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Differential diagnosis of psychogenic polydipsia and diabetes insipidus following acute head trauma : a case report

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THE DIFFERENTIAL DIAGNOSIS OF PSYCHOGENIC POLYDIPSIA AND DIABETES INSIPIDUS FOLLOWING ACUTE HEAD TRAUMA. A CASE REPORT

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Introduction

It is the purpose of this paper to discuss the case report of a patient with a polyuric-polydipsic syndrome. This case was complicated by the fact that the patient suffered acute head trauma following an auto-train collision in which he consequently sustained multiple fractures of the skull, among other traumatic fractures and injuries. The case illustrates many of the classical problems that are presented in a polyuric situation and typifies the necessity of accurate and exact diagnoses because of the acute nature of the disease. It is obvious that prior to laboratory testing, the first consideration had to be that of a traumatically induced diabetes insipidus. However, in proving this diagnosis the differential diagnosis of polyuria was considered and in so doing the ruling in or out of the various possible etiologies brought about the final diagnosis.

I shall present this case history and then follow it with the various diagnostic considerations and discuss how the final diagnostic formulation was conceived. A brief discussion of the other causes of polyuria will also be included and how these things were eliminated. Also included will be a discussion of the various

diagnostic tests that were employed and how and why these tests aided in confirming or rejecting a given diagnostic possibility, in other words, the physiological mechanisms involved, the actual mechanics of the tests and their application to the case itself. These things will necessarily include a brief section on the anatomic physiology of the renal concentration mechanisms including the humoral aspects of control and release of the antidiuretic hormone.

I have had the opportunity to observe this patient myself. His case was presented at the Medical Grand Rounds held at Bishop Clarkson Memorial Hospital on September 19, 1961. The patient was admitted for a 60-day hospital stay at the time of his original problem. I have also had the opportunity for a case follow-up in that the patient was re-admitted February 15, 1963 for mastoidectomy and a discussion of the present disposition of the case will be included. On March 9, 1963, this case report and discussion was presented at the Nebraska Regional Meeting of The American College of Physicians.

I wish to acknowledge the help and cooperation of Dr. George W. Loomis and Dr. Frederick Ware, Jr., without whose personal communications and assistance this paper would not have been possible.

Case report

PRESENT ILLNESS: Mr. J. A., a 14-year-old white male was injured in an auto-train accident on August 25, 1961, at about 11:30 P.M. He was admitted to the hospital for multiple facial lacerations, observation, and determination of the extent of his injuries. The patient was rendered unconscious due to the impact of the crash and at the time of admission was noted to be bleeding from both ears. Past history was non-contributory except for a history of "bed wetting" until 11 years of age. There was no other evidence of psychiatric disturbances, and no history of significant medical illnesses, surgery or trauma. Family history was not revealing.

PHYSICAL EXAMINATION: This was a very lethargic, restless, white male who would respond verbally, with only some of his answers being relevant. His skin was warm, moist and soft with several abrasions and lacerations about his face and skull. Blood was noted to be draining from both ears. The left pupil was noted to be slightly larger than the right with both being sluggishly reactive to light, directly and consensually. His chest was clear. The heart was regular, but the rate was rapid. The abdomen was soft with generalized tenderness present. No rigidity was noted. The right

thigh was reddened and edematous proximally. Deep tendon reflexes appeared to be equal and active and a questionable Babinski reflex was noted on the right.

GENERAL LABORATORY FINDINGS: On admission, hemoglobin 13.8, packed cell volume 45%, RBC 4.88, WBC 17,800, bands 29, segs 53, lymphs 11, monos 7. Urine analysis was mod. yellow, cloudy, 1.018, 5.5, alb-1+, CHO-tr., acetone-negative, less than 50 RBC per high power field, less than 50 WBC per high power field, granules 3+. On 8/29, hemoglobin 9.0, packed cell volume 30%. On 8/30 feces occult blood 4+, hemoglobin 12.2, packed cell volume 37%, 8/31, urine analysis essentially the same as on admission. 9/10, BUN 8.5 mg.%. On 9/11 urine electrolytes essentially normal: Na 38, K 77, (mEq/L), Urea nitrogen (Urine) 638. mg/100ml. Serum electrolytes were also within normal limits: Cl 101, K 4.7, Na 143 (all in mEq.L). Urine Sulkowitch 2+, quantitative urine Ca 5.8 mg/100ml. Alkaline phosphatase 20.5 KA units, serum Ca 6.5 mg/100ml., inorganic phosphorus 4.6 mg.%. Repeat serum Ca 9.3 mg/100ml. Total serum protein 6.5 gm/100ml, albumin 3.2 gm/100ml, and globulin 3.3 gm/ml. A/G ratio 0.9/1. Adrenal function: 17-ketosteriods 12 mg/24 hour (normal for age 8-20), and 17-hydroxysteroids 16 mg/24 hours (normal for age 2-11 mg/24 hours). By the end of the

hospitalization urine analyses became normal without hematuria or pyuria.

X RAY FINDINGS: Skull: An oblique fracture line was present traversing the basisphenoid bone with the fracture line entering the sella turcica. There was a fracture of the left petrous pyramid with increased density suggesting accumulation of blood in the left mastoid air cells. A third fracture line was seen in the mid-portion of the right petrous ridge without displacement. Cervical and lumbar spine: There was a left temporal bone fracture, multiple fractures of mandible, displaced odontoid process, and a compression fracture of L-1. Hip and pelvis: An intertrochanteric and subtrochanteric fracture of the right femur was present, as well as an impacted fracture of the superior ramus of the left pubic bone, and an oblique fracture of the inferior ramus of the left pubis with separation at the symphysis. Chest: Minimal traumatic right pleural effusion was seen, with a fracture of the left second rib and axillary border of the left scapula. Abdomen: Suggested ileus was seen, and the fifth lumbar segment suggested possible damage, and a spina bifida occulta of S-1 was noted.

CLINICAL COURSE: Upon admission, the patient was taken to the operating room for repair of multiple

facial lacerations. His right extremity was placed in traction and a Steinman pin was inserted into the right tibial tuberosity. The patient was maintained on IV fluids and placed on antibiotics. The following morning the patient was essentially unchanged. His urine was grossly clear. The neurosurgical consultant felt that the patient had a severe brain concussion with associated possible sub- or extradural hematoma along with the basilar skull fracture. On August 27, the patient was still restless but more rational. He seemed to be improving. Paraldehyde was given for restlessness. Aspirin was given for fever. On August 28, the patient continued to respond, recognized people and tried to cooperate. His pupils were unchanged. Two units of blood were given at this time because of blood loss anemia. Oral liquids were well tolerated. On August 30, satisfactory progress was noted, and progressive neurological signs were not noted. On September 1, the patient was removed from the critically ill list. The possibility of diabetes insipidus was considered as a complication of injury to the pituitary body because of extremely large oral fluid intake and urinary output volumes. Some deafness was also apparent on September 11. On September 9, studies were begun to determine the cause for the patient's unusually large

fluid intake and output. On September 15, an open reduction of the right hip and wiring of the fractured mandible were performed, and two more units of blood administered due to blood loss during hip pinning. On September 19, the patient continued to ingest large quantities of fluid as well as to excrete an enormous volume of urine. During the first days of admission, the patient's intake was not remarkable, ranging from 2,000 to 3,500 ml., all of which was parenterally administered. Comparable excretion volumes were also noted. On the third hospital day, August 29, intravenous fluids were discontinued and oral intake was 5,015 ml. and output was 4,900 ml. This was approximately the range for the next few days until the 10th day, September 9, when intake jumped to 9,670 ml. For the next 9 days, the intake ranged from this 9,000 ml. level up to 12,985 ml. and then dropped again to 6,000 ml. for 3 days. These intakes were associated with comparable output volumes. During the remainder of the hospital course, the intake volumes were very irregular from day to day, ranging from 6,000 to 25,450ml.

Following a battery of special tests, on the 36th hospital day, the patient began to spontaneously decrease the oral intake of fluids, although gradually and somewhat irregularly, the general downward trend is

established in Figure 1. After 59 hospital days, the patient was dismissed and oral intake was in the range of 3,000 ml. per day. The patient was amnesic concerning the period of heavy intake and remembers little of this.

PRESENT DISPOSITION: The patient continued to maintain normal oral intakes and lived a normal life in his home town. He was re-admitted to the hospital on February 15, 1963, eighteen months later for mastoidectomy. His clinical course shows no evidence of polyuria or polydipsia, being in the 2,000-3,000 ml. range daily. Urine analysis is within normal limits as are random urine and plasma osmolalities (serum: 295 mOsm/L. urine: 445 mOsm/L).

Special Tests

The diagnosis of this case was based mainly on a series of neurohypophyseal function studies and the ability of the kidney to respond. Over a two day period, tests were run which were adapted after those originally described by Hickey and Hare (27) and as later modified by Carter and Robbins (8). The method of De Wardener and Jones (29) was also incorporated into this scheme. On the morning of the first day of testing the patient was given no fluids by mouth after 6 A.M. This dehydration period was carried out for a period of 6 hours during which time catheterized urine collections were made to determine volume per unit of time, specific gravity, urine osmolality. Beginning with the third hour of the dehydration test urine was collected each half hour for the remainder of the 9 hours that day. Initial baseline studies were done at the beginning of the test day. Urine osmolality was done at 1½ hour, 4 hour, 5½ hour, 7 hour, 7 3/4 hour, and 8 3/4 hour intervals. Plasma osmolality was determined at 1½ hour, 5½ hour, 7 hour, and 7 3/4 hour intervals. The osmolal clearance (C_{osm}) and free water clearance (C_{H_2O}) were calculated for each of the urine osmolality determinations, and the value for plasma osmolality

(P_{osm}) was interpolated at the times when this determination was not actually done coincidentally with each urine osmolality determination. After 6 hours dehydration, the patient was rehydrated with 1,600 ml. of water orally over a 45 minute period. At the 6 hour interval, a creatinine clearance test was performed. Following this at the 6½ hour interval, 0.1 Unit of aqueous pitressin was injected intravenously.

On the following day, the test was continued. The patient was hydrated with 20ml. of water per kilogram body weight over a 1 hour period. Then 800 ml. of 3% NaCl was given intravenously over a 25 minute interval. Urine specimens were collected every 15 minutes for determination of volume, specific gravity, and osmolality. Blood was collected each hour for plasma osmolality determinations. One hour after this hypertonic infusion, the patient was rehydrated with free access to oral liquids which consisted of 1,860 ml. over a 1½ hour period. Creatinine clearance was determined at th e 2½ hour point. Aqueous pitressin, 0.2 Units intravenously was administered at 2½ and 3½ hour intervals.

Another attempt at diagnosis was made by giving the patient daily injections of pitressin tannate in oil in an attempt to drive the plasma osmolality down (19) by

plasma dilution from exogenous pitressin induced antidiuresis and result in a decrease intake, the idea being that the thirst center might respond physiologically to a markedly diluted plasma. The results of this test were obtained by determining urine osmolality on each voided specimen and hourly plasma osmolality as well as exact urine volumes. However, the results of this test were generally inconclusive and will not be reported, other than to mention the fact that this test was attempted and the patient did not decrease his intake.

