CERTAIN ENDOCRINAL ASPECTS OF RHEUMATIC AND RHEUMATOID AFFECTIONS

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The connective tissue anabolicaivd metabolk activities are Known to influence and to be infuenced by various hormonal secretion. (Prunty 1953, Aspoe-Hansem 1959, Thus a positive correlation seems to exist between the connective tissue disturbancess on one hand and certain hormonal imbalances which should be involved in the other hand.

Such correlation is well domonstrated in rheumatic and rheumatoid afections and certain other autoimmune diseases which frequently show a dramtic response towards certain hormonal therapies inspite of the fact that the actual nature, rate pathogenesis of the endocrinal involvement is still obscure and a subject matter of many discussions.

Thus the first attention was towards the adrenal cortical function was suggested by Brown (1951) to be responsible for the antimmune involvements and did show an abnormal response to stress due to its hypoactivity as reported by various workes (Selye, 1951, Hill etal 1959; Kelley 1961; Gavsyshova 1954). This view however was opposed by Peterson rtal 1955, mazztonacci 1965, Jchikawa 1966 and Pol 1970, who reported an almost normal secretion and exeretion rates of cortisol in rheumatic and rheumatoid affections. Noverthelless, a certain form of metabolic derangement in the supraenal certicosteroids has been unanimously agreed upon amongst the various workers although its precise is still debated. The liver being the site of many metabolic involvement including particularly the corticosteroid metabolism, as became lately underlined by Bailey etal 1966, Rendal etal 1970, Cockel etal 1971 and Abdl Abul Fad 1972.

The Thyroid gland has also been suspected to have an involvement in rheumatic afections since the first reports. of cartan (1950) in connection with the hypocholestrelemia prevailing in such conditions. Rheumatic fever was reported to proceed thyroid hyperfunction and could play a role in the development of thyrotoxicosis (Pecheneve 1959) Thus hyperthy roidism and rheumatic affections,each of them seem to aggravate the other (Kryzymien & Michalsbei (1959) .When the thyroid function was assessed by labortory aids however, cortra dictory resuls were obtained by different groups of workers: Berezkov 1958, Tzonov 1965 reported hyperfunction, while Wolfson etal 1951, Short

etal 1957 and luper etal 1965, reported hypoactivity of the thyroid in rheumatic children.

The parathyroid function in rheumatics and rheumatoids has not yet been settled due to the wide rangs of opinion as regards the calcuim, phosphourus and alkaline phosphatase status in such affections.

Because of such uncertainity and controversion of the various points of views on this subject, it was decided to carry out a series of invest igations on a total number of over 300 patients sending mostly at the free Rheumatic Heart center as well as in the University hospitals at Cairo, Tanta and Mansoura. All the investigations were Practically conduced on a group of normal children of not less than 100 in number falling within the age groups as those of the patinets. The clinical diagnosis of the rheumatic and the rheumatoid afffections was conduced by Prof. Abdin and was assessed by the different laboratory aids.

The laboratory assessment of the thyroid function was conduced by determining the blood plasma (T4) levels using the ion exchange method (dBiored), the plasma cholestrol, the blood levels and urinary excretion of creatinine and the urinary hydroxyproline excretion.

The blood serium calcium magnesium phosphorus and alkaline phosphatase and the 24hr. urine calcuim and phosphorus. The blood serum total protenin and albumin were also determined.

The suprarenal cortical function was assessed by determining the urinary neutral 17-oxosteroid, the 17-hydroxycorticosteroids and 17 Ketogenic steroids according to Norymberski, Stubbs and Wert 1953.

Blood serum electrolytes: Sodium and potassium were determined by flame photometry.

