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Atomic spectrometry update. Clinical and biological materials, foods and beverages

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This ASU reviews publications that appeared in the twelve months up to the end of October 2001. Analytically, there were few new developments. Indeed, some of the innovations that we have highlighted in the last couple of Updates, such as capillary electrophoresis and movable reduction bed hydride generation, were less evident during this period. In contrast, work to validate the use of XRF for measuring lead in bone in vivo *is moving forward although it is only a few centres that have the capability to carry out this very specialised application. In addition, a non-invasive XRF method of determining skin Fe concentrations to assess liver Fe concentrations in haemochromatosis and β-thalassaemia was presented. Interesting developments in low-cost techniques for dissolution of samples and preconcentration using flow injection are again evident. It appears that, perhaps as more laboratories replace AAS by ICP-MS, the latter technique is being used for work where just one or two analytes were reported. A number of examples were seen of problems in the clinical trace element field relating to the use of newer materials, and techniques in medicine and surgery appeared. Materials for prostheses were highlighted along with the use of relatively high concentrations of some unusual compounds for body organ imaging techniques and radiation therapy. Further applications of techniques for As speciation are featured within the clinical and foods/beverages sections. The most important development was the demonstration of methylated species containing As^{III}, the significance of which is likely to become apparent in the near future. For the first time reports were seen of investigations involving organically produced foods and it will be of interest to see whether this continues. The writing team was strengthened with the inclusion of an experienced Italian colleague, Dr. Marina Patriarca, who helped with the preparation of the section on clinical and biological materials.*

1 Analysis of clinical and biological materials

Our previous annual review on atomic spectrometry in the analysis of clinical and biological materials, foods and beverages was published in April 2001.[1] This Update reviews publications appearing up to October 2001. Table 1 summarises details of the publications while the text describes the more important developments.

1.1 General reviews and articles

Tsalev[2] has argued that both *vapour-generation AAS and ETAAS* should be part of the analyst's repertoire of techniques and they should not be viewed simply as alternatives. In his review, the scope, merits, limitations and sample preparation requirements are discussed for the two approaches and how they can interact with each other in recent trapping of hydrides and vapours in ETAAS is described. Examples of his recent research on environmental and biological samples are outlined.

Speciation of metals and metalloids by *hyphenated techniques* was reviewed by Szpunar.[3] Separation techniques covered include size-exclusion, anion- and cation-exchange, reversed-phase HPLC and flatbed and capillary electrophoresis. Detection by element using AAS, ICP-AES and ICP-MS were compared with detection by molecule using electrospray MS/MS.

1.2 Sampling and sample preparation

1.2.1 Sample digestion. *Low-technology solutions to the dissolution of trace elements* in clinical and biological materials predominate in research this review year. Infra-red heating with tungsten lamps allowed Gouveia *et al.*[4] to heat bovine liver samples with dilute acid in a glass flask in less than 60 s. Total sample preparation time was only 5 min. The method was evaluated by analysis of CRMs and by comparison of results on samples with those obtained after conventional microwave-assisted closed vessel digestion. Results were in agreement at a 95% confidence interval. Bermejo-Barrera *et al.*[5] optimised acid-leaching of trace elements in human hair with ultrasonic agitation. The most important factors were the temperature of the ultrasonic bath (optimum 80–90 °C), the HNO_3 concentration (3.7–4.2 M), and the HCl concentration (3.0–3.5 M); the presence of H_2O_2 did not improve dissolution. The same approach was used to optimise leaching from mussels on heating with microwave energy.[6] Optimal concentrations of HNO_3 were 4.1–5.3 M and of HCl 2.8–3.8 M for leaching of Ca, Cd, Cr, Cu, Fe, Mg, Mn, Pb and Zn in 1.2–3.2 min. For As, Co, Hg and Se, different conditions were required, but all could be extracted in 2 min or less. For example, As was quantitatively leached with HCl concentrations of 4.8–5.3 M in 2 min. Ribeiro *et al.*[7] showed that TMAH could dissolve hair samples in 10 min when heated at 60–70 °C or in 2 h if kept at room temperature. Subsequent determination of As, Cd, Ni and Pb was by ETAAS. Results on CRMs agreed well with certified values and results on samples agreed well with those obtained after conventional acid digestion.

1.2.2 On-line sample preconcentration and preparation. All procedures covered in this review year have used FI for on-line sample pretreatment. *On-line dilution* was used by Wang *et al.*[8] for the determination of As, Cu, Mo, Ni, Pb and Sn in urine by ICP-MS. An internal standard, ^{103}Rh, was added and the dilution factor was 16.5. Calibration was by on-line internal standards.

For *on-line sample preconcentration*, a column is generally used for collecting the element of interest followed by elution at a different pH or with a different solvent. Almeida *et al.*[9] used this approach for the determination of Cu in urine by FAAS. The Cu from 5 ml of digested urine was concentrated on a polyamine chelating ion-exchange column and then eluted allowing determination down to an LOD of 1 μg l^{-1}. In the method of Benkhedda *et al.*,[10] Co was preconcentrated from biological samples by a factor of 15 using ion-pair adsorption on the walls of a PTFE knotted reactor. The ion-pair was formed by the reaction between the negatively charged Co-nitroso R salt complex and the counter ion tetrabutylammonium. The knotted reactor was also used by Liu *et al.*[11] for the collection of Cd, Cu, Fe and Pb trapped by coprecipitation with NiDDC. The precipitate was dissolved in IBMK for determination by FAAS. Enhancement factors of 65, 60, 59 and 58 were obtained for Cd, Cu, Fe and Pb, respectively.

