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Renal Function in Exercise.

By

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With 4 figures in the text.

(Eingegangen am 19. Juni 1937.)

The standard and the maximum blood urea clearances of *Moller, McIntosh* and *Van Slyke* [1] are effective indices of kidney activity. They are expressed as follows:

$$C_s = \frac{U\sqrt{V}}{B} \quad (1)$$

$$C_m = \frac{U\,V}{B} \quad (2)$$

where U = urine nitrogen in mg.%, V = ccm of urine per minute, and B = blood urea nitrogen in mg.%. C_m is used when V is above the augmentation limit of 2 ccm per min. The per cent of average normal C_m is obtained, as developed by the above authors, by dividing the absolute C_m value the mean normal C_m, 75, and multiplying by 100. Similarly the per cent of average normal C_s is obtained by dividing the absolute C_s by 54 and multiplying by 100. The urea clearance values presented here are in terms of per cent of average normal C_s or C_m, and unless qualified the word clearance in this paper will have that meaning.

Some efforts have been made to record kidney function in exercise. *Addis* and *Drury* [2] in 1923 reported the urea clearance ratio, $\frac{\text{hourly urea output}}{\text{urea in 100 ccm. blood}}$ in running to be 70% of the resting value. *MacKay* [3] in 1928 found a clearance value of only 35% during several sets of tennis. *Van Slyke, Alving* and *Rose* [4] in 1932 stated that nearly all of the clearances during severe exercise lay within the range 100 ± 30%. *Benzinger* [5] for exercise of fifteen minutes' duration found clearances of 25 to 75%. In all of *Benzinger*'s experiments clearances rapidly rose to normal after exercise. Recently *Light* and *Warren* [6] reported markedly decreased clearances in football, soccer and basketball players. The average value for 11 schoolboys (age 14 to 20 years) during a full game of football was 47.5. Clearances in soccer and basketball were also depressed to about this level. Average clearance in rest was 136% in this group of adolescents.

Christensen, Krogh and *Lindhard* [7] investigated diuresis as related to heavy muscular exercise, and found that filtration is maintained unaltered during work at the rate of 1,000 kg.-m. per minute on the ergometer. At higher levels of activity they found a reduced filtration, but it rises rapidly to the resting value or even somewhat above during recovery. Diuresis decreased in one experiment to only 20% of the value during rest. They concluded that the fall in diuresis finds a natural explanation in the loss of water by perspiration stimulating tubular reabsorption.

In the present study clearances were obtained on a group of normal subjects, first, while at rest or during slight activity such as walking about the laboratory since "being up and about caused no significant change in urea clearance values from values observed when subjects were in bed before and during excretory periods"[4]. Secondly, clearances were determined on the subjects during and after work on a motor-driven treadmill, oxygen consumption being determined for use as an index of the severity of the exercise. Clearances were also determined on this group following the subcutaneous injection of 1 mg. of adrenalin. Urine was collected during periods of about two hours. Near the mid-point of each period a blood sample was drawn from the ante-cubital vein for urea determination.

Finally, there are presented the clearances of 10 football players obtained during major contests. The playing time of each player was recorded as an index of the amount of exercise. Bladders were emptied and a blood sample obtained about an hour before the game began. Urine and blood samples were obtained immediately after the game. Urine urea nitrogen was determined by *Youngburg*'s modification of *Van Slyke* and *Cullen*'s method[8]. Blood urea nitrogen was determined by *Myers*' titrametric procedure[9].

Controls. Fourteen control tests were run on 12 subjects. The results, contained in Table 1, show an average value of 91. The range, 78—125,

Table 1. Urea Clearance Controls.