Daily input and output records were kept and this data is presented in Figure 1.

Results

INTAKE AND OUTPUT: When it became apparent that the patient was drinking rather unusually large amounts of fluid, accurate daily intake and output records were kept. As can be noted in Figure 1, the patient's intake was not unusual during the first few days of hospitalization but it must be remembered that during this time the patient was in a comatose or semi-comatose state and fluids given were done so mostly by parenteral route. Around the 5th hospital day, the intake consisted of approximately 5,000 ml. followed by a tansient decrease and then a gradual increase on about the 11th day and an early peak on the 15th day, which, interestingly enough, coincides with the day that the patient's jaws were wired for the multiple fractures of the mandible which had been sustained in the accident. In retrospect, it was considered that this point may have been significant if this was to be a truly psychogenic problem with reactive behavior to the threat of not being able to obtain sufficient water based on the fear of not being able to drink enough. This will be discussed below as a diagnostic consideration. If you will then follow along on this graph, you will notice

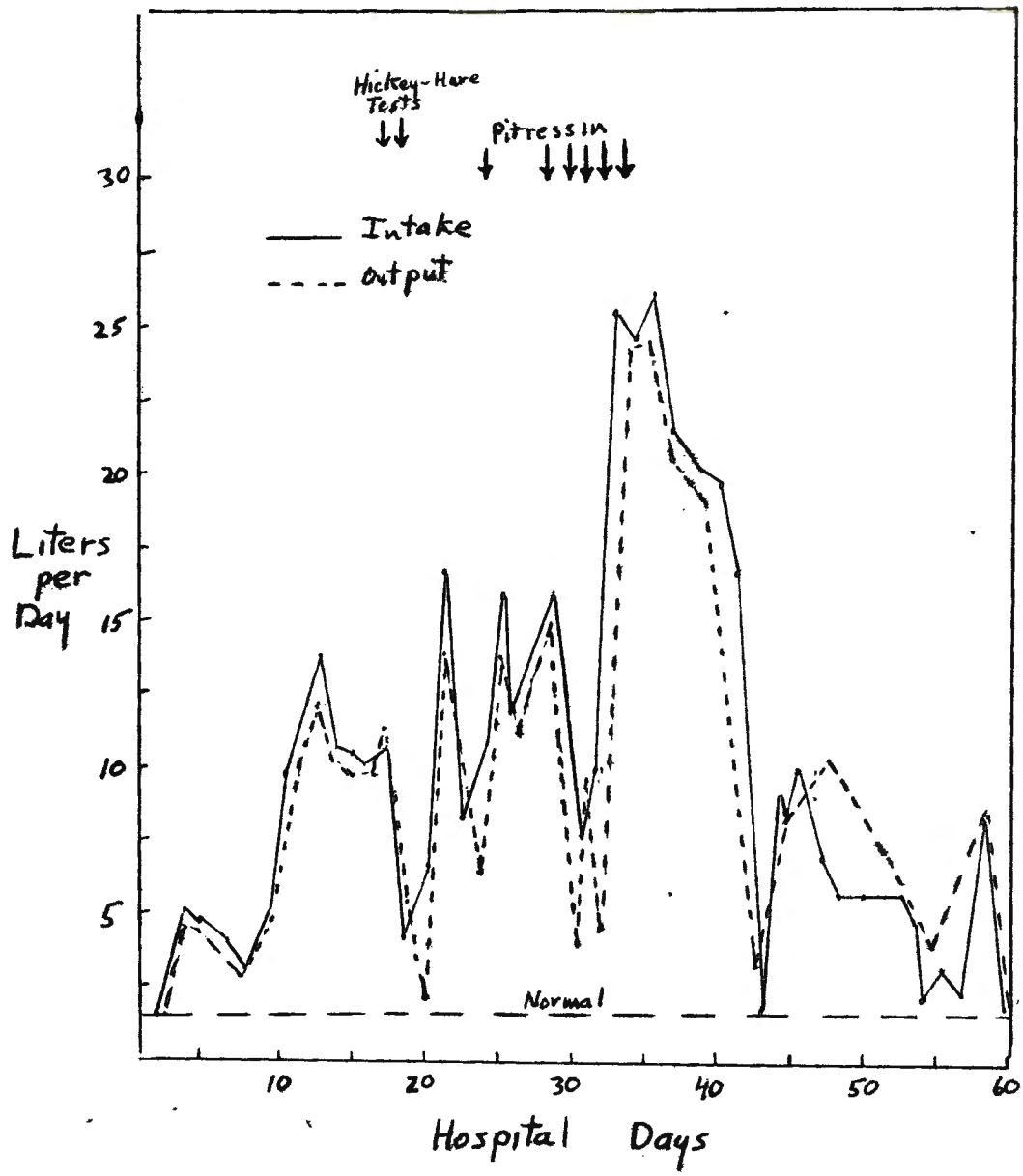


Figure 1. Graph representing entire hospital course with intake (_____) and output (------) volumes. Days are indicated that diagnostic tests were run. Note wide fluctuations in volume, and that output lags slightly behind intake. Normal baseline is shown, and note the return to baseline at the end of hospitalization.

that at this time the intake peaked at around 13,000 ml. appearing to be on the steady increase until interrupted by diagnostic testing including forced fluid deprivation, hypertonic saline injections, and parenteral pitressin injections. It is pertinent that because of the persistant demands of the patient, it was necessary to remove a tooth so that an adequate amount of fluid intake could be obtained with drinking straws and during his peak periods of intake he required almost constant attendance by the nursing staff to provide him with the desired amount of water. The 20th through the 35th day the patient underwent various diagnostic tests which probably accounts for the somewhat overall decrease in volume. However, during the attempt to drive the plasma osmolality down with daily injections of intramuscular pitressin, the patient demonstrated an apparent "release" from the effects of exogenous vasopressin and the intake as well as output rose to the astronomical amount of nearly 26,000 ml. per day! Following this by a few days, the patient began a spontaneous reduction in fluid intake and over the next two week period the volumes turned to near normal levels (note "normal" base line on graph, Figure 1). The urinary output volumes closely parallel the intake

volumes in a general way although overall it can be observed that the output volumes were just slightly less than the intakes, indicating that the patient was usually just a bit ahead on fluid balance.

RESPONSE TO DEHYDRATION: This simplest, and considered by some to be the most significant, test of neurohypophyseal integrity was quite revealing (48). The data obtained here showed an obvious change in urine flow and volume in response to deprivation of fluid. Under rigid control, the patient was not permitted to have any fluid orally after 6 A.M. Values for this data are presented in Table 1 for output volume for each interval of time collected and is calculated in ml./ minute and graphed in Figure 2 as ml. per 15 minutes. These values do not give a clear cut diagnostic result although it is apparent that there is some decrease in urine flow with fluid deprivation. It is difficult to show any significant increase with hydration of 1,600 ml. of fluid.

Urine specific gravities were done on each sample collected and are presented in Table 1 and Figure 2. This showed an increase in concentration of urine with deprivation, higher specific gravity, and a lesser concentration, lower specific gravity, with ingestion of

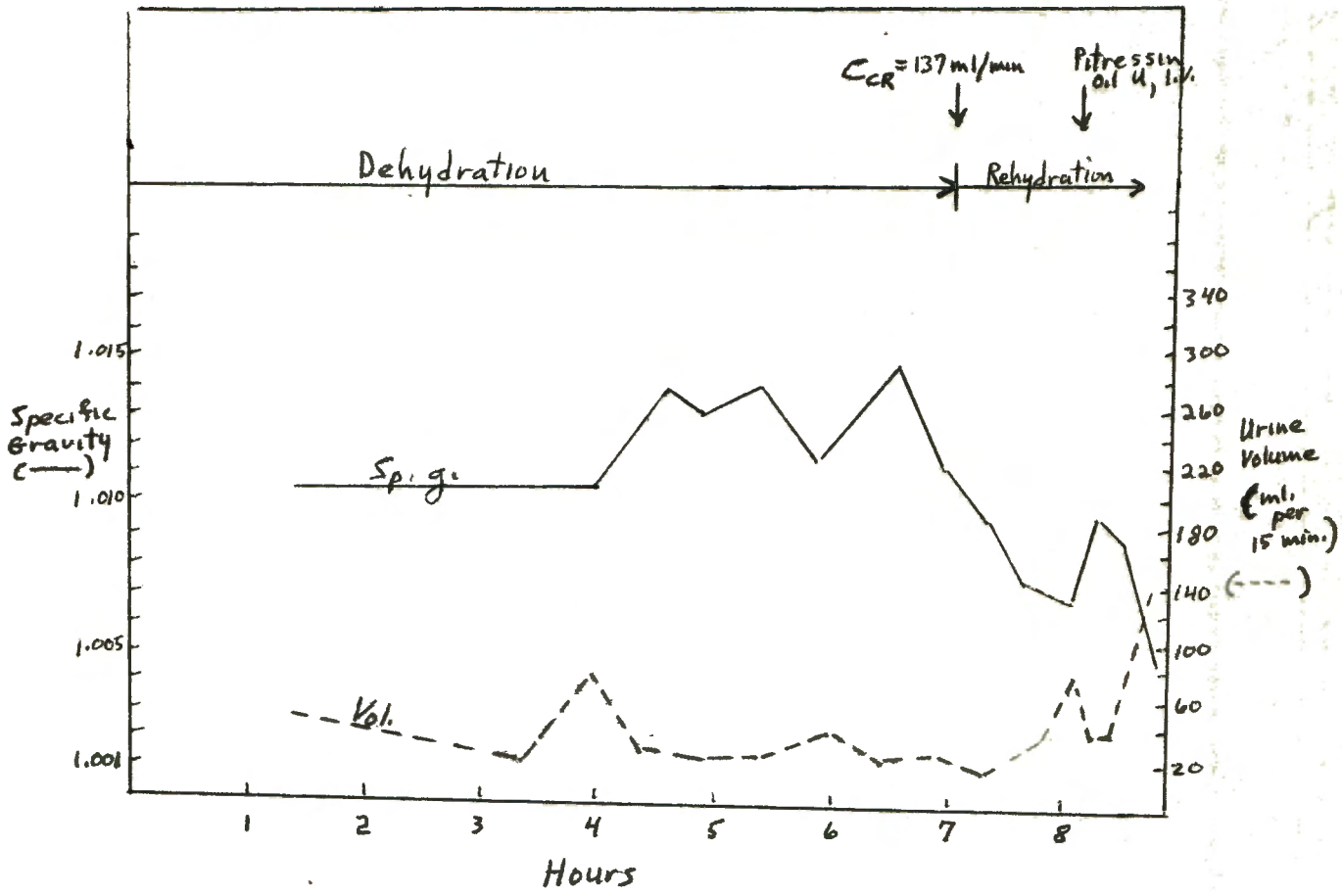


Figure 2. Graph showing specific gravity (_____) and urine volume (------) during dehydration test (see Table 1.). Creatinine clearance obtained at time indicated. Patient was rehydrated and given pitressin as shown.

Table 1.