Wang and Hansen[12,13] have adopted a different approach to on-line preconcentration by using a *renewable column* of a defined volume of ion-exchange beads. The resin beads and 30 μl of 1 : 16 v/v HNO_3 were transported by air-segmentation into the graphite tube of an ET-AA spectrometer for quantitation. While the furnace programme was run, new material was aspirated into the column and the preconcentration of the next sample begun. In this way, Bi could be

determined in urine[13] down to an LOD of 27 ng l^{-1} with an enrichment factor of 33.4 and Ni down to 9 ng l^{-1} with an enrichment factor of 72.1.[12]

1.3 Developments in and applications of multi-element techniques

1.3.1 Atomic emission spectrometry with the inductively coupled plasma and the microwave induced plasma. In a series of papers, Tohno *et al.* used ICP-AES to study the *effects of ageing*. Measurement of the elements Ca, Mg, P and S in the four human cardiac valves[14] showed that Ca and P accumulated most in the aortic valve, about 12–19-fold higher than in the tricuspid valve which showed the least accumulation. In optic, radial and sciatic nerves,[15] the content of P and S remained constant from age 61 to 97 years, but Ca increased with age in the optic nerve, decreased in the sciatic nerve and remained largely unchanged in the radial nerve. Calcium and P concentrations in the trachea[16] were highest in the seventies and decreased thereafter. The Mg concentration, however, remained relatively constant.

To study the binding pattern of *elements in human milk*, Bocca *et al.*[17] coupled size-exclusion HPLC to an ICP-AE spectrometer with a USN nebulizer. Milk samples from 60 lactating mothers were studied. Calcium and Mg were associated with low M_r mass compounds. Copper and Fe were spread across all the five organic fractions seen, whereas Mn concentrated in the first (caseins) and the fifth (low M_r). Zinc was found in highest percentage in the fourth (alpha-lactalbumin).

A screening method for the determination of *Pb in microsamples of blood* was described by Van der Wilp and Karanassios.[18] The blood was diluted with a diluent containing Triton X-100 and 0.5% v/v HNO_3 and 5 μl of this were deposited on a rhenium cup which was dried and ashed close to the torch before final introduction to vaporise the Pb. Precision was 10–15% RSD.

In an evaluation of the potential of ICP-AES for the determination of *trace elements in digested serum*, Rahil-Khazen *et al.*[19] concluded that it could be used for normal levels of B, Ba, Cu, Fe, Li, Se, Sr and Zn and elevated levels of Al, Be, Co, Cr, Ni and Pb. Their method was applied to the determination of reference values for B, Ba, Cd, Cu, Fe, Mn, Li, Se, Sr and Zn in 141 healthy Norwegians.[20] Serum B, Ba and Sr were found to increase with age.

1.3.2 Inductively coupled plasma mass spectrometry and other mass spectrometric techniques. *1.3.2.1 Reviews. Inductively-coupled plasma mass spectrometry and its application in the determination of trace elements in clinical samples* was reviewed by Stastna *et al.*[21] Problems encountered in the analysis of body fluids and tissues were discussed with possible solutions.

1.3.2.2 Multielement determination by ICP-MS. Reference ranges for 25 trace elements in urine samples from a US population were established by Komaromy-Hiller *et al.*[22] using ICP-MS; Cr concentrations, however, were determined by ETAAS. High outliers were assumed to be the result of exposure to the element and were excluded. Results were expressed as a ratio to creatinine. Using sector-field ICP-MS, Alimonti *et al.*[23] determined Cr, Ni and V concentrations in the urine of schoolchildren aged 6–10 years. Ranges established were 0.07–0.76, 0.20–1.23 and 0.02–0.22 μg g^{-1} creatinine for Cr, Ni and V, respectively. Forrer *et al.*[24] reported reference ranges for Al, As, B, Be, Cd, Co, Cu, Fe, Li, Mn, Mo, Ni, Rb, Se, Sr and Zn in human serum determined simultaneously by ICP-MS. Thirty-two elements in human liver and kidney and 20 elements in bone were determined by Benes *et al.*[25] on samples from 70 autopsied individuals. In the liver, the concentrations of Al, As, Cd, Rb and V were higher in men than in women whereas Bi, Cr, Hg and Zn concentrations were lower. Differences between the sexes were also found for concentrations in the kidney and bone.

Reports on *applications of collision cells or reaction cells* in quadrupole ICP-MS in the clinical field are still small in number. Marchante-Gayon *et al.*[26] showed that a collision cell with He and H_2 was effective in reducing interference from polyatomic Ar interferences in the determination of the Se isotopes, ^{78}Se and ^{80}Se. This, when coupled to an HPLC system through a hydraulic high-pressure nebuliser, gave low LODs (30–80 ng l^{-1}) suitable for the speciation of Se in urine. In their study on eight subjects, trimethylselonium was found in the urine of only three subjects, both before and after supplementation, but the main Se-containing constituent was not identified.

Concentration changes of elements in plasma and dialysis fluids of seven patients on haemodialysis were followed by Krachler *et al.*[27] by ICP-MS. In the patients' plasma, concentrations of Cu and Zn continuously increased during dialysis. Concentrations of Ba, Ca, Mg and Sr were above the normal reference range. Plasma Mg concentrations fell during dialysis but at the end were still 50% above the top of the reference range. A further paper[28] looked at the changes in Cd, Co, Cs, Cu, La, Mg, Mo, Rb, Sr, Tl and Zn over 6 months. Concentrations of Cd, Co, Cu, Pb and Zn rose over this period while Cs, Mg, Mo and Rb decreased. Speciation of Cu, Fe and Zn in serum of patients on haemodialysis was achieved by Muniz *et al.*[29] The samples were separated on an anion-exchange column and the eluant was mixed with a solution containing the enriched isotopes ^{57}Fe, ^{65}Cu and ^{67}Zn to allow measurement by isotope dilution with a sector-field ICP-mass spectrometer set at medium resolution. This resolution allowed the main Cu, Fe and Zn isotopes to be separated from polyatomic species. The speciation of patient samples differed from healthy controls, especially in Fe distribution.