Expt. No.	Subject	Activity	Period mins.	Urine vol. ccm./min.	$(Urea\text{-}N)_b$ mg.%	$(Urea\text{-}N)_u$ mg.%	$(Urea\text{-}N)_u$ mg./hr.	Clearance C_s	Clearance C_m	Clearance % of Normal
1	C. H.	slight	66	3.02	25.6	582	1050	—	69	92
	,,	,,	67	1.75	24.7	852	895	46	—	85
7	M. C.	,,	120	.68	13.3	1100	445	68	—	125
9	H. A.	rest*	122	1.03	13.7	671	415	50	—	92
12	H. T. E.	slight	120	.48	16.8	1092	315	46	—	84
	F. C.	,,	120	1.80	17.5	738	795	56	—	101
	W. C.	,,	120	1.55	16.8	630	586	47	—	87
	R. J.	,,	118	.61	14.4	938	344	50	—	92
	D. B. D.	,,	126	.91	16.8	386	481	50	—	92
15	R. P.	rest*	120	3.03	18.2	406	739	—	68	90
	,,	,,	121	.87	13.8	644	336	43	—	80
25	B. D.	slight	120	.75	13.0	728	328	49	—	90
28	A. L.	,,	120	.85	9.6	442	221	42	—	78
34	L. E.	,,	120	.66	13.0	686	275	43	—	79

* Basal.

agrees well with that given by *Van Slyke*, *Alving* and *Rose* [4], viz. 100 ± 30. All but 2 of our subjects were older than the adolescents studied by *Light* and *Warren* [6] in whom the range was 85—241 with an average of 136. Our 2 youngest subjects, aged 19 and 21, showed values of 90 and 125 respectively.

Measured Work. The results of the study of 28 work periods of varying intensity and 16 recovery periods on 8 men are shown in Table 2. The average clearance is 69 per cent of normal. Figure 1 provides a basis for comparing clearances in work with observations made on the same subjects in rest and also after adrenalin.

During work 17 points were below 70, the normal minimum set by *Van Slyke*, et al.[4]. The average of these points is 55, the range being

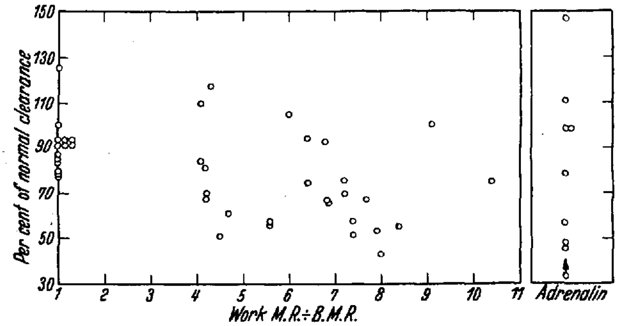

Fig. 1. Urea clearance in normal man. The intensity of work is expressed as the ratio of oxygen consumption in work (Work M. R.) to the basal oxygen consumption (BMR). The clearances when this ratio is unity represent resting state. Observations made after injecting 1 mg. of adrenalin in resting subjects are shown for comparison.

39—69. The other 11 points range from 73 to 117 and average 91. Three of these were on the same subject doing the same grade of work. His initial clearances in work were 92, 73 and 93. In the following periods his clearances ranged from 51 to 66 as shown in Table 2, Expts. 6, 13 and 15. The delayed recovery in Expts. 13 and 15 will be mentioned below.

Four others of the 11 high points were from the work of lightest intensity, Expts. 2 and 10. One other was 74, or below the range of our controls. Finally, the high ano malous clearances in Expts. 22, 23 and 36 may be related to the fact that the two subjects were young and untrained. While Figure 1 reveals no simple relation of clearance value to work duration, it is clear that a decreased clearance in exercise is more common than was reported by *Van Slyke* and his associates [4].

Clearances in continuous and in intermittent work are shown in Figure 2. Within the range of work intensity studied there is no simple relation between clearance and intensity of work, although all but two observations are below 100%. Neither is there a well-defined trend in clearance as work continues; in one case there was a decrease, in two, an

Table 2. Urea Clearance in Exercise.

