Ann. Ist. Super. Sanità, vol. 32, n. 2 (1996), pp. 241-245

French external quality assessment schemes for lead in blood and aluminium in plasma and dialysis water

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Summary. - An external quality assessment scheme (EQAS) for lead in blood was established in France in 1992 at the request of the Ministry of Labour and organised by the Drug Bureau. Participation is mandatory for laboratories wishing to obtain ministerial approval for the determination of blood lead levels. In 1994, two interlaboratory comparative exercises were carried out, each involving the analysis of 3 samples of human blood (2 with and 1 without lead supplementation). Out of 66 enrolled laboratories, 58 and 60 participated in the two exercises, respectively. The scattering of results was quite comparable to that observed in other EQAS. The EQAS for plasma aluminium was established in 1983 at the request of the Commission on Trace Elements of the Société Française de Biologie Clinique. Today, 80 laboratories in 22 countries on 4 continents participate in this scheme. Six exercises are carried out each year, each including 3 plasma samples (2 with and 1 without aluminium supplementation), 2 samples of water supplemented with aluminium and a blank (water). The results obtained in this scheme showed an improvement in the quality of the analyses.

Key words: aluminium, lead, human blood, quality assessment, dialysis water.

Riassunto *(Gli schemi francesi per la valutazione esterna di qualità per il piombo nel sangue e l'alluminio nel plasma umano e nell'acqua per la dialisi)*. - Un programma di valutazione esterna di qualità per il piombo è stato istituito in Francia nel 1992 su richiesta del Ministro del Lavoro e organizzato dall'Agence du médicament - Unité Contrôle National de Qualité. La partecipazione è obbligatoria per i laboratori che intendono ottenere l'autorizzazione ministeriale per la determinazione del piombo nel sangue. Nel 1994 sono stati effettuati due esercizi comparativi interlaboratoriali, ciascuno dei quali comprendeva l'analisi di 3 campioni di sangue umano (2 con e uno senza aggiunta di piombo). Dei 66 laboratori che avevano inizialmente aderito, rispettivamente 58 e 60 hanno preso parte ai due esercizi. La dispersione dei risultati era del tutto confrontabile con quella osservata in altri programmi di valutazione esterna della qualità. Il programma di valutazione esterna di qualità per l'alluminio nel plasma è stato istituito nel 1983 dalla Commissione per gli elementi in traccia della Société Française de Biologie Clinique. Attualmente, vi partecipano 80 laboratori di 22 paesi in 4 continenti. Vengono organizzati sei esercizi all'anno, ciascuno dei quali comprende l'analisi di tre campioni di plasma umano (due con e uno senza aggiunta di alluminio), due campioni di acqua addizionata di alluminio e un bianco (acqua). I risultati ottenuti hanno dimostrato un miglioramento della qualità delle analisi.

Parole chiave: alluminio, piombo, sangue umano, controllo di qualità, acqua di dialisi.

An interlaboratory comparative study of the analysis of lead in human blood

Introduction

The assay of lead in blood is often used to monitor occupational and environmental exposure to lead. As the results may have repercussions on employment and the economy, the assay should be reliable and be interpreted independently of the laboratory carrying out the analysis. Thus, the laboratories involved have the double responsibility for internal and external assessment of the quality of their data, respectively.

For these reasons, the French Ministry of Labour, in collaboration with trade unions and management, has defined a procedure for the approval of qualified laboratories (decrees of 1 February 1988 and 14 November 1990) [1, 2]. To perform "official" determinations of blood lead levels, a laboratory must accept "to undergo any control which may be required, particularly concerning external evaluations of quality". Although no mention is made of the quality requirements for results, the laboratory agrees "to use the analytical methods" recommended and to provide all evidence attesting "its experience or competence in blood lead analysis".

Organization of the scheme

The French external quality assessment scheme (EQAS) is implemented at the request of the Ministry of Labour and set up by the Drug Bureau of the Office of Laboratories and Controls. For purposes of identification, each laboratory is assigned a code number. Only the National Health Laboratory knows the identity of a given laboratory.

The trial was first carried out in November 1992, using control samples at three levels of known lead concentration, obtained by mixing commercial samples of human blood. The validity of this method of sample preparation was checked beforehand. Fifty-two laboratories participated in this exercise, for which the results are reported in Table 1. Results are given in µg/100 ml, i.e. the same unit used in French legislation [1] and in the European Council Directive of 28 July 1982 [3]. The criterion for excluding results was an absolute difference of more than two standard deviations from the general mean.

In 1994, two other trials were carried out, and another three will take place in each of the coming years. Seventy laboratories have already been enrolled.

Preparation and distribution of quality control samples

Human blood, containing EDTA as anticoagulant, was obtained from a blood bank and controlled for HIV, HBS and HBC. After determination of the initial lead concentration, the blood was divided into 3 fractions (A, B, C), 2 of which (B, C) were artificially supplemented with lead. After homogenization, these samples were analysed, distributed in 2 ml tubes and sent to the laboratories. The 3 samples prepared in this manner, stored at + 4 °C, + 20 °C or + 30 °C and analysed at day 0, 7, 21 and 28, showed excellent conservation during the 28-day period. Preparation, recovery and stability studies carried out by O. Guillard during 1993 are detailed in a report prepared for the National Health Laboratory [4].