The hypothalamo-pituitary-adrenal cortex function was assessed by detemining the above urinary steroids before and after intramuscular and oral admenstabo of ACTH and metyrapone respectively. The ACTH was first given on three successive days collecting complete 24hr. urine every time followed by rest period of 7 days .The metyrapone was then given orally on two successive days to the same group of patients with similar collections. The following tables represent sammaries of the results obtained togehter with the necessary atatistical analyses :—

TABLE (1) Shows the range, average and S.D. values for blood plasma thyroxin levels in rheumatic and rheumatoid affections. In rheumatic arthrities with above the upper limit of normality in more than 50% of the cases which indicate a definite tendency towards hyperactivity. This was also the case with rheumatic chorea with carditis and rheumaticcarditis accompanied with heart failure but not in rheumatic chorea simple without carditis. In rheumatoid

TABLE 1:

THE BLOOD PLASMA THYROXINE (T) LEVELS IN RHEUMATIC AND RHEUMATOID AFFECTIONS IN CHILDREN (RANGE, AVERAGE AND S.D. IN ug/100 ml BLOOD PLASMA

	Rh. *tic* Arth.&Card.s	Rh. *tic* Card.&Ht.F.	Rh. *tic* Chorea	Rh.*tic* Chor. with Cardits	Rh.*toid* Arthritis	Normal Control
Rang	5.7 – 10.4	5.2 – 10.2	3.7 – 8.6	4 – 12	4 – 8.8	3.7 – 8.0
Mean	8.4	8.2	6.9	8.1	6.3	5.8
S.D. –	1.49	1.24	1.54	2.03	1.04	1.3
Sig. at P– 0.05	– –	Sig. –	Sig.	* Sig. – –	Sig.	

TABLE 2:

BLOOD PLASMA CREATINE AND CREATININE LEVELS IN RHEUMATIC AND RHEUMATOID CHILDREN (MEAN VALUES IN mg/100 ml.)

	Rh. *tic* Arth.&Card.s		Rh. *tic* Card.&Ht.F.		Rh. *tic* Chorea		Rh.*tic* Chor. with Cardits		Rh.*toid* Arthritis		Normal Control	
	Ctine	*Ctinine*	*Ctine*	*Ctinine*	*Ctine*	*Ctinine*	*Ctine*	*Ctinine*	*Ctine*	*Ctinine*	*Ctine*	*Ctinni*
Mean	0.9	0.7	0.8	0.8	0.5	0.7	0.9	0.6	0.6	0.6	0.4	0.9
S.D. –	0.3	0.4	0.4	0.3	0.3	0.2	0.3	0.2	0.25	0.2	0.2	0.2
Sig. at P– 0.05	–	–	–	–	–	–	–	–	–			

TABLE 3:

URINARY EXCRETION OF CREATINE AND CREATININE IN RHEUMATIC AND RHEUMATOID CHILDREN (mg/24 hr. Urine)

	Rh. *tic* Arth.&Card.s		Rh. *tic* Card.&Ht.F.		Rh. *tic* Chorea		Rh. *tic* Chor. with Cardits		Rh*toid* Arthritis		Normal Control	
	in	*inine*	*in*	*inine*	*in*	*inine*	*in*	*inine*	*in*	*inine*	*in*	*inine*
Mean values	681	194	674	301	690	133	751	275	498	109	859	109
S.D. –	359	134	236	148	170	47	333	140	207	88	309	68
Sig. at P– 0.05	* Sig.		* Sig.				* Sig.					

TABLE 5:

THE FASTING "TRUE" BLOOD SUGAR LEVELS IN RHEUMATIC AND PHEUMATOID CHILDREN (MEAN VALUES IN mg/100 ml.)

	Rh. *tic* Arth.&Card.s	Rh. *tic* Card.&Ht.F.	Rh. *tic* Chorea	Rh.*tic* Chor. with Cardits	Rh*toid* Arthritis	Normal Control
MEAN	83	80	76	84.8	70	72
S. D. –	9.4	7.1	8.6	6.3	4.7	6.7
Sig. at P–0.05	* Sig.	* Sig.	—	* Sig.	—	

TABLE 6:

THE URINARY EXCRETION OF 4–OH–PROLINEIN REHUMATIC AND RHEUMATOID AFFECTIONS IN CHILDREN BELOW 11 YEARS (mg/24 hr.)