To examine the *effect of percutaneous transluminal coronary angioplasty on blood and plasma concentrations of trace elements in patients with heart disease*, Krachler *et al.*[30] measured concentrations by ICP-MS on samples taken 4–12 h prior to and 24–30 h after the operation. Concentrations of Co, Cs, Fe and Rb decreased in both whole blood and plasma. No significant changes were seen in the other elements measured (Ca, Cu, Mg, Pb, Sr and Zn).

Krachler and co-workers[31,32] have also measured *concentrations of 17 elements in osteoarthritic knee-joint effusions* and related them to measurements in the patients' sera. Generally, the knee-joint effusions had lower concentrations than their corresponding sera, with strong correlations between the two concentrations. They reported that the concentrations of Cu and Zn in serum were at or below the reference range for healthy adults.

In *infection*, plasma concentrations of trace elements change markedly, but Funseth *et al.*[33] wished to establish whether these were reflected in the target tissues. In their study, they measured, by ICP-MS, concentrations of 12 trace elements in the myocardium of mice infected with coxsackievirus B3 and in controls. Concentrations of Ca, Cu, Se and Zn increased but Mg decreased.

Menegario *et al.*[34] developed a method to determine concentrations of Ba, Cd, Cu, Pb and Zn in human saliva by ID-ICP-MS using a DIN. Samples were prepared by taking 0.4 ml of saliva, 0.1 ml of concentrated HNO_3 and diluting to 2 ml with H_2O. This was spiked with a solution containing ^{135}Ba, ^{112}Cd, ^{65}Cu, ^{206}Pb and ^{66}Zn. Results obtained by ID were in agreement with those obtained by external calibration on digested samples.

In a study on the *relationship between trace elements and the risk of preeclampsia in pregnancy*, Mahomed *et al.*[35] measured, by ICP-MS, leucocyte Cu, Se and Zn in 171 mothers with proteinuric pregnancy-induced hypertension and 184

normotensive controls. Concentrations of Se and Zn were significantly higher in the patient group with evidence of an increasing risk of preeclampsia with increasing concentrations of Se and Zn.

As a marker of environmental pollution in Poland, Appleton *et al.*[36] measured concentration of Cd, Cu, Pb, Sr and Zn in the teeth of bank voles by ICP-MS. The premise was that heavy metals are incorporated into hydroxyapatite in teeth during its formation and thus provide a permanent record of exposure during the development of the teeth. Higher concentrations of heavy metals in teeth were indeed found to be related to the more polluted areas.

1.3.2.3 Laser ablation ICP-MS. It has been found that Ga inhibits osteoclastic resorption *in vitro*. Ghazi *et al.*,[37] therefore, wished to find whether Ga could diffuse through dentine in teeth to prevent *external root resorption by osteoclasts*. Measurements by laser ablation ICP-MS showed that when the root space was filled with 1.0 M $Ga(NO_3)_3$, the concentration reached in the peripheral root dentine exceeded the 10^{-4} M concentration necessary to inhibit osteoclastic activity.

1.3.2.4 Determination of isotopes by mass spectrometry. Gwiazda and Smith[38] have discussed the *value of measurement of Pb isotopes* by sector field ICP-MS as an economical method for assessing the source of household lead exposure. By measuring $^{207}Pb:^{206}Pb$ and $^{206}Pb:^{204}Pb$ ratios, it was possible to identify the main sources of lead exposure to a child, discard unlikely sources and point to sources of Pb in dust. Case studies were used to illustrate this.

Sector field ICP-MS was used by Latkoczy *et al.*[39] to measure $^{87}Sr:^{86}Sr$ ratios in archaelogical samples of soils and bones. Because ^{87}Rb overlapped the ^{87}Sr peak, a prior separation by on-line anion-exchange HPLC was necessary. The sensitivity of the method was increased by using a shielded torch system and USN.

1.3.2.5 Accelerator mass spectrometry. Iron status affects *absorption of aluminium*, according to a study by Winklhofer *et al.*[40] To three groups of rats, iron-deficient, normal and iron-overloaded, a dose of ^{26}Al was given and they were sacrificed 24 h later. Using AMS, the ^{26}Al was measured in the plasma, urine, femur, liver and spleen. The iron-deficient rats had the highest intestinal Al uptake and the highest concentrations in the spleen, liver and plasma whereas the iron-overloaded rats showed decreased Al uptake and lower tissue concentrations. Transfer of Al from pregnant rats to their fetuses through the placenta and transfer to suckling rats through maternal milk was shown in a study by Yumoto *et al.*[41] Again using injection of ^{26}Al and measurements by AMS, high ^{26}Al concentrations were found in the brain and liver of fetuses or the brain, liver, kidneys and blood of suckling rats.

1.3.3 X-ray fluorescence spectrometry. *1.3.3.1 Elemental mapping. Microbeam imaging* of Fe in a single neuron of patients with Parkinson's disease using SRXRF allowed Ektassabi *et al.*[42] to demonstrate that Fe accumulated in the neuromelanin aggregates co-precipitating with Ca, Cu, S and Zn. The Fe intensity inside the melanin pigment granules of a patient sample was about an order of magnitude greater than in controls. Using an SRXRF microprobe of 100 μm resolution, Carvalho *et al.*[43] measured profiles of Br, Cu, Fe, Pb, Sr and Zn in teeth from populations living on the isolated Portuguese Islands of the Azores. Concentrations of Sr were highest in the external enamel, while concentrations of Br, Fe, Pb and Zn were higher in the inner part of the teeth. Copper and Mn, both present at low concentrations, varied little from region to region.