Processing of raw data

Raw data are processed according to the procedure used by Guillard and Pineau for the "worldwide interlaboratory quality control aluminium" [5]. For each sample, we first calculate the mean (X_1) and standard deviation (SD_1) for all values (n_1, initial calculation). After excluding results lying outside the interval: mean ± 2 SD, we use the remaining data (n_2, final calculation) to determine a new mean (X_2), standard deviation (SD_2) and coefficient of variation (CV_2). After each trial, each participating laboratory receives the results for the three samples in the form of histograms, providing individual results as well as the number of participating laboratories retained (n_2), the mean value (X_2) and the coefficient of variation (CV_2).

Evaluation of laboratory performance

In addition, a more thorough evaluation of the analytical quality of the results of each laboratory is performed according to the following procedure. The quality of results is evaluated in terms of the scores obtained for the two tested parameters: a) comparison with the corrected average value (X_2) for samples A, B and C; b) recovery of the added lead for samples B and C. The scores are expressed as a percentage of the maximum achievable performance.

To calculate these scores, minimum limits of acceptable performance, as regards the corrected average (X_2) and the recovery of added quantities, are determined according to the method of Taylor and Briggs [6, 7]. These limits take the following two factors fully into account: the inverse proportion existing between the concentration and the accuracy of the analysis, and the requirements of clinical biology or occupational health. Consequently, for lead, the corresponding limits (L) are ± 3.0 and ± 5.0 µg/100 ml for concentrations of 10.0 and 60.0 µg/100 ml, respectively (i.e. 0.145 and 0.241 µmol/l for concentrations of 0.482 and 2.89 µmol/l, respectively), which corresponds to the calculation

$$L = X_2 \pm (0.04\ X_2 + 2.6)$$

For each sample, the comparison between the determined value (x) and the corrected average (X_2) then enables us to calculate a score of 100 (accordance) or 0 (a result beyond the tolerance limit), according to the following formula:

$$100 - (100\ |X_2 - x|)/L$$

A similar procedure is carried out to evaluate the recovery of lead added to samples B and C and the two scores are added up.

On the basis of these calculations, the laboratory is awarded a score out of a maximum of 100 for sample A and out of a maximum of 200 for the other two samples (B and C).

Annual ratings and classification for each laboratory

At the end of the year, all scores obtained are added up, and an annual mean is calculated over a scale ranging from a minimum of 0 to a maximum of 200.

A perfect score would thus be 200, although a score of 100 is considered to constitute a good performance if there are no zeros in any of the calculations.

Finally, laboratories are classified according to the decreasing value of the annual mean. This classification has a twin purpose. First, it allows us to provide assistance to laboratories experiencing difficulties with the assay. Secondly, in the event of a series of poor results, we can envisage "a limitation of official approval" in accordance with article 9 of the decree of 14 November 1990 [2].

Table 1. - Results of the first exercise of the French EQAS for lead in human blood (1992)

	Expected concentration (µg/100 ml)	Mean concentration obtained (µg/100 ml)	Standard deviation (µg/100 ml)	CV (%)	No. of participating laboratories
Sample 1	16.4	16.9	2.96	17.52	52
Sample 2	25.5	25.55	3.56	13.93	52
Sample 3	42.9	43.7	6.3	14.42	50

Table 2. - Results of EQAS exercises 2 and 3 (1994)

	Expected concentration (µg/100 ml)	Mean concentration obtained (µg/100 ml)	Standard deviation (µg/100 ml)	CV (%)	No. of participating laboratories
Sample 1	35.2	34.73	6.77	19.49	60
Sample 2	10.4	10.53	2.70	25.61	60
Sample 3	60.8	58.78	8.83	15.02	60
Sample 4	25.3	26.21	4.74	18.09	58
Sample 5	44.8	44.81	6.48	14.47	59
Sample 6	6.23	6.78	1.49	22.01	59

Table 2 shows the good compliance in the two quality assessment exercises carried out in 1994 (respectively 58 and 60 out of 66 laboratories enrolled). The coefficients of variation ranged from 14.47 to 25.61%. The annual average for laboratory scores was 103/200 (55/100 for deviations from corrected average concentrations and 48/100 for deviations from added concentrations). Scores ranged from 0 to 200. Nineteen laboratories had a score above 144 (5 with 200), and 4 had 0.

Worldwide interlaboratory aluminium quality assessment scheme

Organization of the scheme

The international EQAS of the Commission for Trace Elements of the Société Française de Biologie Clinique was created by O. Guillard and has been developed in collaboration with A. Pineau since 1983 [5]. Participation is open to both French and foreign laboratories. Since 1988, analyses have been carried out on dialysis water as well as plasma. The scheme involves a fee for French laboratories but is free of charge for foreign participants.

