Pink Disease in Eastern Anatolia

A Study of 15 Cases of Chronic Mercury Poisoning

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Between May and August 1968, we saw 20 patients whose ages ranged from three to 60 years, who had become ill after eating wheat seed Eight of them were male, and 12 female, and often more than one member of a family was involved. The majority of patients came from neighboring farms, particulary from Peynirli village, which is isolated during the winter.

Materials and Methods

Routine physical and laboratory studies were done on all 20 patients, and five were excluded from our study because mercury was not found in their urine. The wheat seed and flour they used were also examined by means of a qualitative test to determine whether or not they contained any mercury. Besides this, we were informed by the Agricultural Dusting Program Organization that the fungicides used for the wheat seed were Programin and Agroson-GN. Programin contains 2.7 per cent phenylmercuric acetate and Agroson-GN contains 1.5 per cent mercuric acetate phenylethylamine.

The 15 patients were divided into three groups according to their clinical findings. The first group consisted of eight whose ages ranged between three and 18 years. Typical acrodynia (Pink Disease) symptoms were seen in all these patients; they include pellagra-like symptoms of the hands and feet, with no well-defined area between the affected and the normal skin (Figure 1). The patients were seen to rub, twist and chew their fingers because of severe burning and

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Figure 1. Pellagroid-like appearance of the hands in acrodynia.

itching, as a result of which slight ulcers, secondary infections and swelling of the fingers occurred (Figures 1 and 2). Pruritus was generalized in all these patients, and excoriation was marked (Figure 3). Perspiration was common, perhaps because of the inhibitory effect of mercury on the re-absorption capacity of the exocrine glands; as a result of this miliaria was seen in most of the patients. Thirst and sleeplessness were also common

Figure 2. Swelling, hemorrhagic and pustular lesions of the hands in acrodynia.

symptoms. Polylymphoadenopathy was seen in one case, photophobia and hepatomegaly in two, and fever ranging from 38 to 39°C occurred in three patients. Hypertension and muscular fibrillation were not seen in any of them.

Figure 3. Marked excoriation in acrodynia

The second group included five patients aged between 34 and 60 years, three of whom were male and two female. There were no symptoms of acrodynia in these patients. The signs of mercury poisoning in these included insomnia, thirst, abdominal pains and aching of the extremities. In addition to these symptoms, erethism (irritability of the nervous system, psychic disturbances, shyness and uncooparativeness in social and familial activity resembling hyperthyroidism) occurred.

There were only two patients in group three, a mother and daughter. The only symptoms they showed were those of urticaria and edema of the genital regions.

Results

In all three groups, analysis showed the presence of mercury, albumin, a few white blood cells and low gravity (Tables I, II and III). A few casts were present in the urine of one patient from each group.

TABLE I

THE RESULTS OF URINE ANALYSIS OF EIGHT CASES OF ACRODYNIA IN THE FIRST GROUP

Sex	Age	Mercury	Protid	W.B.C.	Gravity	Casts
M	13	3 +	2.8	5–6	1005	1–2
M	9	3 +	0.1	7–8	1000	–
M	17	2 +	0.1	3–4	1015	–
M	12	2 +	0.2	2–3	1005	–
F	18	2 +	0.1	4–5	1010	–
M	3	1 +	1.1	1–2	1005	–
F	10	2 +	0.1	2–3	1012	–
F	8	3 +	2.1	3–4	1010	–

TABLE II

THE RESULTS OF URINE ANALYSIS OF FIVE CASES IN THE SECOND GROUP

Sex	Age	Mercury	Protid	W. B. C.	Gravity	Casts
M	40	3 +	0.2	3–4	1005	–
M	38	1 +	2.2	6–10	1000	–
F	35	1 +	1.6	1–2	1010	–
F	60	1 +	0.1	3–4	1005	–
M	42	3 +	0.1	2–3	1020	1–2

TABLE III

THE RESULTS OF URINE ANALYSIS OF TWO CASES IN THE THIRD GROUP

Sex	Age	Mercury	Protid	W. B. C.	Gravity	Casts
F	15	2 +	0.6	3–4	1005	1-2
F	42	1 +	0.2	4-5	1010	–

Blood examination showed normal cholesterol levels. There was a reversal of the albumin/globulin ratio in two patients of Group 1, in four of group two, and in one of group three. Leukocytosis was seen in only one patient (Tables IV, V and VI).