TESTS FOR EVALUATION OF THE NEUROHYPOPHYSEAL-RENAL SYSTEM

Time		Oral Fluid	Urine Vol.	Urine Vol per Min.	S.G.	U_{osm}	P_{osm}	C_{osm}	C_{H_2O}
1:00	Dehydration test								
1:30	P_{CR}= 0.8mg%		400	3.3	1.011	336	288	3.8	-0.5
3:30			150	1.2	1.011				
4:00	U_{CR}= 56 mg%		155	5.2	1.011	415	(288)*	7.5	-2.3
4:30			65	2.2	1.014				
5:00			50	1.7	1.013				
5:30	U_{CR}= 48mg%		55	1.8	1.014	535	(290)	3.3	-1.5
6:00			90	3.0	1.012				
6:30			60	2.0	1.015				
6:45	P_{CR}= 0.7mg%						290		
7:00	C_{CR}= 137ml/min U_{CR}= 40mg%		73	2.5	1.012	428	(290)	3.5	-1.1
7:30		1600	65	2.2	1.010				
7:45			80	5.3	1.008	250	279	4.7	0.6
7:50	Pitressin 0.1 unit IV								
8:05			115	5.7	1.007				
8:20		115	35	2.3	1.010				
8:35			35	2.3	1.009				
8:50			150	10.0	1.005	134	277	4.8	5.2

1,600 ml. of water orally. Aqueous pitressin intravenously resulted in an increased concentrating ability.

Endogenous creatinine clearance was determined to show that glomerular filtration was in a normal range to rule out this variable as being a significant factor in urine concentrating ability. (3, 24) The determination of the creatinine clearance was done in the usual manner using the formula:

$$C_{CR} = \frac{U_{CR}\ V}{P_{CR}}$$

Creatinine clearance is commonly used for determination of glomerular filtration rate and gives a value not too different from the true amount. Creatinine is excreted into the lumen but also possibly is reabsorbed by the tubules. Also the methods of determination are not specific and include other substances. Probably, then, we have a case of compensating errors resulting in a fairly accurate estimation of glomerular filtration. (4) The value of using inulin or some other substance which gives a more "accurate" result, is therefore, not justified in this case since it involves injecting foreign substances and this endogenous test used is quite sufficient.

PLASMA AND URINE OSMOLALITY: It can be seen (Figure 2) that more refined methods of renal concentrating ability were desirable since urine flow and specific gravities are significant but not exacting and there is an over lapping of results from these rather crude determinations. Urine and plasma osmolalities were determined at regular intervals and are presented in Table 1 and Figure 3. Plasma osmolality remains in the "normal range" although it is slightly higher with deprivation than with ingestion of fluid later in the test. Urine osmolalities demonstrate a definite increase in concentrating ability with deprivation.

OSMOLAL AND FREE WATER CLEARANCES: This is an even more refined method of interpreting the response of the renal concentrating mechanism. A discussion will follow concerning the validity and derivation of this mathematical maneuver. It is clear that with fluid deprivation the free water clearance decreases and becomes a negative value (Figure 4) and osmolar clearance increases relatively and following hydration the free water clearance becomes a positive value, thus a hypotonic urine is being produced, as can be predicted for a normal patient or a patient with an intact

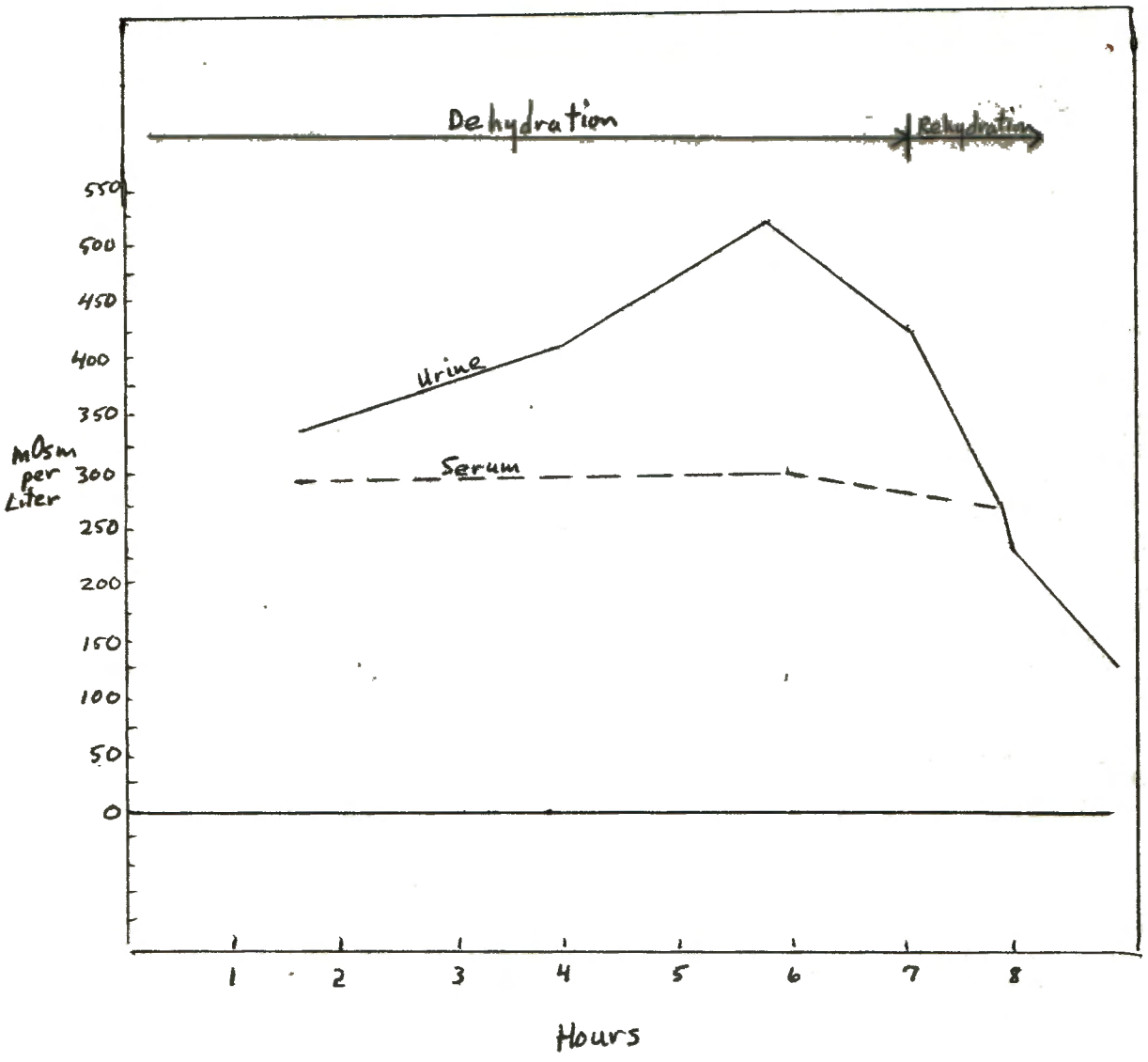
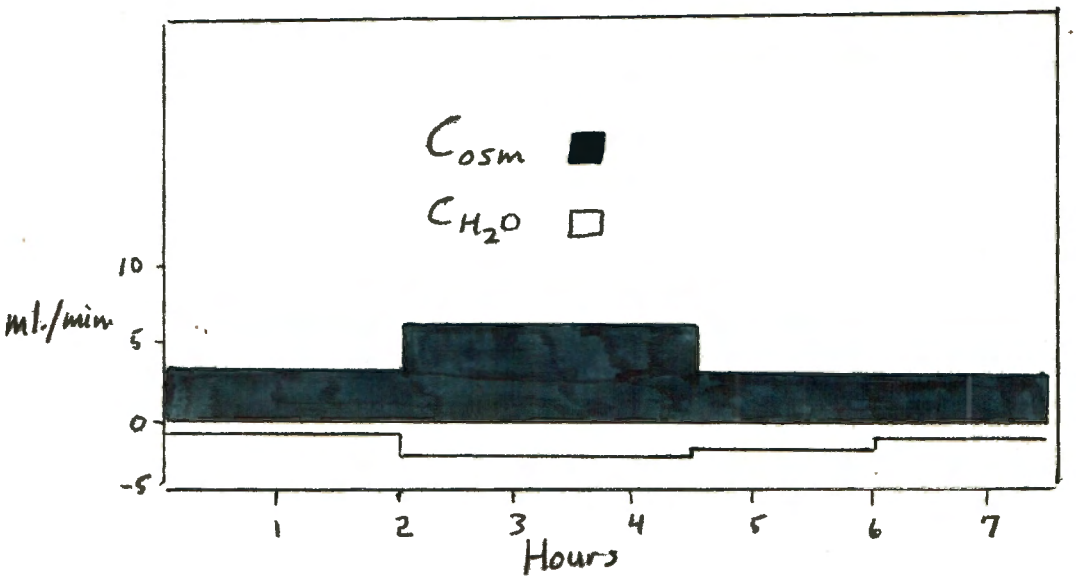


Figure 3. Urine osmolality (————) and serum osmolality (------) during dehydration test. See Table 1 and Figure 2.

Figure 4. Bar graph of free water clearance (C_{H_2O}) and osmolal clearance (C_{osm}) during dehydration test (see Table 1). The negative C_{H_2O} indicates the hypertonic urine produced as a H_2O response to dehydration.



neurohypophyseal system, as will be discussed later.

HICKEY-HARE: This test as devised by Hickey and Hare (27) and modified by Carter and Robbins (8), was performed on the following day. The patient was loaded with the prescribed 20 ml. of water per kilogram body weight. Urine volumes were taken at 15 minute intervals and charted and graphed. Urine flow was at a high rate and the specific gravity was quite low, in the 1.001 area, as would be expected. A single urine osmolality and plasma osmolality was run at the end of this water loading period and the plasma was within normal range and the urine was quite hypotonic to plasma, at 56 mOsm/L (see Table 2 and Figure 5 & 6). The free water clearances calculated (Table 2, Figure 7) clearly show the urine to by hypotonic. Infusion of hypertonic saline resulted in a marked increase in urine specific gravity and a very noticeable decrease in urine flow. Coinciding with this was slight rise in plasma osmolality and very large increase in urine osmolality, rising to a point of 630 mOsm/L, although this overlaps with the period of rehydration, the kidney was then concentrating to a degree even greater than that reflected in the actual laboratory findings at the time. Free water clearance became greatly negative.

Table 2.