Control samples are mailed 6 times per year according to a predetermined schedule. Each set includes 3 samples of human plasma (A, B, C; 2 with and 1 without aluminium supplementation), 2 samples of water with aluminium supplementation (E, F) and a blank (demineralised water). More than 80 laboratories are involved (including 30 in France) in 22 countries on 4 continents. These participating laboratories have about one month to send in their results.

The organisers of the EQAS then evaluate the quality of the results according to the protocol described above in "An interlaboratory comparative study of the analysis of lead in human blood". To calculate scores in terms of percentage of maximum achievable performance, the organisers have first set the minimum limits for acceptable performance. These limits take fully into account both the inverse proportion existing between concentration and accuracy and the requirements of clinical biology. Consequently, for aluminium, the corresponding limits are ± 0.25 and ± 1.5 µmol/l for concentrations of 1 and 10 µmol/l [6, 7].

In the final report for both plasma and water analysis, laboratories are graded in accordance with the declining values of the annual average of their scores. The only ratings included are those of laboratories which sent in at least 50% of their results (i.e. for the exercises 55 through 59 in 1994, a minimum of 8 responses for plasma and 5 for water).

As this means of calculation is particularly strict, a rating above 100 ranks as excellent.

Results and discussion

In 1994, for plasma analysis, only 70 out of 73 laboratories taking part in the EQAS could be classified. Analysis of results gave annual scores ranging from 151.7 to 22.5. Thirty-eight out of the 70 laboratories (54%) ranked higher than average. Although this figure confirms the difficulty of carrying out such assays, it also shows an improvement over the previous year (30/69 laboratories, or 43%, in 1993).

For water analysis, only 63 out of the 70 participants could be classified. Analysis of results showed annual score averages ranging from 150.8 to 7.9, with 30 out of the 63 laboratories (48%) ranking higher than average. This figure once again shows an improvement over the previous assessment (25/60 laboratories, or 38%, in 1993).

Conclusions

The French EQAS for aluminium has been well accepted, with a high percentage of participation. The purpose of this scheme is to assist the laboratories in performing this challenging analyses. The improvement of the quality of the results indicates that this objective has been reached.

Submitted on invitation.
Accepted on 30 October 1995.

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Appendix. - Summary of the schemes

	Lead
Country	France.
Name of scheme	Contrôle national de qualité de plombémie.
Status of scheme	National, compulsory. Run by the "Agence du médicament - Unité Contrôle National de Qualité". *Aims:* to obtain approval for blood lead analysis. *Participants:* 66 hospital, university and private laboratories.
Scheme description	*Control samples*: human blood samples with or without lead supplementation, prepared in house. Target value: mean of results after exclusion of outliers (data outside the interval: mean ± 2 SD). *Organization of EQA exercises*: 3 exercises beginning in 1995, including 3 samples each (9 samples per year). Mail distribution: a two-week delay for sending in results by mail or fax. *Elaboration of results and evaluation of laboratory performance*: evaluation of the results in terms of comparison to the target value and recovery of the added amounts. Scores and acceptability limits as defined by Taylor & Briggs [6, 7]. *Measures against poor performers*: laboratories not obtaining the average are refused ministerial approval. *Financial support*: a fee is charged: 2,002 FF/year.
Organization	Mlle Otz or Mme Burg Agence du Médicament Unité Contrôle National de Qualité 93285 Saint-Denis, France Tel (33) 48 13 24 01. Fax (33) 48 13 23 56
Analyte and matrix covered	Lead in total human blood.
	Aluminium
Country	France.
Name of scheme	Worldwide interlaboratory aluminium quality control.
Status of scheme	International, voluntary. Run by the Laboratoire de Biochimie-Toxicologie. *Aims:* self-evaluation of the quality of analytical work: to confirm the validity of the analytic approach used by laboratories. *Participants:* 80 in 22 countries on 4 continents (30 French laboratories).
Scheme description	*Control samples*: human plasma (3 samples), water (2 samples), blank (1 sample). Enrichment by addition of known amounts of aluminium. Monoelemental samples in plastic vials. Target value: mean of results after exclusion of outliers (data outside the interval: mean ± 2 SD). *Organization of EQA exercises*: six annual exercises, each including 3 plasma samples, 2 water samples and one blank. Mail distribution: one-month delay for sending in results by mail or fax. *Elaboration of results and evaluation of laboratory performance*: evaluation of the results in terms of comparison to the target value and recovery of the added amounts. Scores and acceptability limits as defined by Taylor & Briggs [6, 7]. *Financial support*: free of charge for foreign participants; a fee (500 FF) for French participants.
Organization	Olivier Guillard Ph. D. and Prof. A. Pineau Laboratoire de Biochimie - Toxicologie CHU Poitiers 350 Avenue Jacques Coeur - BP 577 86021 Poitiers Cedex, France Tel (33) 49 44 44 44, extension 42734. Fax (33) 49 44 38 34
Analyte and matrices covered	Aluminium in human plasma and dialysis water.