Expt. No.	Subject	Activity	Period	Urine vol.	$(Urea\text{-}N)_b$	$(Urea\text{-}N)_u$		Clearance		
			mins.	ccm./min.	mg.%	mg.%	mg./hr.	C_s	C_m	% of Normal
2	H. A.	4.2×BMR	34	1.35	30.6	977	792	37	—	69
		4.2×BMR	61	1.02	31.7	1117	715	36	—	66
		4.2×BMR	60	.48	30.2	1900	547	43	—	80
3	H. A.	7.4×BMR	94	.59	13.3	464	164	27	—	50
		slight	86	.38	13.3	822	187	38	—	71
		7.4×BMR	123	.36	16.5	831	180	30	—	56
4	H. A.	7.2×BMR	126	.33	18.2	1168	231	37	—	68
		7.2×BMR	150	.31	18.2	1319	245	40	—	74
6	R. P.	6.8×BMR	29	5.24	22.4	294	925	—	69	92
		6.8×BMR	61	1.81	22.4	482	522	29	—	54
		6.8×BMR	62	1.24	22.4	588	440	29	—	54
8	R. P.	5.6×BMR	122	.73	20.1	734	319	31	—	57
		rest	60	.45	19.4	722	195	25	—	46
		5.6×BMR	121	.48	19.4	840	242	30	—	56
		rest	59	.38	19.4	816	185	26	—	48
		6.1×BMR	122	.48	27.3	927	267	23	—	43
10	R. P.	4.1×BMR	121	.55	12.9	778	258	45	—	83
		rest	59	.47	13.6	—	—	—	—	—
		4.1×BMR	122	.42	13.2	1192	300	59	—	109
		rest	56	.38	12.7	1242	324	60	—	110
		4.1×BMR	124	.39	12.6	1285	300	63	—	117
11	H. A.	4.5×BMR	152	1.86	15.7	313	350	27	—	50
		slight	100	.55	15.3	734	242	36	—	66
		4.7×BMR	185	.44	16.8	818	216	32	—	60
13	R. P.	rest*	1212	.87	13.8	644	336	43	—	80
		6.4×BMR	123	.50	14.0	784	235	39	—	73
		rest	120	.34	15.4	755	151	28	—	53
		rest	120	.25	15.1	836	125	28	—	51
15	R. P.	rest*	120	3.03	18.2	406	738	—	68	90
		6.4×BMR	125	3.80	16.1	297	675	—	70	93
		slight	116	1.07	13.7	400	257	30	—	56
		„	133	.76	15.8	650	293	36	—	66
19	D.B.D.	8.4×BMR	132	.37	17.3	818	186	29	—	54
		slight	65	.45	17.4	805	148	31	—	58
		„	81	.33	16.9	1290	165	44	—	81
16	F. C.	7.7×BMR	135	.66	12.8	561	227	36	—	66
		slight	58	.59	15.3	543	181	28	—	50
22	M. C.	6.0×BMR	127	.77	14.7	937	420	56	—	104
		slight	121	.59	14.0	1084	378	60	—	110
23	B. D.	9.1×BMR	132	1.08	11.9	626	403	54	—	100
		slight	115	.85	12.3	666	340	50	—	92
26	A. L.	8.0×BMR	130	.84	12.2	300	147	23	—	42
		slight	122	.67	10.0	696	281	57	—	106
30	L. E.	7.9×BMR	125	1.57	8.5	193	182	28	—	52
		slight	120	1.04	8.5	288	180	34	—	63
32	M. C.	6.3×BMR	126	.57	7.5	209	72	21	—	39
36	B. D.	10.4×BMR	124	.43	13.8	860	224	41	—	75

* Basal.

increase and in four, little or no change. The same figure shows the rate of urine secretion. Under the conditions of these experiments there is little dependence of urine secretion on work intensity although the rate of secretion in many instances was less than one-half normal. The diminished rate of urine flow no doubt depends on sweat losses, as suggested by *Christensen, Krogh* and *Lindhard*[7], but it may also depend on movement of water from blood serum to tissues.