TESTS FOR EVALUATION OF NEUROHYPOPHYSEAL-RENAL SYSTEM (2nd day)

Time		Oral Fluid	Urine Vol.	Urine Vol per Min.	S.G.	U_{osm}	P_{osm}	C_{osm}	C_{H_2O}
1:00	Hydration 20ml/Kg	400							
1;15		400	90	6.0	1.004				
1:30		400	115	7.7	1.003				
1:45		400	200	13.3	1.002				
2:00			330	22.0	1.002	56	296	4.2	17.8
2:15	Hypertonic saline		360	24.0	1.001	67	(298)	5.4	18.6
2:30	(800 ml 3% NaCl IV in 25 min.)		235	15.5	1.002	119	307	6.0	9.5
2:45			120	8.0	1.007	404	(307)	10.5	-2.5
3:00			85	5.7	1.012	540	(307)	10.0	-4.3
3:15	U_{CR} = 18mg%		105	7.0	1.013	528	(300)	12.3	-5.3
3:30	U_{CR}=16mg%, P_{CR}=0.6mg% C_{CR}=193ml/min.		101	6.7	1.013	549	294	12.5	-5.8
3:45	Rehydration	1860	110	7.3	1.012	575	(294)	14.3	-7.0
4:00		↓	45	3.0	1.016	630	(294)	6.4	-3.4
4:15			85	5.7	1.011	440	(294)	8.5	-2.8

(continued)

Table 2.(con't)

TESTS (day #2, continued)

Time	Oral Fluid	Urine Vol.	Urine Vol per Min.	S.G.	Uosm	P_{osm}	C_{osm}	C_{H_2O}
(cont'd)								
4:30 Pitressin	150	150	10.0	1.005	235	294	8.0	2.0
4:45 0.2 units IV	200	200	13.3	1.003	164	(293)	7.4	5.9
5:00	215	215	14.3	1.004	236	(292)	11.6	2.7
5:15	345	345	23.0	1.002	136	(291)	10.7	12.3
5:30 Pitressin	345	345	23.0	1.001	141	(290)	11.2	11.8
5:45 0.2 units IV	250	250	16.7	1.002	270	(290)	15.5	1.2
6:00	210	210	12.0	1.004	263	289	12.7	1.3
6:15	400	400	26.7	1.001	103	(289)	9.5	17.2
6:30	510	510	34.0	1.001	102	(289)	12.0	22.0

*( ) = estimated

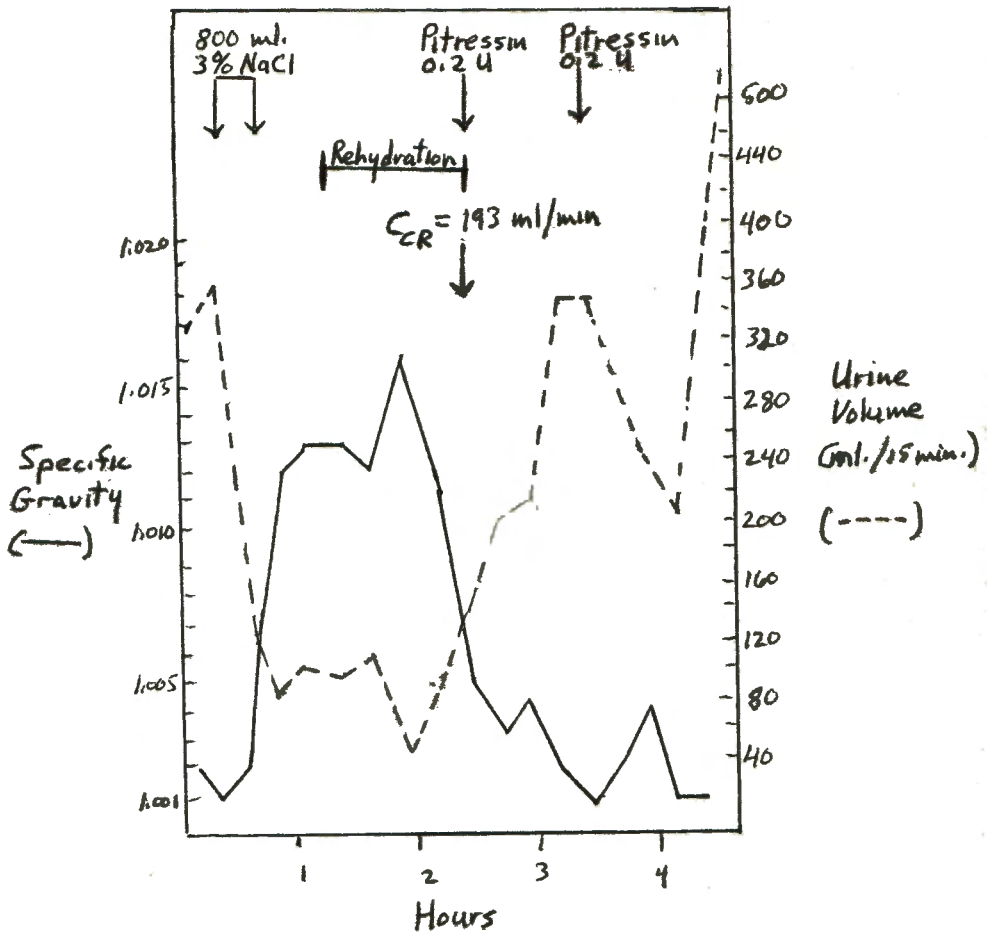


Figure 5. Results of Hickey-Hare test showing specific gravity (———) and urine volume (ml./15min.) (------) in response to hypertonic saline and aqueous pitressin intravenously. The patient was loaded with 20ml. of water per kilogram one hour prior to test. See Table 2.

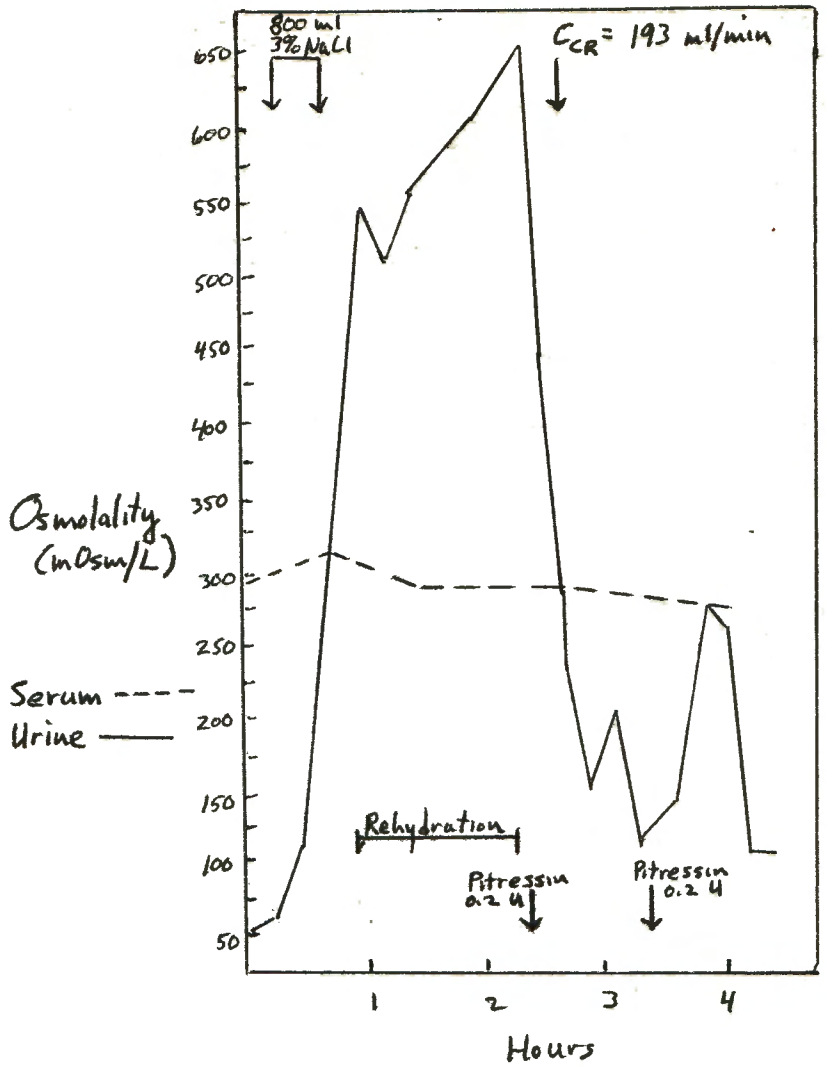


Figure 6. Hickey-Hare test showing urine (———) and serum (------) osmolality in response to hypertonic saline and aqueous pitressin intravenously. See Table 2.

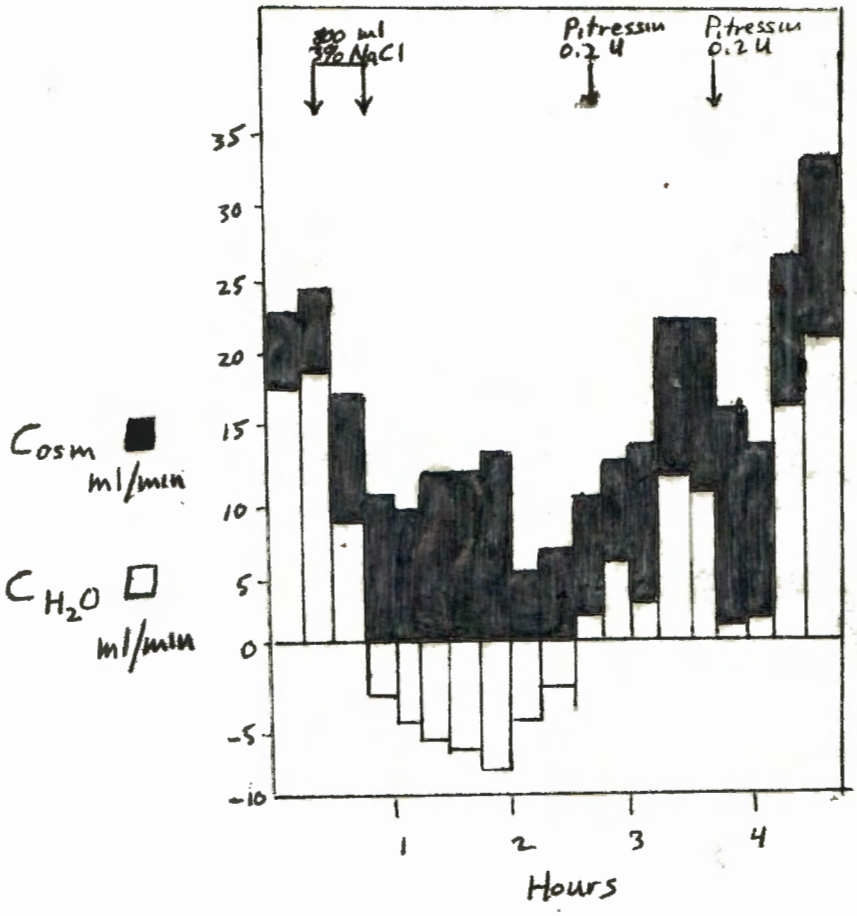


Figure 7. Bar graph illustrating osmolal and free water clearance during Hickey-Hare test. See Table 2.

Endogenous creatinine clearance was again determined to show that the glomerular filtration rate was adequate. Following a period of rehydration, the patient again put out a hypotonic urine by the indices of specific gravity, urine flow, urine osmolality and a positive free water clearance. Pitressin intravenously resulted in a rather equivocal response at first and then upon re-injection of another 0.2 Units, the indices showed a concentrated urine but not as great as that produced by hypotonic saline infusion.

RANDOM OSMOLALITIES: It is interesting that during the hospital course, the patient was able to concentrate urine to a very high degree, 847 mOsm/L, during a period of testing, and at one time during a very high water intake the urine osmolality was as low as 33mOsm/L, (see Figure 8), theoretically the lowest that is physiologically possible (see later discussion).