	Rh. *tic* Arth.&Card.s	Rh. *tic* Card.&Ht.F.	Rh. *tic* Chorea	Rh.*tic* Chor. with Cardits	Rh*toid* Arthritis	Normal Control
Range	45.6 –64.4	42.5 – 58.7	180 – 49.5	38.8 – 52.5	14.4 – 32.0	19.3 – 57
Mean	52	47.8	28.5	45.7	20.8	31.8
Sig. at P– 0.05	* Sig.	* Sig.	—	* Sig.	* Sig.	

TABLE 7:

BLOOD SERUM CALCIUM LEVELS IN RHEUMATIC AND REUMATOID AFFECTION IN CHILDREN (Rrange and mean values in mEg/1)

	Rh. *tic* Arth.&Card.s	Rh. *tic* Card.&Ht.F.	Rh. *tic* Chorea	Rh.*tic* Chor. with Cardits	Rh*toid* Arthritis	Normal Control
Range	3.5 – 5.2	3.9 – 5.5	4.4 – 6.0	3.3 – 5.6	3.7 – 5.6	4.7 – 6
Mean	4.2	4.6	5.0	4.6	4.8	5.1
S.D. –	0.58	0.53	0.64	0.53	0.5	0.36
Sig. at P– 0.05	* Sig.	* Sig.	—	* Sig.	—	

TABLE 9:

THE BLOOD SERUM ELECROLYTES IN RHEUMATIC AND RHEUMATOID CHILDREN (AVERAGE VA:JES IN m Eg/1)

	Control		Rh.tic Arth. Card.		Rh.tic Card & Ht.F.		Rh.tic Chorea		Rheumatic Chorea with Card.		Rh.tic. Arthrites	
	Na	*K*	*Na*	*K*	*Na*	*K*	*Na*	*K*	*Na*	*K*	*Na*	*K*
Mean	139	4.3	139	4.1	141	4.9	138.8	4.2	139.5	4.2	139.5	4.2
S.D. –	2.8	1.3	1.9	0.2	2.3	0.3	2.6	0.2	2.4	0.4	3.1	0.3
Sig. at P– 0.05	—	—	—	—	—	—	—	—	—	—	—	—

TABLE 10:

URINARY N-7- OXOSTEROID EXCRETION IN RHEMATIC AND RHEUMAT OID CHILD REN 5-11 YEARS OLD (mg/24 hr,)

	Normal Controls	Rh.tic Arthrx Card.	Rh.tic Arth. & card. with Ht. F.	Rh.ticChorea	Rh.tic Chorea & Card	Rheumatoid Arthritis
Range	1.8 – 4.3	1.8 – 3.3	1.3 – 2.9	1.7 – 4.2	1.6 – 3.9	1.4 – 2.9
Mean	3.1	2.6	2.2	2.5	2.3	2.1
S.D. –	0.64	0.28	0.45	0.84	0.34	0.16
Sig. at P– 0.05	* Sig.	* Sig.	—	* Sig.	* Sig.	

TABLE 11:

URINARY CORTICOSTEROID EXCRETION IN RHEUMATIC AND HEUMATOID CHILD-REN 5–11 YEARS OLD (mg/24 hr) RANGE AND MEAN VALUES)

	Normal Control	Rhic Arth. & Card.	Rhic. Arth. & Ht. F.	Rhic. Chorea	Rhic Chorea & Cardits	Rheumatoid Arthritis.
17 Oxogein Corticoids	1.8 – 5.9	1.6 – 5.2	0.7 – 4.3	1.8 – 4.7	1.2 – 4.3	1.7 – 2.8
Mean	3.4	2.4	2.4	2.9	2.2	2.1
17 Hydrox. Corticoid	1.8 – 6.5	1.8 – 4.5	1.7 – 4.3	1.9 – 5.2	1.7 – 4.5	0.9 – 2.8
Mean	3.4	2.8	2.6	3.0	2.4	2.1
Sig	*	*	*	*	*	*

TABLE 12:

HYPOTHALAMO-PETUITARY – ADRENAL CORTEX

ASSESSMENT IN RHEUMATIC CARDITIS CHILDREN 5–11 YEARS (MEAN VALUES FOR 15 CHILDREN)

EFFECT ACTH AND METYRAPONE ADMINSTRATION ON THE URINARY EXCRETION OF CORTICOSTEROIDS.