1.3.3.2 Fundamental developments in in vivo *XRF determination of lead in bone.* Bateman *et al.*[44] showed that two new digital spectroscopy systems allowed *improvements in LOD* in the determination of Pb in bone by ^{109}Cd-based XRF. A conventional analogue amplifier system gave an LOD of 6–10 μg g bone mineral^{-1} but with a Canberra DSA-2000 or an ORTEC DSPECPLUS system the LOD was reduced to 1.2–2.5 and 0.5–1.0 μg g bone mineral^{-1}, respectively. The feasibility of combining the K- and L-XRF methods for the determination of Pb in bone was investigated by Lee *et al.*[45] Their system used a ^{109}Cd source and Ge and Si(Li) detectors for the K and L X-rays, respectively. Monte Carlo simulated results indicated an improved LOD over a conventional single detector system.

Calibration of in vivo *XRF determination of Pb in bone* is normally with phantoms of material (often plaster of Paris) containing known amounts of Pb. Then a coherent conversion factor (CCF) is applied which converts between the response in the standards and that in human bone. Todd[46] looked critically at the the effect on the CCF of various factors. He concluded that impurities in plaster or bone matrices, coherent scatter from non-bone tissue and the individual subject's measurement geometry were all minor or negligible effects and also that a synthetic apatite matrix was more representative of bone than plaster of Paris. In a further paper,[47] he addressed the treatment of the calibration-line intercept and proposed refinements to the accepted method of subtracting the phantom calibration line from the in vivo measurements to calculate the in vivo concentrations. Spitz et al.[48] developed a new type of phantom which reproduced the anatomy of the human leg and had components (polyurethane and $CaCO_3$) that exhibited the same density, energy transmission and Ca content as cortical bone, bone marrow and muscle.

The effect of measurement location was studied by Todd *et al.*[49] On bare bone, the measured XRF intensity and its uncertainty increased towards the proximal and distal ends of the tibia but in an intact leg, there was no effect of proximal–distal location but the uncertainty was increased towards the ends. In their study on two young male cadavers, Hoppin *et al.*[50] showed considerable differences in mean bone Pb concentrations in the left and right legs of the same individual (mean mid-point bone Pb 0.8 and 2.0 μg g bone mineral^{-1} in a 17-year old and 3.6 and 6.0 μg g bone mineral^{-1} in a 20-year old).

1.3.3.3. Applications of in vivo *XRF determination of lead in bone.* It has been apparent in recent years that the development of *in vivo* XRF methods has rekindled a *large interest in studies on environmental and occupational lead exposure*. This measurement is important as bone is the main storage tissue for Pb and its Pb concentration reflects Pb accumulated over the subject's lifetime. It would appear to be a reliable index of exposure although, as is evident in the previous section, there is room for improvement in the methodology and in the understanding of the biological variability in the measurement.

Changes in *bone Pb concentrations of workers* in a lead smelter were studied by Brito and co-workers.[51,52] Following improvements in industrial hygiene, tibia Pb concentrations in 51 subjects had fallen to a mean of 33 μg g bone mineral^{-1} from a mean of 39 μg g bone mineral^{-1} in a previous study five years earlier. However, surprisingly, calcaneous Pb had not fallen significantly from a level of 64 μg g bone mineral^{-1}. In a more extensive study on 327 individuals,[52] the findings were confirmed and by looking at subgroups of subjects, it was found that workers aged under 40 had a shorter half-life for release of Pb from the tibia than their older colleagues. In addition, those with a lifetime average blood lead less than or equal to 25 μg per 100 ml (1.21 μmol l^{-1}) had a shorter tibia half-life than those with a higher blood lead. High tibia Pb concentrations were found in lead workers in Taiwan by Todd *et al.*[53] using *in vivo* XRF. In 43 workers, the mean and

maximum tibia Pb concentrations were 54 μg g bone mineral^{-1} and 193 μg g bone mineral^{-1}, respectively, corresponding to blood Pb concentrations of 44 μg 100 ml^{-1} (2.12 μmol l^{-1}) and 92 μg 100 ml^{-1} (4.64 μmol l^{-1}), respectively.

As part of an extensive study (The Normative Ageing Study), Cheng *et al.*[54] studied the relationship between *environmental Pb exposure* as measured by blood and bone Pb concentrations and the development of hypertension in 833 participants. A positive association was found between the baseline bone Pb level and the incidence of hypertension but no association was found with blood Pb level. In a study of 156 boys aged between 11 and 14 years, Campbell *et al.*[55] found that those children in the highest bone lead quartile had decreased performance in the most difficult language processing tasks. There was no difference in the easier tasks, however. Tibial Pb concentrations were measured by *in vivo* XRF.

1.3.3.4 Determination of other elements by in vivo *XRF.* In order to establish whether *skin* Fe levels measured by *in vivo* XRF could be used to monitor iron overload, Farquharson *et al.*[56] injected rats with iron-dextran and then treated them with an iron chelator. Non-haem Fe concentrations in the liver, heart and spleen were measured colorimetrically. The skin Fe concentration correlated strongly with the concentration of Fe in the inner organs and they foresaw that this technique had great potential in the diagnosis and treatment of hereditary haemochromatosis and β-thalassaemia.

Kadhim *et al.*[57] developed a method for measuring Pt concentrations in the *kidneys* of patients receiving Pt-based chemotherapy drugs. The optimal conditions included an operating voltage of 220 kV, a 0.25 nm Sn filter and a polarizer made of Cu and Si. With a measurement time of 2000 s, the LOD was 16 μg g^{-1}. To support the development of a system for *in vivo* determination of Cd in kidney using ^{133}Xe as an excitation source, Al-Ghorabie[58] used Monte Carlo simulation to show that, for distances between the skin and kidney surface of 30–60 mm, Cd concentrations of 15–60 μg g^{-1} could be detected.

1.3.3.5 Other applications of X-ray techniques. In a comparison of *Fe concentrations in the liver* of 50 Greenlandic Inuit and 72 Danes by XRF, Milman *et al.*[59] reported no significant overall difference between the two groups or between genders. However, in the age group less than 50, the Inuit had a significantly lower Fe content than the Danes and for age greater than 50 the Inuit had higher liver Fe than the Danes.