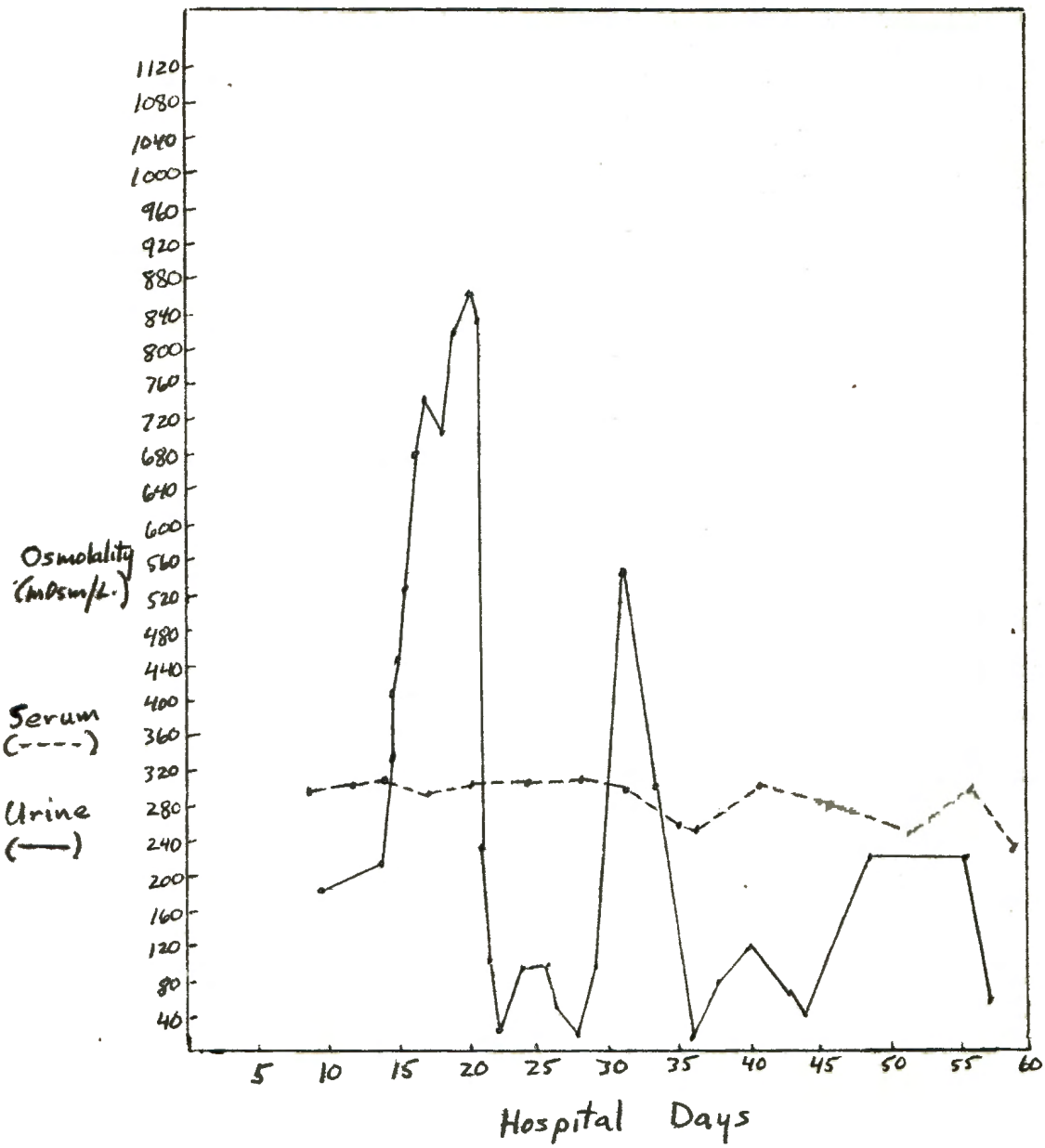


Figure 8. Graph of random urine (———) and serum (------) osmolalities to show only the wide range of values, varying from 33 mOsm/L to 847 mOsm/L. These fluctuations were not spontaneous, but reflect the results of diagnostic tests on several occasions.

A Review of the General Physiological Principles

THE RENAL CONCENTRATING MECHANISM: The normal glomerular filtration rate of 125 ml/minute comprises about 20% of the cardiac output and consists of about one liter per minute. This so-called "arteriovenous fistula" maintains a fairly constant rate of blood flow over a rather wide range of arterial pressures which is effected by vascular dilatation and constriction within the kidney. The glomerular filtration tends to be even more regular than renal blood flow, being controlled by renal efferent and afferent arterioles. This one liter of blood which perfuses the kidneys consists of approximately 650 ml. of plasma which makes up the glomerular and peritubular perfusate (12). By observing Figure 9, it can be seen that as the glomerular filtrate enters the proximal tubule it is isotonic to plasma. In this proximal tubule active transport reabsorption of sodium occurs from the tubule to the interstitium (38). It is also believed that passive reabsorption of urea occurs here also. (36) Water is passively absorbed in the proximal tubule as it is carried along with the actively reabsorbed sodium (38). As the tubular fluid progresses down the

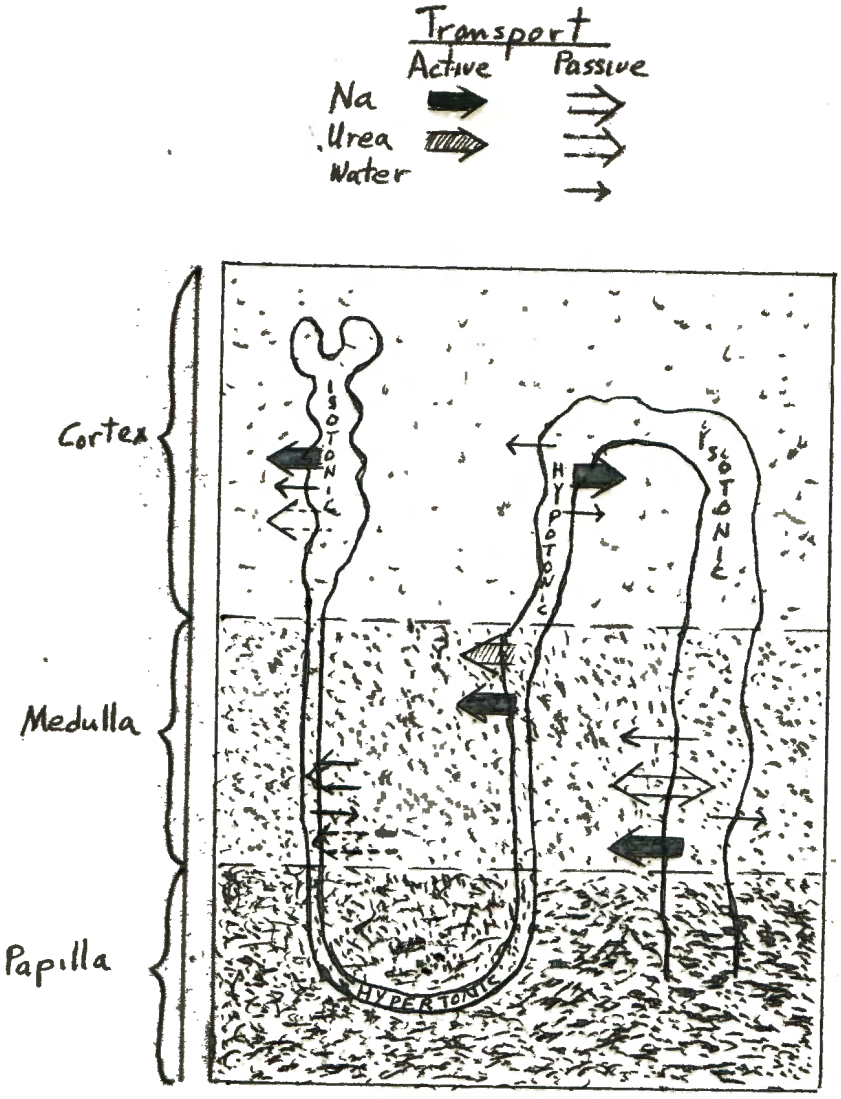


Figure 9. Diagramatic representation of nephron and interstitium. Cortex is isotonic to plasma and as fluid progresses toward the medulla and papilla, the concentration becomes greater as indicated by the gradation of stippling. This diagram is that seen in antidiuresis. Sites of Na, urea, and water reabsorption are indicated. There is no quantitative significance to the size of the arrows.

nephron it becomes more and more concentrated with sodium, chloride, and urea, during an antidiuresis that is (22). The thin loop of Henle then contains fluid which becomes greater concentrated due to the obligatory reabsorption to the more concentrated interstitium. This theory of a countercurrent multiplier system as advanced in 1957 by Hargitay, Kuhn, and Wirz (54) and confirmed by Gottschalk by his classical micropuncture techniques in 1960 (22) demonstrates that as one progresses into the real medulla the interstitium becomes more concentrated and the hairpin structure of the loop of Henle remains in equilibrium with this interstitium. As the intraluminal fluid then advances up the ascending loop, again there is active reabsorption of sodium and by the time this fluid reaches the distal tubule it is again hypotonic to plasma. The detailed discussion of this multiplier system is the topic of quite another subject and I will not attempt to cover the scope of that in this paper.

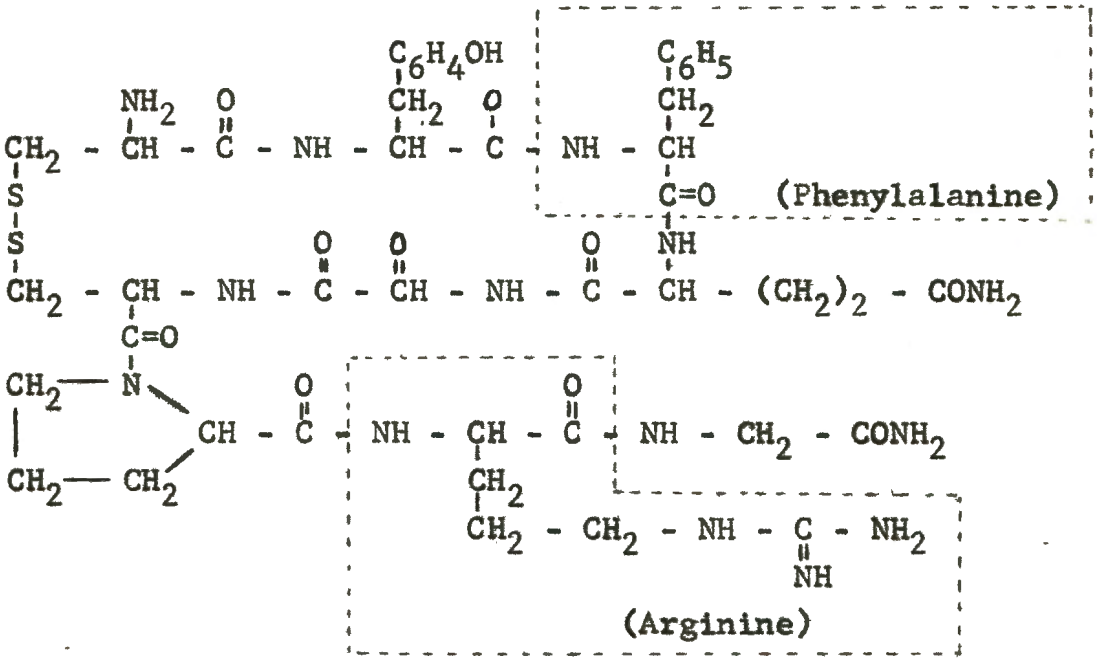
It is at this point in the distal tubule where a large amount of water is contained and in the case of an antidiuresis, it is reabsorbed. The amount of water reabsorbed is directly dependant on the permeability of the tubule at this point, and this is controlled by the

presence or absence of the antidiuretic hormone (20). It has been determined that the action of ADH is, indeed, at this point and also it is thought to act in the area of the collecting duct (20). Sodium is also actively reabsorbed at this point and, of course, urea is free to pass either way through the tubular epithelium according to the needs of the body fluid state (37). The kidney is able to produce urine four to five times more concentrated (12,000 to 14,000 mOsm/L) than plasma, (300 mOsm/L) or one-seventh to one-tenth (30 to 40 mOsm/L), as concentrated.