The removal of mercury from the body was accelerated by the use of 2.3 Dimercaprol (BAL). Mercury disappeared from the urine after the fifth to seventh administration of BAL, but reappeared four to five days after discontinuation. BAL was again given for four or five days, and this time there was no reappearance of mercury in the urine after discontinuation of the treatment.

TABLE IV

THE RESULTS OF BLOOD EXAMINATIONS OF EIGHT CASES OF ACRODYNIA IN THE FIRST GROUP

Sex	Age	Urea	Cholesterol	Al/gl
M	13	18	160	2.8/3.1
M	9	18	160	3.2/2.2
M	17	11	150	4.5/2.0
M	12	18	150	4.6/2.7
F	18	16	150	3.5/2.3
M	3	16	160	3.5/2.5
F	10	12	140	3.5/2.6
F	8	18	150	3.2/4.0

TABLE V

THE RESULTS OF BLOOD EXAMINATIONS OF FIVE CASES IN THE SECOND GROUP

Sex	Age	Urea	Cholesterol	Al/gl
M	40	14	150	3.1/2.1
M	38	18	230	2.8/3.5
F	35	16	230	2.0/3.0
F	60	18	160	2.9/3.1
M	42	16	160	3.5/3.5

TABLE VI

THE RESULTS OF BLOOD EXAMINATIONS OF TWO CASES IN THE THIRD GROUP

Sex	Age	Urea	Cholesterol	Al/gl
F	15	16	140	4.0/4.2
F	42	14	160	3.2/1.7

In one case of acrodynia during the BAL therapy a sudden unpitting edema of the lacrimal parotis glands, including the area of the thyroid, occurred (Figures 4 and 5). The edema disappeared within three days after the administration of corticosteroids (Figure 6).

During the therapy, all of the symptoms gradually disappeared, and mercury was no longer detectable in the urine, but other abnormal laboratory findings persisted for longer.

Figure 4 and **5.** Swelling of the parotid, lacrimal glands and the neck of a patient with acrodynia during BAL therapy.

Figure 6. The same patient after corticosteroid therapy.

Discussion

Because of the long winters and short summers in Eastern Anatolia, the main source of support for the population is livestock. During the

winter many of the villages are completely isolated, so that when their stock of flour is depleted they are unable to obtain more. Under these circumstances they often fall back upon their supply of wheat seed as a source of flour. At the same time, because of the severe weather, they are often unable to wash wheat seed before making flour from it. The village, Peynirli Köy, from which most of our patients came, was completely isolated because of closed roads.

Announcements were made by radio warning of the danger of eating wheat seed, but as in Peynirli it was a question of eating seed or starving, the villagers ignored these.

Under ideal circumstances the amount of mercury in the urine should be measured quantitatively, since it is known that mercury may be found in concentrations of 0.0001-0.001 mg per lt in normal persons. Because of this, the qualitative determination of mercury cannot be used to distinguish between normal and pathological amounts. The qualitative method that we used, however, was not sensitive enough to detect the small amounts found in normal persons. Thus in the 20 patients suffering from wheat seed mercury poisoning, the qualitative test was found to be sufficient for distinguishing between normal and pathological amounts of mercury in the urine.

It has been widely stated that mercury produces the symptoms of acrodynia only in children. Our findings were similar in that Group 1 (aged from three to 18 years) showed symptoms of acrodynia, and Group 2 (aged from 23-60 years) had no symptoms of this disease. It has been suggested that the disease is usually found in babies and very small children,[2 6 7 8] however, we found five patients over 10 years of age with symptoms of acrodynia. Also there were two cases after puberty, as can be seen in Table 1. The study by Çam,[3] in southeastern Anatolia also showed that acrodynia may be seen in older children; he found children up to 18 years of age with symptoms. It is our opinion that the constitution of the individual as well as age is a factor in the development of acrodynia. This is supported by the fact that in our study one 15-year-old girl was found to have only urticaria, while another patient 18 years of age had typical acrodynia. The former's 13-year-old brother also had acrodynia.