(1) 17-*Oxogenic Urinary Steroid Excretion mg*/24 *hrs.*

		Responce to i.m. A C T H		
BASAL		IST DAY	2ND DAY	3RD DAY
Normal control	3.9	12.4	12.7	15.5
		(–213%)	(–220%)	(–280%)
Rh. Arth. x Card.	2.5	6.2	6.8	6.8
		(–140%)	(–170%)	(–170%)
		* Sig.	* £	*

(2) 17–*OH Corticostuiroel excretion in mg*/24 hrs.

	BASAL	1ST DAY	2ND DAY
Normal Control:	4.45	14.05	17.4
		(–315%)	(–390%)
Rhic. Arth & Card:	3.06	9.25	9.53
Sig Test.		(–309%)	(–358%)

arthritis however, there was much less tendency towards hyperthyroxoemia although about 20% of thecases were either or slightly exceeding the high norma levels.

TABLE (2) Represents the mean values for the blood plasma creatine and creatinine levels in rheumatic or rehumatoid affections. The creatine levels showed slight to mederate but everytime significant increases in all carditis cases but much less so in rheumatoid afections.

TABLE (3) Shows the urinary excretion of creatine and creatinine in the above cases which alse illustrates the significantly increased urinry excretion of creatine in craditis cases particularly in those with heart failure.

TABLE (4) Shows the blood plasma cholestrol levels, the mean values for carditis cases were significantly reduced as compared with the control group as well as the rheumatoid cases.

TABLE (5) Gives the avarage fasting true blood sugar levels in rheumatic and rheumatoid children. There was mild but significant elevation in most of the rheumatic carditis group.

TABLE (6) gives the range and average urinary excertion ot 4(OH) proline in rheumatic and rheumatoid children below 11 years. The marked increas in the excretion of this metabolite in carditis cases was demonstrable. In simple chorea involvements; the excretion was within normal while in rheumatoid affections it was significantly subnormal.

In children above II years of age, however, such changes were not so prominent.

TABLE (7) illustrates the blood serum in rheumatic and rheumatoid affections. There was mild but significant deminution in the mean values of carditis cases as compared with the normals the chorea and the rheumatoid groups. This might possibly be attribted to either some hyper acti vity or certain changes in the plasma proteins since the non diffusible fraction of the serum is associated with albuim.

TABLE (8) demonstrates the mean values for total plasma proteins and albumin fraction in rheumatic and rheumatoid children. There was variable degrees of hypernatraemia in rheumatic carditis with mild hyperprnatraemia in the rheumatiod group. The albumin fractoins were significantly on the low side of normal in all groups as Compared with contrls.

TABLE (9) show the blood serum electrolyte levels. The mean values showed no significant avriation in the different patient groups as Compared with normal

TABLE (10) shows the respective urinary 17-oxsteroid and corticosteroid excretion in the dierent groups of patients as composed with normal child ren

at the same age groups which showed significant deminutions in the rheumatic carditis groups as well as the rheumatoid children.

The effect of ACTH parentral and oral metayrapone adminstration is illustrated in the following table (II) in this table the response to ACTH was subnormal .This indicates a mild to moderate degree of suprarenal hypofunction while the hypophesial and possibly the hypothalamic functions were within normal in rheumatic affections.

Our findings could thus be summarisc as follows :—

(1) The data obtained concerning the T4 and cholesteral levels in blood plasma and the creatine levels in blood and urine together with the hydroxyproline urinary excretion, indicate that.

— The functional state of the thyroid gland seemed to be on the side of chemical hyperactivity in active rheumatic carditis with or without heart failure, and to a less extest in chorea with carditis but not in rheumatoid arthitis.