It can be stated that urine is concentrated not by adding solute to it, but rather by removing water from the intraluminal fluid, as is done in the distal tubule and collecting duct. On the other hand, urine is diluted by reabsorbing solute, as in active transport of sodium, reabsorption of chloride, and urea transfer, both active and passive. Urine remains dilute when there is increased solute opposing passage at the freely permeable membrane of the distal tubules and when water cannot permeate the tubular epithelium due to absence of ADH or other causes resulting in impermeability (23). ADH is essential to production of a hypertonic urine, although Berliner's experiment provides evidence of production of a slightly hypertonic urine in the absence of the hormone. It is believed that this phenomenon is

the result of decreased glomerular filtration rate and an associated decrease in sodium reaching the tubular fluid (3).

ANTIDIURETIC HORMONE: This is a chemical compound which consists of eight linked amino acids of which phenylalanine is the third and arginine is the eighth (in man and oxen). It's structure as depicted by Du Vigneaud, et. al (45) is as follows:



This structure presented is arginine vasopressin. It differs from species to species by alterations in the amino acid at the 8th link where arginine is placed.

The monumental work by Verney and the presentation

of his results in the Croonian Lecture in 1947 (43) is the most significant work done on the antidiuretic hormone and the factors which determine its release in which he, among many other things, cannulated scores upon scores of dogs and by manipulation and injections of the carotid artery system came up with much of the first definitive data. It is well excepted that ADH is produced in the area of the supraoptic and paraventricular nuclei of the hypothalamus. The hormone is not produced, as was once believed, by the posterior pituitary gland but instead it has been shown that the hormone is transported distally from the neurohypophysis via the axones of the supraoptico-hypophyseal tract and stored in the end plates about the vascular channels in the posterior pituitary gland. Upon its release it is secreted directly into the blood stream in these vascular channels (15).

Figure 10 diagrammatically depicts the nephron and the action in the presence and in the absence of ADH.

The presence of ADH cannot be detected in blood under normal conditions with the present assay methods, but Bisset (5) has found it possible to detect the presence of an "antidiuretic substance" in central blood, that is blood taken from the jugular vein, in

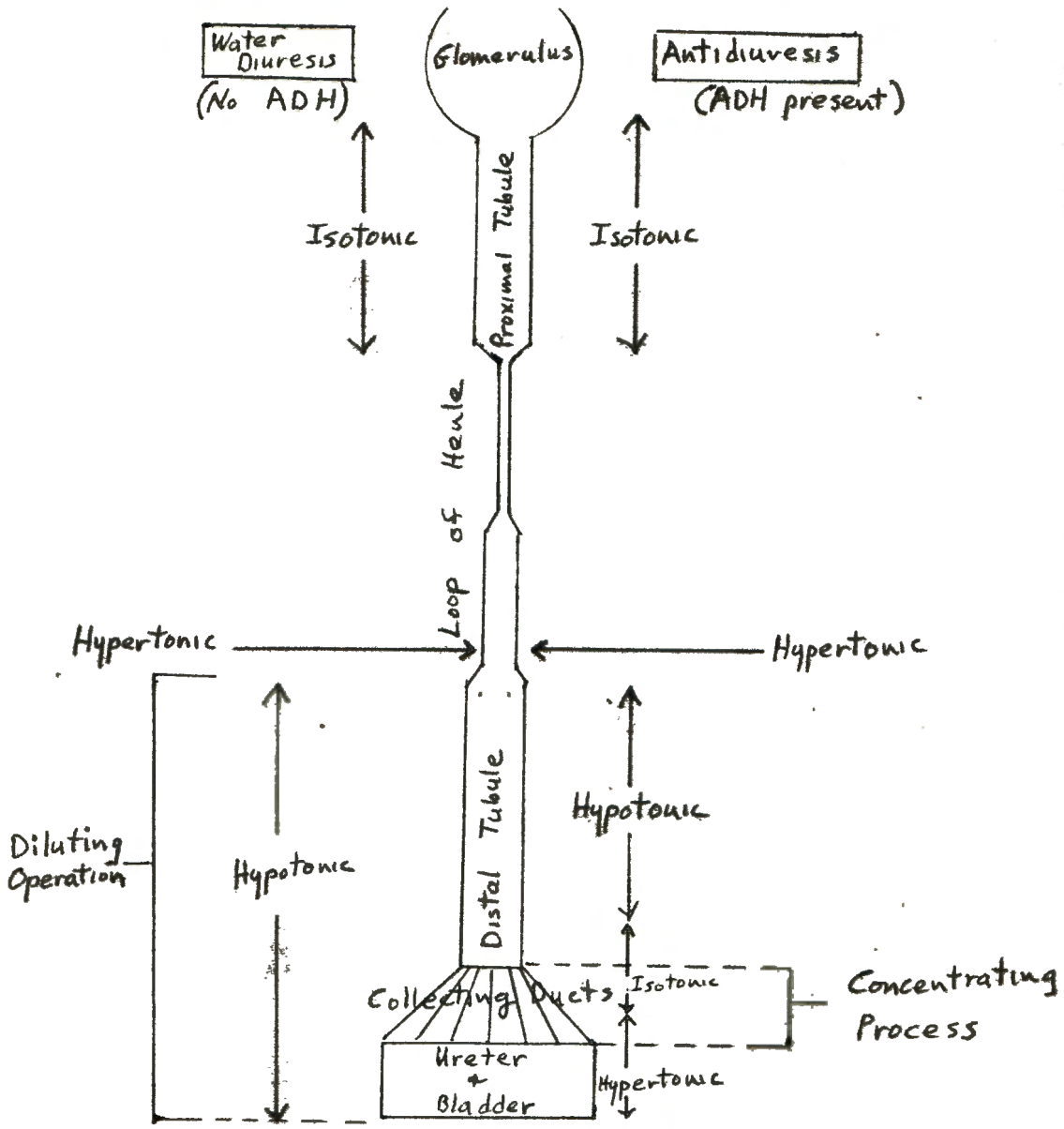


Figure 10. Schematic drawing of nephrons in presence and absence of ADH. After Robinson, 1962 (36).

conditions of very strong stimulation of the neurohypophysis, and at the same time this activity is undetectable in "peripheral" blood. Even with powerful stimulation, the antidiuretic activity can be detected only in very concentrated extracts. This procedure is very difficult and is not practical for clinical determinations. Therefore, the only practical way of evaluating the activity of the antidiuretic substance clinically, is the response of the renal system to tests of neurohypophyseal integrity, as outlined above.

RELEASE OF ADH: The need for water conservation by the body is a stimulus for secretion of this hormone and its action is inversely proportional to the water load (16). In an attempt to lump together the factors which stimulate the release of ADH, one can divide the stimuli into four large groups: 1) change in body fluid tonicity, i.e., increased tonicity, 2) decreased extracellular fluid volume, 3) emotion, and 4) direct pharmacological stimulation.

The first condition, rise in body fluid tonicity, (28) is a stimulus for antidiuresis (1). Verney, in 1957, stated that a rise in osmotic pressure of as little as 1% was sufficient stimulus for release of ADH (43). This principle is the basis for the infusion of

hypertonic saline as a test of ability to produce ADH. Verney proved this by carotid artery infusions of saline. He confirmed the opinion that the arterial osmotic pressure acts as a stimulus to the hypophysis and it was not due to any "direct action" on the kidneys. He also showed that there was some specificity to NaCl because he also used infusions of sodium sulfate, dextrose, and urea. Sodium sulfate and dextrose were not as good a stimulus as NaCl but were indistinguishable from each other. Urea, however, was inactive as a stimulus for release of ADH. Gilman, in 1957, (21) indicated that perhaps it was the shrinkage of the cells in the body fluid rather than the increased tonicity since both urea and NaCl increase tonicity but urea passes freely into the cells and does not shrink the cells while NaCl does not enter the cells and does shrink them. He concluded that perhaps there were specialized receptor-cells in the hypothalamus which respond to shrinkage.

Decrease in fluid volume has been postulated as a stimulus, either with or without change in tonicity (40). It is also felt that a decrease in intracellular volume as well as extracellular volume may be a stimulus. According to Strauss (40), the left atrium sup-

posedly contains pressure receptors which elicit reflex responses in the hypothalamus when volume decreases, and thus there is a decreased pressure in the left atrium.

Stress has been documented as a stimulus for the release of antidiuretic hormone by many (10, 18, 24, 43). This was shown by Verney (43) to be independant of renal nerves and endogenous adrenaline, as well as changes in blood presure.

Direct pharmacologic action of administered substances has been shown to stimulate antidiuresis. Both nicotine and acteycholine have been used in the testing of neurohypophyseal function (9, 10, 18, 33).

This method of diagnosis has, in general, become rather unpopular because of the unpleasantness of the side reactions (sweating, nausea and vomiting, dyspnea and feeling of impending doom) which accompany a large enough dosage to elicit the desired antidiuretic response, and are somewhat unreliable in the data supplied by the response (9, 10, 33). Therefore, this pharmacological testing has little value clinically.

THE HYPOTHALAMIC THIRST CENTER AND OSMORECEPTORS: The concept of thirst is integrated in the hypothalamus, It is the conscious response to stimlli. Andersson (1) stimulated the hypothalamus in the region of the supra-

optic nucleus and promoted drinking in goats. He found that destruction of this area destroyed the desire to drink altogether. This response is transmitted to the cortical level and interpreted in the conscious awareness by the phenomenon of thirst. The origin of thirst may arise either centrally or peripherally. It was first thought that the basis for thirst was merely a dry mouth. But this is not a complete explanation since water deprivation produces thirst before it produces a dry mouth (18). Moreover, thirst is not relieved by simply wetting the mouth. Neither does an increase in salivary flow abolish the thirst. On the other hand, a dry mouth does not necessarily make a patient thirsty, as in the administration of atropine which may produce a dry mouth, but usually there is no complaint of thirst. Thirst may be the response to an increase in body fluid tonicity. Wolf (55) calculated a rise as little as 1% of osmotic pressure produces thirst. Verney (43) found that a similar rise is sufficient for the release of ADH. Also Wolf found that this small increment will produce a decrease in salivary flow. Thus, the central effect on thirst is reinforced by dryness of the mouth. Thirst accompanies a number of clinical states associated

with a decrease in extracellular volume without any change in tonicity (40). This symptom may often be the first sign of gastrointestinal hemorrhage, it often follows the removal of ascitic fluid, and may precede the appearance of edema in congestive heart failure or the nephrotic syndrome. It is felt that this is a reflection of the decreased circulating blood volume as interpreted by the receptors of the left atrium which are sensitive to pressure, as mentioned above.