The concentration of urea in urine and the rate of urea excretion in the foregoing experiments are shown in Figure 3. In most instances

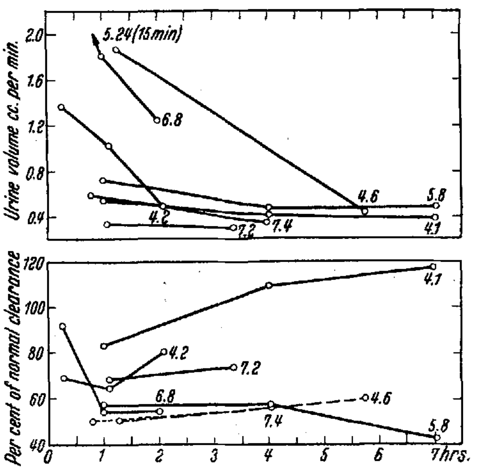

Fig. 2.

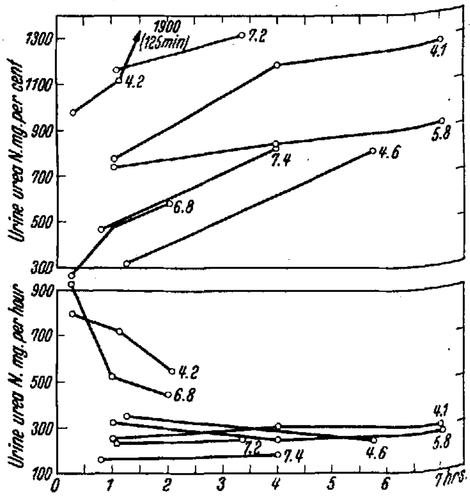

Fig. 3.

Fig. 2. Urea clearance (below) and urine flow (above) in relation to duration and intensity of work.

Fig. 3. Rate of urea excretion (below) and urea concentration in urine (above) in relation to duration and intensity of work.

the excretion of urea nitrogen is below the ordinary rest level of about 300 mg per hour, although *Wilson* and associates[10] report that a rise in urea excretion results from exercise of long duration. The concentration of urea in urine rises without exception, reflecting the successful conservation of water. The concentration of urea in blood (Table 2) rarely showed marked alteration during the course of these experiments, but one would not expect significant increases in blood urea concentration during such a period unless marked retention had occurred. The excretion of some urea by the sweat glands and the large volume of body water in which urea is dissolved explain the absence of changes in blood urea despite alterations in renal function.

Recovery. The 16 observations on recovery (Table 2) show declines in volume output in all cases. Concentration of urea nitrogen in urine rose distinctly in 11 instances and fell slightly in 5. The output per hour, however, was lower in 12 instances. One-half of the urea clearances were greater than during work, but 11 remained below for from 1 to 4 hours.

Experiments 13 and 15, previously referred to, reveal no rapid rise of clearances to normal after 2 hours' exercise. *Benzinger*'s conclusion, based on a study of recovery after 15 minutes' work, is not applicable to recovery after prolonged exercise. The other recovery figures bear this out with the exception of Expt. 26. Experiments 8, 13, 15 and 16 show that the effect of prolonged and heavy exercise on urea clearance may be evident for as long as four hours after the exercise is concluded. This will be mentioned in the interpretation of the clearances during football play.

Adrenalin. Results of the injection of 1 mg of adrenalin on 7 subjects are given in Table 3. They are plotted, for comparison, to the right in Figure 1. The clearance values ranged from 33 to 147. The average was 78 for a period of 2 hours after the injection. The two young men, inexperienced as laboratory subjects, gave values of 147 and 98 in their first test. On repeating the test they were 33 and 68 respectively: Expts. 21, 33, 24 and 35. Five of the 9 values which were below the normal range averaged 50.

Table 3. Urea Clearances. (Following injection of 1 mg. adrenalin.)

