table II) is quite variable. However, there is a marked sodium excretion the first night in Tokyo. The peak of sodium excretion follows the steroid excretion peak very well and corresponds to a group of subjects studied previously(1) but not to the traveler's own pattern in Minneapolis. Sodium excretion is erratic except for the Tokyo study, so the significance of the variations cannot be evaluated.

It is clear that 17-hydroxycorticosteroid excretion reverted to a pattern synchronized with Korean time with displacement of the peak of excretion by approximately 9 hours from CST (USA). This occurred by 11 days after leaving Minneapolis (9 days after leaving Seattle). The striking difference between the first study and the others is apparent at a glance. The amplitude of variation and particularly the decrease at night on all subsequent curves is not as great as one in Minneapolis. There is a small secondary peak of excretion at either the 18 to 21 or 21 to 24 hour period in all but one of the curves during the Korean sojourn.

Discussion. Mammals can adapt or their rhythm becomes synchronized only slowly when subjected to sudden changes in environmental routine. Halberg(3,4) has found that it takes one week or longer for mice to resynchronize the daily rhythm in blood eosinophils with an abruptly inverted lighting schedule. When mice are kept under otherwise controlled conditions significant shifts in phase have been established by 2 weeks after lighting inversion for diverse daily periodic functions, the daily rhythms of mitoses in pinnal epidermis or liver, those of hepatic nucleic acid metabolism and the rhythm of corticosterone in blood are but some of the cases in point(5). In turning to data on human beings, Burton has twice studied his temperature rhythm, when flying from London, Ontario, across the Atlantic to England. He thus altered his routine of living by a phase shift of 5 hours and found that it took 3 to 4 days for his Canadian temperature rhythm to fall in step with the English rhythm (6).

The data of this paper, in turn, show that in man excretory patterns related to cortical adrenal function also can be adjusted to a new schedule of lighting and activity, in 9

days at least. In good agreement with the results obtained on experimental animals it is also apparent that there is not a complete adjustment immediately following a change in routine. The synchronization with a new time schedule also is apparent in the electrolyte excretion.

Summary. 1) Excretion of 17-hydroxycorticosteroids in the urine was measured at frequent intervals throughout 30 hours at 5 different times following a shift from CST to Japanese and Korean time. The excretion was synchronized with CST immediately after arrival in Japan, but became synchronized with the new time schedule by 9 days. 2) Sodium and potassium excretion patterns are similar to that of a previous study on Central Standard Time but synchronized with the new time schedule also in 9 days.

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Wound Healing: Glycoproteins of Wound Tissue. I. Studies of Hexosamine, Hexose, and Uronic Acids Content.* (24675)

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The importance of connective tissue in wound healing is well recognized. However, little is known about the complicated sequence of events by which connective tissue is formed. Kao, Boucek, and Noble(1) recently reported studies of connective tissue formed following implantation of polyvinyl sponge. Robertson, *et al.*(2) found that following injection of carrageenin suspension into scorbutic guinea pigs, granulomatous repair tissue contained more hexosamine containing polysaccharide material than that formed under the same conditions by normal animals. Slack(3), using a similar suspension, found that increase in polysaccharide material in scorbutic guinea pig tissue was due to increase of hyaluronic-acid-like material, but that chondroitin sulfate decreased. Schilling *et al.*(4) have described a technic for study of wound fluid utilizing stainless steel cylinders which are implanted subcutaneously in animals. This procedure allows removal of numerous samples at various time intervals for studies of tissue and fluid components. The following describes serial studies of hexosamine, hexose, and uronic acid contents of wound tissue formed around such cylinders.

Methods. Stainless steel cylinders were implanted subcutaneously in dogs as previously described for guinea pigs(4). The cylinders used were of #46 mesh and were 1 cm in diameter by 5.5 cm long. Two lucite plastic rings 9.5 mm in diameter and approximately 3 mm thick were placed in each cylinder to keep it from collapsing during the healing process. At stated intervals the cylinders were removed, the fluid within cylinder was drawn off, and extraneous tissue was stripped from the outside of cylinder. The cylinder was opened by longitudinal scissor cut, and the tissue was lyophilyzed still attached to the cylinder. The dry tissue was stripped by hand from the stainless steel mesh and extracted in Soxhlet extractor for 24 hours with diethyl ether to remove lipid material. The extracted tissues were ground to pass through

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