A range of elements in white and grey matter of the brain were measured by Boruchowska *et al.*[60] using *particle-induced X-ray emission*. The elements Ca, Cu, Fe, K, Mn, S and Zn were found in higher concentrations in grey matter. Zinc concentrations in the white matter were found to increase with age. A study by Akanle *et al.*[61] on maternal breast milk in Nigeria showed that breast milk for preterm infants had higher concentrations of Cl, Cu, Fe, K, Mg, Mn, Na and Zn and lower concentrations of Br and P than milk from term mothers. Concentrations of Al, Ca, I and Rb were not significantly different. Measurements were by INAA and PIXE.

A sensitive method for the determination of Au and Pd in urine using *total reflection X-ray fluorescence* was developed by Messerschmidt *et al.*[62] The elements were separated by reductive co-precipitation with Hg, followed by evaporation of the Hg. Concentrations in occupationally exposed and non-exposed individuals could be measured down to LODs of 2.0 μg l^{-1} for As and 2.5 ng l^{-1} for Pd.

1.3.4 Other multi-element techniques and studies. A simple direct method for *simultaneous determination* of Al, Cu, Cr and Mn in urine using a commercial simultaneous ET-AA spectrometer was reported by Lin and Huang.[63] The modifier was Pd used in conjunction with a purge gas of 5% H_2 in Ar, which was found to lead to smaller and more uniform Pd particles. Samples and standards were simply diluted 1 + 1. Accuracy was confirmed by analysis of a urine CRM and by recovery studies.

Normal values for As and Se in *human lung tissue* were determined by Kraus *et al.*[64] using HGAAS. Samples taken from 50 persons at autopsy gave As results from <1 to 74 ng g^{-1} dry wt and Se concentrations from <3 to 574 ng g^{-1} dry wt. Smoking habits, age and lung disease did not appear to affect the concentrations.

Release of trace metals from metal prostheses is a topical subject. Brodner *et al.*[65] measured serum Co and Cr in patients post-operation by ETAAS. They found that patients with chronic renal failure had maximum serum Co values 100-fold higher than the median values for patients with the same prosthesis but no known renal disease. They concluded that metal-on-metal bearings should not be inserted into patients with chronic renal failure. Schaffer *et al.*[66] reported increased Co and Cr levels in the blood and urine of patients with hip replacement operations. They measured concentrations by ETAAS in 76 patients and 26 controls. Significant correlations were found between blood and urine concentrations for both elements and between Co and Cr concentrations. Release of Cr and Ni from fixed orthodontic appliances into saliva was studied by Kocadereli *et al.*[67] Saliva samples were taken before insertion and 1 week, 1 month and 2 months after insertion. Measurements by ETAAS showed no significant difference between the results and those in a control group with no appliances, leading to the conclusion that there was no significant release of Cr and Ni in the first two months.

A study from six medical centres in Taiwan[68] investigated the prevalence of abnormal Al, Cd, Cu, Hg, Pb and Zn concentrations in the blood of *patients on haemodialysis*. Measurements by AAS showed that 78% of the patients had low plasma Zn, 31% had high plasma Al and 73% had high blood Cd levels. The majority had normal plasma Cu, blood Pb and blood Hg concentrations.

Factors that influence the concentration of *trace elements in human milk* were investigated by Silvestre *et al.*[69] Copper, Fe and Zn were determined by FAAS. Iron concentrations were higher in hind-milk samples and at the night-time feeding and depended on which breast the sample was taken from. Copper and Zn concentrations showed no such differences. The Zn concentration in transitional milk was lower than in colostrum but no significant differences were seen in Cu and Fe concentrations. They concluded that a standardised sampling protocol procedure was important to obtain comparable results. They applied this to a longitudinal study[70] to follow changes at 5 stages up to a time of 3 months. Zinc concentrations fell from 7.99 mg l^{-1} to 1.05 mg l^{-1}, whereas Fe concentrations varied little (from 0.56 to 0.40 mg l^{-1}). Overall, the Cu concentration fell from 0.38 mg l^{-1} to 0.19 mg l^{-1}, but these workers identified two distinct patterns of increase or decrease on transition from colostrum to transitional milk. Concentrations of Cu, Fe, Mn and Zn in milk from Kuwaiti mothers were measured by Al-Awadi and Srikumar[71] by AAS and compared with concentrations in milk from non-Kuwaiti mothers. The Kuwaiti mothers had significantly higher Cu, Fe, Mn, Zn and total protein concentrations in their milk than the non-Kuwaiti mothers. Turan *et al.*[72] reported concentrations of Cu, Cd, Cr, Mn, Pb and Ni in colostrum samples which were determined after wet ashing by ETAAS with a modifier of W, Pd and citric acid. Iron and Zn concentrations were additionally determined by FAAS. An *in vitro* method to predict the availability of Ca, Fe and Zn in infant formulae and human milk was developed by Bosscher *et al.*[73] Continuous-phase dialysis against a simulated intraluminal gastric juice

appropriate for infants less than 6 months modelled availability and the dialysates were analysed by AAS. Human milk showed higher availability of Fe and Zn than all forms of formula but the availability of Ca was similar.

Methods for the determination of trace elements in blood fractions were developed by Prohaska *et al.*[74] using ETAAS with Zeeman-effect background correction. Samples of erythrocytes, plasma and lymphocytes were diluted with a solution containing HNO_3 and Triton X-100 and an appropriate modifier added to allow separate determination of Cd, Cr, Cu, Mn and Se.