Expt. No.	Subject	Activity	Period mins.	Urine vol. ccm./min.	$(Urea\text{-}N)_b$ mg.%	$(Urea\text{-}N)_u$ mg.%	$(Urea\text{-}N)_u$ mg./hr.	Clearance C_s	Clearance C_m	Clearance % of Normal
17	D. B. D.	slight	63	.33	16.8	714	141	24	—	45
		,,	74	.29	17.4	773	136	24	—	45
18	R. J.	,,	59	.41	10.6	556	139	34	—	62
		,,	59	.26	10.7	588	94	28	—	52
20	F. C.	,,	120	.73	16.3	1151	506	60	—	111
21	B. D.	,,	120	.45	11.3	1383	374	80	—	147
24	M. C.	,,	121	.49	16.8	1275	373	53	—	98
		,,	118	.64	14.9	1205	455	65	—	126
		,,	120	.61	14.2	857	308	47	—	87
31	A. L.	,,	126	1.58	8.8	179	175	26	—	48
33	B. D.	,,	109	.58	10.2	240	87	18	—	33
34	L. E.	,,	125	.66	11.8	773	307	53	—	98
35	M. C.	,,	126	.38	16.5	984	226	37	—	68

Football. Data on the 10 football players is presented in Table 4 and Figure 4. From the figure it appears that the clearance values are roughly inversely proportional to the playing time. Though the data are few, the lower part of the curve agrees with the average value of 47.5 reported by *Light* and *Warren* [6] for 11 boys who played a full game of football. The inverse relation of clearance values to playing time and the lack of close relation between intensity of work and urea clearance (Figure 1) are not necessarily inconsistent. Football players are in action for only about a quarter of an hour. Our clearance study covers a period of about 4 hours and hence includes both work and recovery.

Table 4. Urea Clearance During Football Playing.

Subject	Period	Playing time	Urine vol.	$(Urea\text{-}N)_b$	$(Urea\text{-}N)_u$		Clearance	
	min.	min.	ccm./min.	mg.%	mg.%	mg./hr.	C_s	% of Normal
J	201	30	.37	20.4	854	190	26	47
D	201	12	.60	17.4	925	333	41	77
N	211	55	.71	17.5	404	172	34	36
S	209	15	.67	11.9	534	214	37	68
A	209	25	.61	14.6	560	205	30	56
H	170	0	2.26	12.5	391	531	70*	93
K	180	0	1.25	19.3	739	554	44	81
O	226	17	.56	21.6	909	305	32	59
Wi	236	18	.80	18.7	602	289	29	53
Wa	211	28	.72	23.1	910	393	33	62

* C_m.

Two clearances obtained on players who sat on the bench throughout the game were 81 and 93. Apparently urea clearance, like blood sugar [11], lactic acid [12] and the leucocyte count [13], is unaffected by this experience. Yet the injection of 1 mg. of adrenalin tends to lower the urea clearance and to markedly increase the other values mentioned.

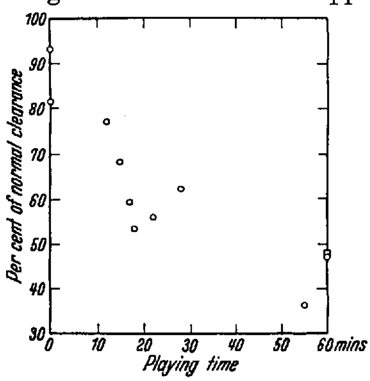

Fig. 4. Urea clearance in football players in relation to duration of play.

Mechanics of Urea Excretion. The filtration-reabsorption theory assumas that water and crystalloids leave the blood in the glomeruli forming an ultra-filtrate of the blood with the same concentration of the diffusible substances, from which about 97% of the water and some of the diffusible substances are reabsorbed through the tubular epithelium.