Verney's experiments (43) justified the use of the term osmoreceptors. This term was descriptive of the autonomic receptive elements with which the neurohypophysis was linked and through whose activation the pituitary antidiuretic substance is released. He speculated that they were not in the carotid sinus but rather were limited to the hypothalamus. By stimulation and destruction techniques, he found that they were probably located in the anterior hypothalamic region but that functioning properly depended on the nervous connections with thalamic paraventricular nucleus. Dingman (15) reported that the site of the osmoreceptors was probably somewhere in the posterior pituitary gland or in the pituitary stalk rather than the supraoptic neurones or that no such structures

exist and ADH is stored in the perivascular regions of the posterior pituitary may be released directly into the blood stream when a hypertonic blood perfuses the gland. He supported this by finding that experimental destruction of the posterior pituitary gland resulted in a "diabetes insipidus-like syndrome" despite the preservation of hypothalamic neurosecretory function. However, I believe that the majority of the current authors agree with the thinking of Verney, in that the site of the osmoreceptors probably resides in the anterior hypothalamus.

The Concept of Free Water and Osmolal Clearance

The mathematical calculation of free water clearance and osmolal clearance by the kidney is a refined but very important procedure in the differentiation of pituitary polyuria and non-pituitary polyuria. The hydropenic kidney conserves water and excretes osmotically concentrated urine. The formulation of this theory is credited to H. W. Smith (38). It is based on the idea of dividing the volume of urine produced into two quantities.

$$V = C_{osm} + C_{H_2O}$$

In this formula, the volume of urine (V) is equal to the sum of the two quantities osmolal clearance (C_{osm}) and free water clearance (C_{H_2O}). Osmolal clearance is defined as that volume of urine which could contain the solutes excreted per minute at a concentration identical with that of plasma filtrate, i.e., isotonic with plasma. Recall, that the glomerular filtrate is isotonic with plasma and therefore the changes that take place are due to tubular transfer of water. The free water clearance is defined as the volume of water which makes theoretical

solute free portion of the given volume of urine. The C_{H_2O} thus has a positive value only when the urine is hypotonic, that is, when it has more water per unit volume than does the plasma. It obviously becomes a negative value when the urine is hypertonic, or when the urine is concentrated in excess of the plasma or glomerular filtrate. The negative free water clearance may be equated with the volume of water extracted from the isosmotic fluid which enters the tubules in the third operation which probably occurs in the collecting tubule. This formula takes added meaning with the introduction of another calculation.

$$C_{osm} = \frac{U_{osm}V}{P_{osm}}$$

The isotonic fraction of the urine (C_{osm}) is calculated by dividing the total solute excretion (U_{osm} V) by the osmolality of the plasma (P_{osm}). The total solute excretion is given by the product of urine flow (V) and urine osmolality (U_{osm}).

Therefore, if one can determine the urine and plasma osmolality, by substitution in the above formula, the osmolal clearance can be calculated. Since,

$$V = C_{osm} + C_{H_2O}$$

then by mathematical transposition of terms,

$$C_{H_2O} = V - C_{osm}$$

and knowing the urine volume and having calculated the osmolal clearance, the free water clearance can be determined. These numbers are conveniently diagramed in bar type graphs for presentation of data. (Figure 7)

It is difficult for some to visualize the free water quantity as a negative number as in the case of a hypertonic urine, and this value often takes on more meaning when assigned a positive number. This can be done again by considering that in a hypertonic urine a certain amount of free water has been extracted by the tubules and this is often referred to as the tubular free water ($T^C_{H_2O}$). Then if,

$$T^C_{H_2O} = -C_{H_2O}$$

by changing all signs of both sides of the equation,

$$-C_{H_2O} = V - C_{osm}$$

clear the minus sign and substituting,

$$T^{c}_{H_2O} = V - C_{osm}$$

or the negative free water clearance in hypertonic urine production becomes a positive entity if it is referred to as the tubular extraction of free water (T_{H_2O}).

It can then be stated that providing that no water has escaped the free water clearance is the volume of water originally containing the salt reabsorbed in the tubules. The capacity of these segments to reabsorb sodium then limits the amount of water that can be excreted above that of the isotonic substance.

The extremes of high and low urine concentration occurs when solute excretion is relatively decreased. The division of urine into the two portions makes this more understandable. When the solute load becomes greater dilute urine tends to become more concentrated or closer to isotonicity, and concentrated urine becomes more dilute or progresses toward isotonicity.

Etiology of Polyuria

The causes of polyuria as defined by De Wardener are set forth in a classification by site of pathology which is causing the polyuria (48, 49). The two causes of polyuria which are most pertinent are both the result of a diminished circulating antidiuretic hormone. This can be either the result of an impaired ability to secrete the hormone, such as in true diabetes insipidus, or the other general category is that of a decreased need or stimulation to secrete the hormone, as in primary polydipsia. There are other points of the classifications in both of these general categories. In the former, the inability to secrete antidiuretic hormone, there is a situation of a persistent defect such as classical diabetes insipidus where there is an organic lesion of the supropticoparaventricular region of the hypothalamus where the hormone is produced or lesions of the pituitary stalk through which the hormone is transmitted to the other possible site of the lesion, the posterior pituitary gland (7). It has been postulated that there can also be a transient defect in the ability to secrete the antidiuretic hormone, in contradistinction to absence of proper stimuli, as will be discussed below, in cases of compulsive water

drinking, where there possibly is, in addition to absent stimulus, a transient inability to produce the hormone even when proper stimuli are provided (46, 47, 50). It has also been shown that in potassium deficiency the neurohypophyseal system is related to the direct cause of the polyuria in that there is a transient inability to secrete the hormone (11, 18, 31, 39).

The latter general category, decreased need to secrete the hormone, first of all, is the case of psychogenic polydipsia which is felt to be the result of purely psychological disturbances without organic involvement. Again under this category of decreased need to secrete ADH, we must consider the case of potassium deficiency. Another problem which must be considered, especially in this case report, is the possibility of a lesion in the thirst center and the osmoreceptors which receive and transmit the response to changes in plasma osmolality. The possibility of an organic lesion here with disassociation of the thirst center from normal homeostatic mechanisms, whereby this control center may be completely knocked out and destroy the ability of the hypothalamus to produce the hormone because there are no stimuli presented to it by the osmoreceptor systems. These

are extremely uncommon but it appears that this must be considered a distinct possibility in this case. The polyuria of potassium deficiency is due to at least two mechanisms. The first being that of a primary increase in thirst, and secondly, that of an impaired ability to concentrate urine. Thirst may possibly be due to an impaired ability to secrete the antidiuretic hormone (31) as a result of hypokalemia. Another possibility under this heading is that of hypercalcuria and hypercalcemia. The reasons for polyuria being associated with this condition are not clear. It probably resembles the situation of potassium deficiency. In addition, there can be some actual primary polydipsia. It probably is due to an increased amount of ionized calcium in transit through the tubule cells and not due to precipitation of calcium in the tubules as was once thought (49). It has been observed by De Wardener (49) that in patients with elevated serum calcium levels that the urine will remain hypotonic even with exogenous administration of pitressin but a normal response can be obtained if the serum calcium is returned to normal and the patient is again administered pitressin, i.e., a hypertonic urine is produced.

There are, in addition, pathologic states in which polyuria is present in the presence of adequate circula-

ting antidiuretic hormone. This is the category where one must consider that the tubule wall has an impaired ability to respond to the hormone. This can be either congenital or acquired. There are two congenital types. (47) Nephrogenic diabetes insipidus is a problem of the tubular defect being the single defect. This situation is a familial, sex-linked condition of males. There have, however, been reported cases of heterozygous female carriers of this disease in whom there is mild concentrating impairment. In this nephrogenic type of diabetes insipidus, the urine osmolality is always less that that of the plasma and remains so even after exogenous administration of pitressin or after fluid deprivation and often the results are identical with both (13). There cases are usually not compatible with life, although some of the more mildly affected patients do survive to adulthood. The other congenital tubular defect is associated with several tubular lesions. It is that of Fanconi's syndrome. It is usually of later onset than nephrogenic diabetes insipidus and is often overshadowed by other systemic complications, such as rickets. This is associated with an acquired potassium deficiency due to excessive loss of potassium in the stool because of the diarrheal and sprue-like problem.

At this point it should be mentioned that the second major group is an acquired defect in the tubular response to circulating antidiuretic hormone exists in conditions previously listed under other headings above. These can also be classified at this point, and there are hypercalcuria and hypercalcemia, potassium deficiency, compulsive water drinking and diabetes insipidus (17, 25, 26, 50).

A third major group of pathologic conditions can be described as a loss of the ability of the interstitial fluid of the medulla to produce a hypertonic medium under which the mechanism of the counter current multiplier system may operate. It has been suggested that this condition is represented by partial renal artery occlusion, chronic pyelonephritis, and widespread gradual destruction of the nephrons as is found in most instances of chronic renal failure (2, 6, 51, 52).

A final broad group of etiological conditions are those things which result in a relative osmotic diuresis (30) because of an increased solute load per nephron. This occurs in cases where there is a normal number of functionally existing nephrons as in glycosuria and in an instance of salt diuresis following relief of a urinary obstruction. In a condition where there is a greatly reduced number of functioning nephrons, as in

chronic renal failure where a normal solute output is presented, the result is a relative osmotic diuresis because there are fewer normal nephrons to handle normal load presented.

Physiological Basis of the Differentiation of Diabetes Insipidus vs. Compulsive Water Drinking

De Wardener sets forth four criteria for making the clinical diagnosis of these two possibilities (47, 48, 49). An assessment of: 1) clinical features of the disease, 2) response to long acting vasopressin, 3) response to tests of neurohypophyseal integrity, and, 4) plasma osmolality.