In a study of trace elements in the spinal cord of horses with equine *motor neuron disease*, Polack *et al.*[75] found that Cu concentrations were significantly higher than in control horses. No significant difference was found in the other elements measured (Al, Ca, Cd, Co, Cr, Cu, Fe, Hg, K, Mg, Mn, Na, Ni, P, Pb, Se and Zn) using the techniques of ICP-AES, ETAAS, CVAAS and fluorimetry. They concluded that Cu was possibly involved in the pathogenesis of this disease. Interestingly, Pamphlett *et al.*[76] carried out a study on human sporadic motor neuron disease by ICP-MS and ETAAS. Of the elements they measured in blood, plasma and red cells (Cd, Cu, Hg, Pb and Se), only plasma Cd was found to be significantly different from controls; Cu concentrations did not differ.

Human tooth enamel was analysed by Reitznerova *et al.*[77] for Cu, Fe, Mg, Mn, Pb and Se by FAAS, ETAAS, ICP-AES and ICP-MS. Successive layers of 50 μm thickness were etched off with 3 M $HClO_4$ up to a depth of 200 μm. The Cu, Fe, Mn, Pb and Zn concentrations decreased with successive layers whereas the Mg and Sr concentrations increased.

Savarino *et al.*[78] may have found the *secret of a healthy long life*. They measured serum Se and Zn concentrations by ETAAS and FAAS, respectively, in two groups of "healthy" elderly people. The first group aged between 91 and 110 (90 subjects) had significantly higher Se and Zn concentrations than a second group aged between 60 and 90 (62 subjects). Moreover, 84.4% of these nonagenarians/centenarians had both Se and Zn concentrations equal to or greater than the lowest values of the elderly group.

1.4 Developments in single element techniques

Tungsten-filament atomisers for determination of blood lead by ETAAS have featured in previous reviews. Zhou *et al.*[79] completed a comparison of three types—short and long wire filaments based on Osram W-filaments and a third etched filament produced by lithographic imaging and photoetching. Whole blood was diluted 1 + 4 with a modifier containing phosphate, Triton X-100 and HNO_3. The long wire filament proved the best with an LOD of 0.05–0.10 μmol l^{-1} and a lifetime of 60–70 firings. Within-run precision was better than 10% RSD.

Cathode materials for *electrolytic hydride generation* were investigated by Denkhaus *et al.*[80] Glassy carbon was suitable for hydride generation with As^{III}, Sb^{III}, Se^{IV} and Sn^{IV}. However, Hg–Ag could generate stibine from both Sb^{III} and Sb^{V} and arsine from As^{III} and As^{V} with efficiencies greater than 90%. The method was applied to the determination of As and Se by HGAAS in CRMs and tissue from cancer patients. Machado *et al.*[81] used electrochemical hydride generation in an FI system coupled to a flame-heated T-tube in an AA spectrometer for the determination of Se. The electrolytic cell consisted of two reservoirs each with a Pt electrode and separated by a Nafion membrane. One cell contained the sample and the other an electrolytic solution. Optimised conditions allowed an LOD of 10 μg l^{-1} to be reached and a throughput of 30 determinations h^{-1}. Accuracy was established by analysing food and animal CRMs.

1.5 Reference materials

Parr *et al.*[82] reported *improved values* for Cs, I, Sr, Th and U in NIST Diet, Bone Meal and Bovine Muscle SRMs. Seven laboratories in five countries took part in this study using ICP-MS and instrumental and radiochemical NAA.

1.6 Hair and nail analysis

Using sector-field ICP-MS, Rodushkin and Axelsson[83] determined *reference values* for 71 elements in hair and fingernail samples for an urban population living in the north-east of Sweden. A strong correlation between hair and nail concentrations for the elements Bi, Cd, Hg, Pb and Sb was seen as evidence for reliable assessment for exposure to these elements. Reference values for 13 essential elements and 6 toxic elements in hair from urban schoolchildren aged between 3 and 15 years were established by Senofonte *et al.*[84] using ICP-AES. Certain elements showed significant differences according to age and sex. For example, the mean Ca concentration was 336 μg g^{-1} in boys and 537 μg g^{-1} in girls. A study by Sakai *et al.*[85] on growing children showed higher Cu and Mn concentrations in the hair of boys than in girls. They found that Cu, Mn and Zn concentrations decreased from 6 months to 14 years for boys and 6 months to 12 years in girls then increasing up to 20 years for both sexes. Measurements were made with ETAAS and ICP-AES. Selenium concentrations in hair samples from mothers and their children were determined by Barrera *et al.*[86] using ETAAS after digestion with HNO_3–H_2O_2. Concentrations in the child (mean 0.77 ± 0.25 μg g^{-1}) were higher than in the mother's hair (mean 0.54 ± 0.34 μg g^{-1}).

Toribara[87] has described the results of the analysis of a single hair sample from a chemistry professor five months after *exposure to dimethylmercury* in a laboratory incident. Analysis by XRF along the length of the hair showed a large peak corresponding to the date when exposure occurred. A later peak corresponded to release of Hg on chelation therapy. The professor died five months later.

Rahman *et al.*[88] developed a continuous-flow vapour-generation system coupled to an *atomic-fluorescence detector* for determination of As, Bi, Hg, Sb and Se in hair after microwave digestion. For Hg, a two-stage digestion with HNO_3–H_2O_2 was used whereas for the others a common digestion with HCl–H_2O_2 was preferred. The LODs were 0.2 ng g^{-1} for Hg and between 2 and 10 ng g^{-1} for the others. Accuracy was demonstrated by the agreement of the results obtained on analysis of a CRM with the certified values. Application of AFS to the determination of Hg in hair for a population survey was described by Pellizzari *et al.*[89] Using 5 mg samples, Hg could be determined down to an LOD of 12 ng g^{-1} with a duplicate sample precision of 12.5% RSD and allowed measurable values in 95% of the population surveyed. The mean Hg concentration was 287 ng g^{-1}.

