

PRACTICAL SIGNIFICANCE OF DIAGNOSTIC MOBILIZATION OF LEAD

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1. On the basis of many years' experience with the diagnostic mobilization of lead in out-patients it is recommended to take urine samples six hours after injection.
2. As maximum permissible concentration after the lead mobilization a value within 0.8–1.0 mg/24 hrs (or 0.45–0.56 mg/hrs.) is suggested.
3. With the values exceeding 3 mg/24 hrs. in 90% of cases at least two positive laboratory tests can be expected. Anemia is most frequently present when values reach 5 mg.
4. This method is recommended for the diagnosis of atypical cases, for the control of treatment and when a decision is to be reached whether a patient is to return to work with lead.

Shortly after CaEDTA had been introduced into the therapy of chronic lead poisoning owing to its property of forming with lead constant complexes easily soluble in water and excreted by the kidney, thought was given to the possibility of assessing the degree of the poisoning by the amount of lead excreted. *Rieders and Brieger (1955)* (1) were the first to draw attention to this relation, and many authors have since tried to make use of lead mobilization after the injection of EDTA for the diagnosis of chronic lead poisoning. (*Teisinger, J., Srbová, 1956, 1958 J. (2a., 2b.)*, *Bastienier, H., Deslypère, P., de Graef-Millet, 1957 (3)*, *Désaille, H., Albahary, D., Truhaut, R., Boudène, C. 1957 (4)*, *Zahorski, W., Myślak, Z. 1957 (5)*). No doubt, the tests used until now (stippled cells, porphyrinuria, blood lead level, determination of lead in urine) are good but there are still cases which are not very typical and where the diagnosis of lead poisoning is difficult. This is why the test of diagnostic lead mobilization has become widely used, although at the beginning a total 24 hour amount of urine was used. This fact, of course, made the examination rather difficult and suitable for in-patients only. This is why several authors tried to work out a mobilization method which would be suitable for out-patients as well. In Czechoslovakia such a method was introduced in 1961 (*Teisinger, J., Srbová, J.*) (6). According to this method it is sufficient to take the urine sample after the intake

of one litre of tea and after the intravenous injection of 10 ml. of »Edtocal Spofa«* (two grams of the substance) six hours thereafter.

Since this amount of lead excreted in the course of the first six hours represents 56% of the total amount of the lead eliminated within 24 hours it is possible to calculate the total daily amount. According to our previous measurement this amount does not exceed 0.350 mg in unexposed persons. The recent paper by *Ružička* (7) proves that the method is suitable for practice.

Abroad, this method is also being introduced into out-patient practice under different names (Chelaton test, evoked plumburia) and different intervals for urine sampling are suggested. We chose a six-hour time, because the fractionated examination of urine after injection revealed that the maximum of lead elimination during that time was most constant. *Albahary, Truhaut et al.* 1961 (8) recommend that urine samples should be collected 10 hours after the injection of 0.5 g of the substance or within 20–30 minutes after the administration of 1 g of the aerosol substance in a 20% solution. Recently, however, *Byczkowska* and *Antczak* (9) have recommended the sampling to be done eight hours after the injection of 1 g of the substance in a 5% solution, because according to their experience 80% of the total daily amount are eliminated during that interval. No doubt that in a longer period of time a greater amount of lead is eliminated and the calculation is consequently more accurate. But it should be taken into consideration that this is only an orientation method and that the 8-hour time is relatively long for out-patient practice. The Polish authors confirmed our data concerning the amount eliminated in six hours. According to their investigation during that time 56–60% are eliminated from the daily amount.

Now, after a few years' experience with the method, we are able to provide further details about the relation of the amount of lead eliminated after mobilization to clinical signs.

Unfortunately we cannot yet speak about the amount of lead deposit in the organism, though this would be advantageous, because the relation of the eliminated amount to this deposit has not been known. Under the term deposit the amount of lead in parenchymatous organs is understood because only this deposit can bring about toxic manifestations, and not the deposit in the bone, which is apparently not directly affected by EDTA. In our previous experiments it was found that PbEDTA had a lower rate of elimination than CaEDTA.