First to be discussed will be the clinical features of the two entities (see Figure 1). The pattern of the patient's drinking habits may be a tip off as to the basic pathology involved. The cause and effect relationship applies well here when one considers that by definition, compulsive water drinking is a situation whereby due to some mental aberration, the patient has a markedly increased fluid intake and the effect is the polyuria. The pattern of this group would probably vary widely and fluctuate irregularly due to the varying mood and compulsion of the patient. In contrast to this, the diabetes insipidus patient has as its primary cause of polyuria, the inability to conserve water due to a persistent defect in the ability to secrete antidiuretic hormone due to an abnormality of the neurohypo-

physis. These patients will have a regular and fairly constant daily intake of fluid because of the set and unvarying mechanism of loss of water which requires a fairly regular intake to keep up. The pattern of the symptoms can be of assistance in making the differentiation (32). The compulsive water drinker often has a long standing history of frequent and obvious remissions and exacerbations. He will have periods of apparent relief only to relapse and again fall back into times of excessive intake (35). The incidence of these two diseases is interesting, although it does not apply in this particular case report. Compulsive water drinkers are characteristically postmenopausal women and diabetes insipidus is present equally in both sexes and is found most commonly before the age of 20, statistically speaking of the "average" patient, that is. In compulsive water drinking there is usually no other evidence of structural or systemic disease while in diabetes insipidus these factors are often present, possibly in the form of head trauma, which particularly confused the issue in this case report, and in diseases such as a supracellar cyst of the neurohypophysis, granuloma, neoplasm, syphilis, leukemia, etc. (40, 42). Compulsive water drinkers often have a history of previous mental disturbances ranging from conversion reactions,

hypochondriasis, compulsive eating, and there is a report of one patient who was caught pouring water into the bed pan in an attempt at increasing the apparent seriousness of polyuria to the observer. Mental disturbances are not typical of the diabetes insipidus patient. The compulsive water drinker may present with a chief complaint of headache, dizziness, and lassitude as a reflection of water intoxication while the diabetes insipidus patient, in contrast, may present with complaints of thirst and polyuria even though the former patient may also have this problem of thirst and polyuria to a terrific degree.

The second category for basis of the diagnosis is placed on the response to intramuscular injections of vasopressin tannate in oil, usually in the dosage of 5 Units. The compulsive water drinker typically has a rather early and marked decrease in urine flow but the thirst and excessive amount of intake will probably not change. In a few hours, the patient may feel distended, nauseated, and torpid, in other words feels much worse. However, the diabetes insipidus patient also has an early decrease in urine flow but within a few hours, thirst is diminished and the patient clearly feels relieved, grateful, and much improved generally.

The point of differentiation as suggested by

De Wardener is the response to tests of the neurohypophseal integrity. Since methods are not presently available for direct determinations of blood levels of antidiuretic hormone (5), the response to the various methods of testing are observed by changes in urine concentration. Basically, three tests assume the major role. First is the response to increased plasma osmolality and the contraction of the extracellular fluid volume by means rigidly controlled fluid deprivation. The second phase of this test is to evaluate response to increased plasma osmolality by means of a hypertonic saline infusion. And the third phase of the test is that of direct pharmocological stimulation, classically by the use of some such substance as nicotine. However, the use of nicotine in this test has been somewhat less popular because it is basically an unreliable test and since it is necessary to use such large doses of this drug in order to attain an antidiuretic response that the patient may become quite ill and very uncomfortable from the side effects. This test was not used in this case.

It has generally been concluded that the best test of neurohypophyseal integrity is that of fluid deprivation (29, 48, 49, 47). Jones (29) concluded that urine

following dehydration is more concentrated than after pitressin stimulation because of the mechanism which allows a greater proportion of tubular water to be reabsorbed independantly of rate of solute output and which works equally well in the presence of antidiuretic hormone or pitressin. He then goes on to say that the reason that the urine becomes more concentrated in patients with intact neurohypophyseal systems is that there is some factor which creates an adjunctive effect when there is a combination of dehydration and antidiuretic hormone, which there would be if the patient were able to secrete his own antidiuretic hormone. De Wardener has found infrequent cases of compulsive water drinkers in which the response to fluid deprivation was less than the response to exogenous pitressin and he postulates that in these cases there is probably present some renal tubular impairment, either from the long standing polyuria or from other causes. These patients also, it was concluded, probably have some degree of transient inhibition of neurohypophyseal activity. The physiological basis for the use of fluid deprivation in making a diagnostic evaluation of the polyuric patient rests with the principle that the renal concentrating process is conditioned to an im-

portant degree by the state of hydration of body tissues, including the cells of the renal tubules. Deprivation of fluid, obviously, decreases the hydrated state and acts as a stimulus for release of ADH, probably by two mechanisma: 1) increased tonicity of the extracellular and intracellar fluids, and, 2) by decrease of the circulating blood volume. These stimuli are originated at the osmoreceptors or the hypothalamus and by the pressure receptors of the left atrium, respectively.

The response to 2.5 to 5% hypertonic saline at a given rate following a water loading period of one hour was originally described by Hickey and Hare (27). Later other workers, Carter and Robbins (8) confirmed these experiments with a large series of tests. This test stimulates the neurohypophysis to secrete antidiuretic hormone because of a rise in vascular osmotic pressure. Barlow and De Wardener (47) report at least two disadvantages to this latter phase of the test in that they have found an osmotic diuresis may result and subsequently no change or little change in urine flow is obtained. They also report some isolated cases of precipitation of cardiac failure resulting from electrolyte imbalance.

De Wardener's fourth criteria for making the differentiation is the plasma osmolality determinations in these patients. He asserts that compulsive water drinkers will have a normal to slightly decreased osmolality in the range of 269 ± 14 mOsm/L. On the other hand diabetes insipidus patients tend to have a normal to slightly higher plasma osmolality in the range of 295 ± 15 mOsm/L. He states the normal range as being 280 ± 6 mOsm/L. This, of course, is not entirely reliable but it does tend to reflect the etiologh of the two diseases, In the former condition the patient initially increases intake and polyuria is the response, the patient tends to be ahead of the water balance. While in diabetes insipidus there is polyuria with thirst the result of contraction and concentration of body fluids and the patient is always a little behind on fluid balance.

A summary of the differentiation between compulsive water drinking and diabetes insipidus is seen in Table 3 (14, 46, 47, 48).

Table 3.

Differential Diagnosis of Compulsive Water Drinking (CWD) & Diabetes Insipidus (DI)

	CWD	DI
1. pattern of drinking	fluctuates widely; irreglar	constant day to day
2. pattern of symptoms	remissions & relapses	persist w/o remissions
3. incidence	postmenopausal women	equal in both sexes; before age 20
4. evidence of structural lesions	usually no evidence	often present: suprasellar cyst, neoplasms, trauma, etc.
5. confusing chief complaint	may complain of headache, dizziness, lassitude rather than thirst & polyuria	usually straight forward: complain of thirst & polyuria
6. previous mental disturbance	often present	usually negative
7. response to vasopressin (PIT)	decreased urine flow; thirst & intake unchanged; pt. feels worse	decreased urine flow & thirst; pt. feels much better
8. neurohypoph. tests (1) FD (2) hypertonic fl. (3) nicotine stim.	 urine conc. urine conc. urine conc.	 no change no change no change
9. comparison of #7 & #8	greater conc. with FD no matter how low, than with PIT	lesser conc. with FD no matter how high, than with PIT
10. plasma osmolality	slightly low	slightly high

Conclusion

It is the purpose of this paper to present a case report and discussion of a young boy who was severly injured in an auto-train accident and of the many injuries received, multiple fractures about the head and skull, including radiologically evident fracture lines of the basisphenoid bone and of the sella turcica itself. This patient developed a post-traumatic polyuria and polydipsia, which is the concern of this presentation.

This problem presented offers a good opportunity to investigate and review the physiological principles of the neurohypophyseal functions and of the renal concentrating mechanisma and the inter-relationship which exists. Because of the nature of the injuries, the onset and magnitude of polydipsia and polyuria, one had to be clinically suspicious of diabetes insipidus. However, the unique situation is that the neurohypophyseal function was proven to be intact, at least the antidiuretic system was operating. This problem then became one of the primary polydipsic type, as other causes of polyuria were ruled out by history, physical and laboratory evaluation. There was no

familial history of nephrogenic diabetes insipidus, the serum and urine electrolytes were normal, and urinary excretory function was normal.

The terms psychogenic polydipsia and compulsive water drinking and their hybrid, compulsive polydipsia, are all taken to be synonymous and interchangeable in this thesis. However, by De Wardener's definition, this problem is usually related to previously existing psychotic tendencies or other mental disturbances of the psyche. Here the only significant past history one finds is enuresis until eleven years of age, hardly basis for labeling one psychotic. The present disposition of the patient is that of a normally acting and appearing, young teenage male, certainly with no overt signs and symptoms of disturbed psyche. He had always been a "heavy water drinker" perhaps above or at least high normal range, though no accurate intake volumes are available. He has had no recurrances to date, nearly 18 months later. It has been considered that on the day that his jaw was wired for the multiple fractures, his intake became markedly increased. But it had been significantly above normal prior to this procedure. It is significant also that the patient is amnesic about this period of excessive intake.

It is possible this problem was not one of compulsive water drinking in the usual meaning of the term. It was an obvious primary polydipsia problem but whether or not it was compulsive or purely psychogenic is covered with some shadow of a doubt. It is possible that this problem was one of a transient organic lesion to the hypothalamic thirst center with an intact ADH secretory system. An attempt to prove this was made by daily injections of pitressin in an effort to drive the plasma osmolality down and institute a decrease of intake by the patient who had free access to water, thinking that perhaps the osmoreceptor control was intact but that perhaps there was a disassociation of the thirst center and the ADH system, and possibly the threshold of the thirst center was "set" at a different level. It was postulated that perhaps if the plasma tonicity was forced down very low, he would respond with a decrease in intake voluntarily. However, the results of this attempt were not very helpful because the patient responded by increasing his intake to the highest peak of the polydipsic episode. This was only significant in that primary polydipsics often do not decrease their intake in this instance. He also probably demonstrated some evidence of "resistance" or "release" from the exogenous vasopressin substance.

It was conclusively proven by tests of neurohypophseal function outlined above that this patient did not have diabetes insipidus or a diabetes insipidus-like syndrome. A truely compulsive or psychogenic problem seems unlikely in face of a negative psychiatric history both before and after. The existence of a transient organic lesion of the thirst center seems possible in view of the severe head trauma and hemorrhage of the intracranial vault, but definitive diagnosis is not possible in the absence of a pathologic diagnosis.

This patient had a primary polydipsic syndrome with an intact ADH system and an intact renal concentrating system.

Summary

In this thesis, a case report is presented which is that of a post-traumatic polydipsia and polyuria. The patient had multiple fractures and injuries, including basal skull fractures and more specifically, a fracture entering the sella turcica. The patient at admission was semi-comatose and blood was oozing from both ears. Initial laboratory findings are presented as are those of special tests of the neurohypophseal integrity. These include fluid deprivation, hypertonic saline infusion, parenteral pitressin, the latter two being consistent with the so-called Hickey-Hare test.

Results are presented along with illustrative graphs and charts, all of which, in general, are consistent with that of a primary polydipsic syndrome with intact ADH system.

A review of the physiological principles involved are presented including a brief discussion of the renal concentrating mechanism, the chemical structure, the site of production and storage, the factors determing its release, and its mode of action, as well as the hypothalamic thirst center and the osmoreceptors. A

rather detailed discussion is given on the concept of free water and osmolal clearance.

The pathophysiology of polyuria is presented as a section and then separate from that is a discussion of the basis for differentiating the two most prominent polyuric-polydipsic syndromes and the two which are the title of this thesis, diabetes insipidus and psychogenic polydipsia.

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