Differences between *major and trace elements in black and grey hairs* from the same individual were found in a study by Tsai *et al.*[90] Grey hairs had lower concentrations of Ca, Cu, Fe, K, Mn, Na, K and Zn than black hairs but differences in Fe, K and Zn failed to reach statistical significance. They concluded that reduction in hair mineral and trace element concentrations could be one of the factors associated with greying of hair.

MacPherson and Bacso[91] reported the results of an extensive study to examine further their earlier findings of an inverse relationship between *hair calcium and coronary heart disease* (CHD). Hair samples were collected from 4393 males in 40 different health districts in the UK and analysed by XRF. Standardised mortality ratios for CHD for each region showed significant relationships to hair calcium, water hardness and sunshine hours. Scotland with the highest mortality from CHD showed the lowest hair calcium, the softest water

and the least sunshine hours, whereas South-East England had the lowest mortality from CHD, the highest hair Ca, the hardest water and the most sunshine hours. This is an important study but does not clarify whether hair calcium is directly related to CHD or simply related to the hardness of the water. It will be interesting to see how this work develops.

Confirmation that *hair Pb* is not a reliable guide to an individual's exposure to Pb was produced in a study by Campbell and Toribara.[92] Children being screened for lead exposure by a standard blood lead measurement also provided hair samples. Measurement of Pb at the root of the hair by XRF failed to distinguish between children with low and high blood lead concentrations.

1.7 Drugs and pharmaceuticals

Interest in the determination of *trace element contamination in pharmaceuticals* has always been very limited. The "heavy metals test" prescribed by the US, European and British Pharmacopeia involves a crude colorimetric test. Wang *et al.*[93] developed an alternative method using ICP-MS which was fast and sensitive and allowed all the elements possible by this technique to be surveyed. Lead concentrations in calcium supplements were measured by Scelfo and Flegal[94] using sector-field ICP-MS. Two-thirds of the calcium supplements exceeded the 1999 California limit for an acceptable Pb level (1.5 μg per daily dose of supplement).

Concentrations of *potentially toxic elements in traditional Chinese medicines* were determined by Chuang *et al.*[95] using AAS. Concentrations of As, Cd, Co, Mn and Pb were higher in medicines of mineral origin than in those derived from plants and animals. Copper concentrations were higher in products of animal origin. The concentrations of heavy metals in many medicines exceeded those allowed by health agencies in several countries. Speciation of the As in the Chinese medicines, realgar and orpiment, was made by He *et al.*[96] using ion-chromatography and HG-ETAAS. Concentrations of As^{III}, As^{V} and dimethylarsinic acid (DMA) could be quantified.

An on-line FI method was developed by Sweileh[97] to determine Cu, Fe and Zn in *nutritional supplements*. The powdered multi-vitamin tablet was inserted into a special chamber and carried by the digestion solution to a heated coil. The analytes were retained as their chloro-complexes on an anion-exchange mini-column. After a brief column wash, the elements were eluted with dilute HNO_3 for determination by AAS. Two different derivatization approaches were compared by Pelaez *et al.*[98] for the determination of selenomethionine in nutritional supplements by GC-ICP-MS. The preferred method involved esterification of the carboxylic acid group of the seleno-amino acid with propan-2-ol and then acylation of the amino group with trifluoroacetic acid anhydride. Concentrations of V contamination in infusion solutions were measured by Heinemann and Vogt[99] using ETAAS. Albumin solutions showed V concentrations greater than 600 μg l^{-1}. In a multi-trace element solution used in total parenteral nutrition, 14.8 μg l^{-1} V was found.

1.8 Marine and freshwater biology

Arsenic species in oyster tissue were extracted with methanol–H_2O with 40 W microwave power for 5 min in a method developed by Vilano and Rubio.[100] Subsequent measurements were made with LC–UV irradiation–HG-AFS. Three species were detected, arsenobetaine (AB) (87%), an arsenosugar (4.9%) and DMA (4.7%). A similar method described by Suner *et al.*[101] was used for speciation of AB, arsenocholine (AC), trimethylarsine oxide (TMAO) and tetramethylarsonium ion (TMI) in fish CRMs.

1.9 Progress for individual elements

1.9.1 Aluminium. Yokel and McNamara[102] presented a review of the toxicokinetics of Al, which updated a review undertaken by the same authors in 1990. The review highlighted the role played by AMS in enabling studies of Al toxicokinetics under physiological conditions. Common sources of Al exposure were identified and bioavailability of Al from food was considered to have been inadequately investigated. Two groups examined the speciation of Al in serum. Polak *et al.*[103] determined low M_r Al complexes in serum using anion exchange fast protein LC with off-line determination of Al by ETAAS. Using an NH_4NO_3–H_2O linear elution gradient, these workers separated the following Al species: Al-phosphate, Al-citrate and ternary Al-citrate-phosphate, which were characterised by ES-MS-MS. Different distribution patterns were observed in individual subjects. Canteros-Picotto *et al.*[104] used HPLC coupled with *determination of Al by AAS to examine Al speciation in serum after administration of desferrioxamine to dialysis patients*. Serum was ultrafiltered and the filtrate injected into the chromatograph. An "unknown" Al species other than aluminoxamine was identified in the early elution fraction.

Two groups reported the findings of studies to investigate the *impact of Al on the immune system*. Graske *et al.*[105] determined Al in urine of volunteers, administered daily doses of $Al(OH)_3$ antacid, using ICP-MS. Blood samples were taken to measure circulating concentrations of immunoglobulins, interleukins and lymphocyte sub-populations. During a 6 week period of three daily doses of 590 mg $Al(OH)_3$, urine Al levels rose to values 10–20 fold higher than in controls but no major differences were found between the groups in the measured immunological parameters. Kosch *et al.*[106] compared intracellular concentrations of Al in lymphocytes from haemodialysis patients and healthy controls. Intracellular Al levels were determined using AAS. In B-lymphocytes intracellular Al was significantly increased from dialysis patients (2.9 μg g^{-1} protein) compared with controls (1.4 μg g^{-1} protein). Levels of Al in dialysis fluids are still a cause for concern. Martin and Cannata[107] presented the findings of a multi-centre study of Al concentrations in dialysis solutions from all Spanish dialysis centres. The authors reported that over 80% of centres had dialysate Al concentrations below 2 μg l^{-1} compared with only 45% in 1990. However, they highlighted that there was still a proportion of centres (4%) with dialysate fluids having high concentrations (>10 μg l^{-1}) of Al.