Byczkowska and *Antczak* have made an interesting observation recently. They have found that in the subjects unexposed to lead 90% of the total daily amount of lead were excreted after eight hours, whereas in the exposed group where the deposit was higher only 80% were eliminated. The difference is small but statistically significant. It is evident that the amount of the deposit affects the elimination rate, i. e. the more PbEDTA – the longer the elimination.

* »Edtocal« is the Czechoslovak preparation of the firm Spofa in which CaNa_2EDTA is contained in a 20% solution.

From the point of view of practice the most important thing is to find out what amount of lead eliminated in the urine after the mobilizing injection can be considered indicative of lead hazard.

To answer this question we have analyzed the results obtained from a group of 50 persons working with lead, where the effect of lead was evidenced by certain tests (stippled cell count, porphyrinuria, blood lead level). A finding of more than 1000 basophil stippled cells/1,000,000, porphyrinuria higher than 0.150 mg/litre and the blood lead level exceeding 0.070 mg % was considered positive. By statistical analysis, for which I am indebted to Mr. Roth from the Institute of Industrial Hygiene and Occupational Diseases in Prague, it was found out that in 88% of the subjects who had at least two positive tests, the result of mobilization - calculated for 24 hours - was higher than 3 mg, what corresponds to about 1.7/6 hrs. Only in rare cases was the eliminated amount lower e. g. 1.8 mg/24 hrs.

After this correlation has been established it is possible to say that when at least two tests are positive it is not necessary to carry out lead mobilization, which is a more laborious and time-consuming test. In our opinion lead mobilization ought to be used only in cases these tests are uncertain, or when it is necessary to distinguish porphyrinuria of a different origin. This method need not be considered a routine test in the preventive examinations of all subjects exposed to lead.

However, the test has proved suitable for the check-up of the persons who have been treated for lead intoxication and who are to return to their previous work after some time. It is certainly a well-known fact nowadays that after the treatment the above mentioned tests quickly become negative, though at the same time lead deposit may still be considerably high. Since these persons should not be advised to return too early to work with lead, in such cases the test proves advantageous.

Only in rare cases did we check up the patients who had negative laboratory tests and eliminated 3 mg/24 hrs after mobilization. As such examinations were not performed systematically, we cannot say how frequent such cases were. These cases probably relate to very resistant subjects ranked among the so-called carriers of lead. A thorough follow-up of such persons is, of course, to be recommended, because according to my experience, some great exposure will later certainly cause a manifestation of lead intoxication.

From the diagnostic point of view the mobilization test has no particular significance in cases with clear manifestation, such as subjective complaints of fatigue, lassitude, indigestion, constipation or diarrhoea, colic or even pain in the joints. I am mentioning only the symptoms that occur quite frequently nowadays and not the cases of classical intoxication accompanied by severe nervous disorders which are rather rare.

As to the objective signs, I consider the above mentioned tests and anemia typical of chronic poisoning. The objective evaluation of a neurologic examination, which reveals certain vegetative disturbances already in the early stages, is still underrated. This examination, howe-

ver, is seldom carried out in a systematic way. If we evaluate our 50 cases carefully we can see that 28 of them had no subjective complaints. The remaining 22 has some of the disturbances mentioned above. Laboratory tests in both groups were positive in the same degree. Under these conditions we assessed intoxication only in cases with subjective complaints and with anemia. Anemia was more frequent in persons with subjective complaints. In the other group where patients did not report any complaints, lead intoxication was not diagnosed and the case was regarded as the so-called laboratory intoxication which is not considered as an occupational disease, the patient was not subjected to any treatment, the case was solved by removing the person to a non-hazard work, and his working ability remained unchanged. It is therefore evident that in such cases the diagnosis was based on the patient's information, who might have simulated or dissimulated and there was no possibility for us to make an objective check-up of his complaint. Unfortunately, in such cases even the mobilization of lead was of no help, because in both cases practically the same positive result was obtained. For the time being we have not advanced in this respect and the diagnosis of actual intoxication in such cases remains uncertain, unless all cases with positive laboratory tests are regarded as lead intoxications. From the point of view of practice this would be of no advantage at all.