It is usually suggested in western textbooks that hypertension may be seen in acrodynia. In our study, however, this was not the case; it is more reasonable to expect hypentension in acute mercury poisoning than in chronic forms such as acrodynia. Our patients with the disease also showed no evidence of acute renal insufficiency, and only one showed polylymphoadenopathy, with marked excoriation (Figure 3). This adenopathy

was due to secondary infection rather than being specific, or caused by dermatopathic lymphadenitis. None of the other patients with pruritus showed lymphoadenopathy.

In the second group, the patients aged from 36 to 60 years did not show typical symptoms of acrodynia, but rather aching of the extremities, abdominal pain, insomnia, anorexia and erethism. The milder symptoms in adults are most likely due to lower concentrations of mercury per kilogram of body weight. Even though a child may eat a similar amount of bread, the amount of mercury would produce a higher concentration of mercury per kilogram of body weight, and thus more severe symptoms. It might be questioned whether a child would eat the same amount of bread as an adult, but in the eastern part of Turkey the main food of a child is bread, and it is probable that the children eat even more a day than their elders.

The only patients in group three, a mother and her 15-year-old daughter, showed only urticaria and an angioneurotic edema of the genital area. In the same family, a boy of 13 showed typical symptoms of acrodynia. Çam[3] in his study of mercury poisoning also found patients with urticaria and edema. These findings suggest that mercury may occasionally cause a type of hypersensitivity rather than acrodynia.

A low gravity of urine, consistent albuminuria and leukocytes in the urine were common laboratory findings. There was reversal of the albumin-globulin ratio in seven out of 15 patients. This was due to the exretion of albumin through the urine. No nephrotic syndrome was observed in any of the patients, which is related to the fact that the blood cholesterol level was normal in all groups. Probably mercury was not the only cause of the abnormal laboratory findings,and one may suspect that the phenyl groups in the fungicides also played a part.

D-penicillamine, which is an isomere of dimethylcystein, has been reported to have more effect on the treatment of chronic mercury poisoning than BAL.[1 5 6 8] Unfortunately we were unable to obtain any for our patients and were forced to use BAL in its place, but we obtained satisfactory results as have other authors.[2 4] The therapeutic mechanism of both substances is by means of the more selective affinity for -SH groups of proteins and enzymes, and also for the amino, carbonyl and hydroxyl groups for which mercury also has an affinity.

During the BAL therapy, a non-pitting edema of all lacrimal glands and of the thyroid gland area suddenly appeared in one patient with acrodynia (Figures 4 and 5). Since the excretion of mercury also takes place

through the lacrimal glands, we believe that this acute edema was due to the irritating effect of the mercury on the glands during its excretion. Such side effects of the therapy are not serious complications since they disappeared within a few days after corticosteroid therapy and had no sequels (Figure 6).

From the findings in the three groups of chronic mercury poisoning, we may conclude that the occurrence of acrodynia symptoms depends on various factors such as the age of the individual, his constitution, and the relative amount of mercury in the tissue.

Contrary to classical texts, acrodynia, at least in this part of the world, is found in higher age groups, up to 18 years of age. In these same texts, it is stated that hypertension is a symptom of mercury poisoning; we found no evidence of hypertension in any of the patients. This symptom depends upon the amount of mercury intake and would tend to be found in acute rather than chronic poisoning.

Finally, we might mention that acrodynia is not a rare disease in Turkey, since populations in certain areas are forced to eat wheat seed during the winter months. Thus, dermatologists as well as pediatricians should be alert to the possibility of acrodynia in any patient showing neuropsychic, gastrointestinal and skin symptoms as well as signs of disturbance of the kidney.

Summary

In our clinic, 20 patients were examined who became ill from eating wheat seed which had been treated by fungicides containing mercury. Of these 20 patients, 15 showed the presence of mercury in their urine. They were selected for a more complete study and were divided into three groups according to their symptoms.

The symptoms and their implications for each group have been discussed. From the results of our study, we believe that the symptoms of mercury poisoning depend upon the amount of mercury in the tissues, the age and the constitution of the individual. We also found that acrodynia may occur in persons aged up to 18 years, and that hypertension is not commonly seen in this disease.

One must be alert to the possibility of chronic mercury poisoning in Turkey, especially in areas where the population is forced to eat wheat seed because of a shortage of flour during the winter.

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