(2) The parathyroid function as judged by the blood serum calcium and inorganic phosphorus levels and their urinary excretion together with the blood sreum alkaline phosphatase activity, does not seem to be affected.

(3) (3) The studies conducted on the urinary oxosteriod and corticosteroid excretion before and after ACTH adminstration showed subnormality with respect to the adrenocorltcoidal function in most group of rheumatic and rheumatoid affections. The mineralocrticoidal function, on the other hands, did not seem to be appreciably affected as judged from the minimal changes in most groups of rheumatic and rheumatoid affections. The mineralocrticoidal function, on the other hands, did not seem to be appreciably affected as judged from the minimal changes in the eelectrolyte patiern of these patients.

(4) The hypothalamo pituitary adrenocorttical function as assessed by the intramuscular ACTH and the oral metyraponae dministration effect on the urinary corticosteroid excretion, seemsed to be within normal response in different reheumatic and rheumatoid affections.

REFERENCES

Abdin, Z.H. & Eissa, A. (1965) Ann. Rheum. Dis. 24, 389

Asboe-Hansen, G. (1959), Amer. J. Med. 26, 470.

Bensley, S.H. (1955) canad. Arch. Arch. & Rheum. Soe. P. 61.

Berezkov, L.F (1958) Periatriya P. 7, 79.

Brown, E.E. (1951), Arch. Pediat. 68, 565.

Cockel, R., Kendall, M.J., Becker, J.F. & Hawkins, C.F. (1971)

Coburn, A.F. (1950) J. Am. Diet, Ass. 26, 345.

Annal Rheum, Dis. 30, 166.

EL-Kinnishi, M.H., M.D Thesis 1972 Mansoura Faculty of Medicine, Mansoura-University.

Grayzel, E.F. & Longson, D.(1964), Lancet 11,66.

Hill, S.R. Jr; Holley, H.L; Ulloa, A, Starnen, WR. Hibbit., LL and MCNeil, J.H. (1959) Arth & Rheum. 2, 114.

Ichikawa, Y. (1966), Metobolism, 15, 613.

Kelley V.C. (1961) "Inflammation & Diseases of Connective Tissue" P. 575 Eds Mills. L.C. & Moyer J.H. Saunder, Philad and Londor.

Kendall, M.J., Cockel, R. Becker, J. & Hawkins C.F. (1970) Ann. Rheum. Dis 29, 5.

Krzymien, H. & Mickalski, J. (1969) Rheumat 7, 31.

Lu Pu, N. Ch., Balaceame, M.; Niculeseo, Z.D., Crob anu, V. & Ston, M. (1964) Rov. Reun. Med. Int. 1, 19.

Mazziconacci, P., Bicoux, M. & Girard, F (1965) Ann. Pediat. (Paris) 41, 1623 Pal, S.B. (1970) Clin. Chem. Acta. 29, 129.

Pechenaya, R.B. (1959) Prob. Endokr. 5, 57.

Prunty, F.T.G. (1933) Brit. Med. J. 2: 615, 673.

Selye, H. (1951) Am. J. Med. 10, 549.

Selye, H. (1951), Am. J. Med. 10, 549.

Short, C.L., Bauer, W.; Reynoleb, W.E. (1957) "Rheumatoid Arthritis, Common Wealth Fund Puplication" Camburdge mass, Harvard, Univ, press.

Tzonev, T. (1965) Vatrenchi Bolg. 4, 28.

Wolfoson, W.Q; Beierwaltes, W.H.; Robenson, W.D., Duff, I.F.; Jones J.R. Knorpp, C.T.; Sieminski, J.S. & Eya, M. (1951) Procceedings of second clinical ACTH Conference Therapeuties Vol. 11. Bakiston co N.Y.

Peterson R.E.; Wyrgasrden, J.B.; Guerre, S.L.; Bradie, B.B. & Bumin, J.J. (1955) J. clin. Jnvest 34, 1779.