Lassen and *Husfeldt* [14] believe that the filtration is proportional to the available pressure for filtration, i. e., the *forward* hydrostatic pressure in the glomeruli, the *back* colloid osmotic pressure, and the *back* hydrostatic pressure in the glomerular capsule. They have demonstrated that glomerular filtration is directly affected by change in blood pressure.

Bock, *Van Caulert*, *Dill*, *Fölling* and *Hurxthal* [15] have recorded a change in pulse pressure from a value of 22 mm. Hg in rest to 70 mm. Hg (the diastolic pressure remaining unchanged) within the first minute of exercise requiring an oxygen consumption of about two liters per minute. The urea clearances here recorded did not change in the same direction as the pulse pressure.

The plasma protein content rose from 6.8% in rest to 7.3% after completing 6 hours of exercise (H. A., Expt. 11, Table 2) at an oxygen consumption of 1.1 Liters per minute. *Dill*, *Talbott* and *Edwards* [16] recorded an average change from 6.86 to 7.60% from rest to work for 17 to 18 minutes with an oxygen consumption of 2.4 liters per minute. *Keys* and *Taylor* [17] in 8 experiments which produced exhaustion in one minute found a rise from 7.11 to 7.99 gm. per cent in plasma protein content. The colloidal osmotic pressure, however, generally decreased due, it was suggested, to change of the mean size of the protein molecules. No changes in measurements of colloidal osmotic pressure seem to have been made in exercise of long duration. It is improbable that changes of the order we have observed in urea clearances can be due to changes in concentration or properties of serum proteins.

A likely explanation of reduced urea clearances in exercise is that renal blood flow is diminished due to the demand of heavily working muscles and the possible dehydration of the blood by sweating [4]. *Van Slyke Rhoads*, *Hiller* and *Alving* [18] have shown that the urea excretion varies directly with renal blood flow. The shunting of blood from the splanchnic region in exercise has long been assumed. *MacKeith* [19] in accounting for anuria in running stated that it may be due to the dilatation of the cutaneous vessels and constriction of the splanchnic vessels, for the maintenance of blood pressure.

Winton and *Bayliss* [20] in a summary of factors controlling urine flow include adrenalin as one of the elements effecting a fall in glomerular capillary pressure with consequent decrease in kidney function. *Raymond-Hamet* [21] has reported that adrenalin can provoke renal vaso-constriction; evidence for the secretion of adrenalin in athletic contests is found in the augmented concentration of blood sugar. The interrelation of adrenalin secretion, renal vaso-constriction, and diminished urea clearance is entirely possible; the experiments recorded above do not substantiate or deny this view.

Summary. Fourteen control tests for urea clearance on 12 subjects gave an average of 91% and a range of 78—125%. In work of varying intensity over a fixed time, the clearance values range from 39 to 117 per cent and are usually low. They have a roughly inverse relation to the intensity of work. In five of seven resting subjects urea clearance values were markedly lowered after injecting subcutaneously 1 mg. of adrenalin. From the clearance values obtained in recovery it appears that the effect of exercise on the urea clearance by the kidney may persist for several hours.

Studies made under controlled conditions in the laboratory were supplemented by observations made on football players. In this case the period was 4 hours in length, so that an over-all effect of exercise and recovery is measured. The American game of football involves intense emotional stimulation as well as physical exercise. It is intermittent

in character with no more than 15 minutes during which the ball is in motion in the 60 minutes of playing time. With rest periods included, the game lasts about 2 hours. Our conclusion is that there is a cumulative effect of football play on renal function; to be sure, this is a temporary phenomenon but it is of interest both to clinical and to research medicine.

The clinical observer in competitive athletics has been looking to the physiologist year by year to ascertain the physiological factors making up the conglomerate picture of physical fatigue. The trained athlete is becoming more and more completely understood, and although one does not comprehend all factors making up the balance of a well trained athlete, one is still learning. Through studies in physical fatigue the physiologist is advencing toward the complete comprehension of strenuous muscular exercise.

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