From the medical point of view this could not do any harm to the worker who dissimulates, because he will be given another job where intoxication cannot advance any further. In the group with subjective complaints where we could find some rare cases of simulation, there might of course occur an economic loss, because the patient will be reported disabled, will get higher allowances and will ask for financial recompensation. For this reason we should be very careful before diagnosing lead intoxication when the symptoms are only scarce and we should ask the factory's physician to give us a report on the trustworthiness of the patient. Invalidity claims in such cases are out of the question.

I should like to add that in cases with anemia (18) we found a significantly increased elimination of lead, i. e. the average was 5.05 mg compared to cases without anemia, where the average was 3.77 mg/24 hrs ($p < 0.05$).

It is natural that from the point of view of a clinician lead mobilization in many cases can be significant for differential diagnosis, especially in atypical and latent cases. It has often been stressed that this is above all a question of clinical experience.

I should like to point out that the penicillin which is for some reason administered shortly before the diagnostic mobilization, can considerably alter the result. In the organism penicillin changes into penicillamine which is highly complex-forming and has a mobilizing action. The lead deposit in the body decreases accordingly.

On the basis of our present experience we can make out a rough scheme for the evaluation of the numerical results of diagnostic mobilization.

The values exceeding 0.350 mg/24 hrs signify that the person is in close contact with lead. But according to our observations when the values are within 0.8–1 mg/24 hrs the effect of lead is not yet manifested, because the organism is apparently able to tolerate minor changes. An exception relates to the instances of short and severe exposure, where the flow of lead is quick and the lead content in the organism quickly increases.

Incomplete positive laboratory tests, usually without subjective complaints, can be found within the values 0.8–1 mg or even 3 mg/24 hrs. But under the above mentioned conditions lead intoxication cannot be excluded.

With the values exceeding 3 mg in 90% of cases at least two tests are positive and very often signs of intoxication are manifest. The values over 5 mg are usually accompanied with anemia which can, however, be present even when the values are lower.

The values within 0.8–1 mg./24 hr. can be taken as the maximum permissible concentration, while the values above this limit can be accompanied by pathologic signs. This proposal is in good agreement with previous proposals of other authors:

Maximum permissible concentration of lead in urine after EDTA mobilization:

Authors:	6 hrs	10 hrs	24 hrs
Brieger, H., Rieders, F. (10) . . .			1.0 mg
Albahary, C., Truhaut, R. et al. (8)		0.8 mg/l 0.4 mg/l*	
Teisinger, J.	0.450–0.650 mg		0.8–1.0 mg
Byczkowska, Z., Antczak, K (9)			1.0 mg

* 10 hrs after the administration of aerosol.

With regard to the correlation between the mobilization test and the concentration of lead in the air I want to mention the observation of *Ružička* (7) who found an average of 0.468 ± 0.286 mg/24 hrs of lead in urine in persons exposed to concentrations below the Czechoslovak M. A. C., i. e. 0.05 mg/m³, and who can be regarded consequently as a group with low exposure.

As to the way of expressing the result of the test, I am of the opinion that it is better to express it as the absolute value than as the concentration per 1 litre of urine at least until the relation between the excretion of lead and diuresis is established,

In the end I should like to add that penicillamine too has a similar effect on the elimination of lead, as was found by some authors and confirmed by *Srbová* and myself.

References

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Sadržaj

PRAKTIČNO ZNAČENJE DIJAGNOSTIČKE MOBILIZACIJE OLOVA

Na temelju dugogodišnjeg iskustva s dijagnostičkom mobilizacijom olova kod ambulantnih pacijenata, preporučuje se uzimanje uzoraka urina šest sati nakon injekcije.

Vrijednost u granicama od 0,8–1,0 mg/24 sata (ili 0,45–0,56 mg/6 sati) preporučuje se kao maksimalno dopuštena koncentracija nakon mobilizacije olova.

Kad su vrijednosti veće od 3 mg/24 sata mogu se u 90% slučajeva očekivati bar dva pozitivna laboratorijska testa. Anemija se najčešće pojavljuje kad vrijednosti dosežu 5 mg.

Ova se metoda može preporučiti za dijagnostiku atipičnih slučajeva, za kontrolu liječenja i kad treba donijeti odluku da li je pacijent sposoban da se ponovo vrati radu s olovom.

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