Riihimaki *et al.*[108] investigated the relationship *between body burden of Al and central nervous system (CNS) function* in a group of Al welders. Workers were divided into three exposure groups based on aggregated estimates of Al body burden. Both serum and urine Al concentrations were determined using ETAAS with Zeeman effect background correction. Median levels of serum Al were 0.08 μmol l^{-1}, 0.14 μmol l^{-1} and 0.46 μmol l^{-1} for controls, low exposure and high exposure groups, respectively. Corresponding urine Al levels were 0.4 μmol l^{-1}, 1.8 μmol l^{-1} and 7.1 μmol l^{-1}, respectively. The authors reported that both objective and subjective measures of CNS function showed dose dependent changes associated with increased Al body burden. They established that urine Al levels of 4.6 μmol l^{-1} and serum Al levels of 0.25–0.35 μmol l^{-1} were threshold values for adverse effects on CNS function.

1.9.2 Antimony. Krachler and Emons[109] used HPLC coupled on-line to ICP-MS for the determination of *Sb species in urine*. Separation of Sb^{V} from Sb^{III} was achieved using a PRP-X100 anion exchange column with a 20 mM EDTA mobile phase, whilst satisfactory separation of trimethyl antimony dichloride ($TMSbCl_2$) and Sb^{V} was obtained using an ION-120 anion exchange column with a mobile phase containing 2 mM NH_4HCO_3 and 1 mM tartaric acid. To

overcome the interference from Na on Sb^V that was observed when a USN was used for direct introduction of the eluent into the plasma, an HG system was interfaced between the HPLC system and the the ICP-mass spectrometer. The reported LODs were 20 ng l^{-1}, 12 ng l^{-1} and 8 ng l^{-1} for Sb^V, $TMSbCl_2$ and Sb^{III}, respectively. The method was used to determine Sb species in urine from a group of occupationally exposed workers. The predominant species was Sb^V followed by $TMSbCl_2$. The Sb^{III} species could not be detected in all urine samples. The sum of measured Sb species in the urine specimens ranged from 51 to 78% of the total Sb concentration.

1.9.3 Arsenic. Reference values for As in human lung tissue were reported by Kraus *et al.*[64] At 50 autopsies, tissue samples were taken from each lung lobe and hilar lymph node. Tissues were dried and wet digested for quantitative determination of As by HG-AAS. A reference range for As of <1–74 ng g^{-1} dry weight was established and As was noted to accumulate in the hilar lymph node tissue. As in previous years *almost all the reported studies on As have been concerned with speciation* in different matrices. Do *et al.*[110] developed a method for quantitative determination of As species in urine using HPLC coupled to HG ICP-AES. Four As species, As^{III}, As^V monomethylarsonate (MMA) and DMA were satisfactorily resolved using a non-polar C18 column. The researchers determined all four species in urine samples from individuals administered an i.v. dose of As_2O_3. Mester and Pawliszyn[111] described a method for the determination of DMA and MMA in human urine using solid phase micro-extraction (SPME) and GC-MS. The methylated As species were derivatised with thioglycol methylate and extracted on SPME fibres coated with polydimethylsiloxane. Reported LODs for the two species were 0.12 μg l^{-1} and 0.29 μg l^{-1} for DMA and MMA, respectively. In the light of discrepancies in the reported values for As species in the NIST CRM 2670–human urine, Wei *et al.*[112] conducted a detailed comparison of direct nebulisation ICP-MS and HG-ICP-MS for determination of As species in this CRM following their separation by ion chromatography. The authors established optimum elution conditions for separation of five As species. A photo-reactor interface was incorporated into the HG system to facilitate determination of non-hydride active As species. A value of 77.7 μg l^{-1} for the sum of the five As species was determined using direct nebulisation compared with a value of 71.1 μg l^{-1} using HG for sample introduction.

Nakazato and colleagues[113] reported a *sensitive method for the determination of eight inorganic and organic As species in biological matrices using a combination of LC-ICP-MS and LC-HG-ICP-MS*. Good chromatographic separation of the As species was achieved with a carboxylated methacrylate resin ion-exchange column and Na_2SO_4 mobile phase. With nebulisation injection of the LC eluent, reported LODs for the species ranged from 0.067 to 0.34 μg l^{-1}. With HG–ICP-MS LODs for As^{III}, As^V, DMA, MMA and TMAO were improved to 0.016–0.075 μg l^{-1}, but AB, AC and TMI-salt were not detected. The method was validated by analysis of urine and tuna CRMs

Methylated As species containing As^{III} have been recognised as potent enzyme inhibitors and cytotoxins and thus formation of $methylarsenic^{III}$ species may be considered to be an activation of As toxicity rather than detoxification. Two groups reported the findings of studies to determine methylated As^{III} species in biological samples. Gregus *et al.*[114] used HPLC coupled with HG-AFS to determine biliary and urinary As species in rats exposed to As^{III} and As^V. They identified MMA^{III} in bile but not in urine and hypothesised that acid MMA^{III} was subsequently oxidised to MMA^V and excreted in urine. Del Razo *et al.*[115] developed a method for differential determination of methylated As^{III} and As^V species. The method was based on the pH dependent differences in generation of hydrides from As species containing either As^{III} or As^V. Only hydrides from As^{III} species were generated at pH 6, whereas at pH 2 hydrides were generated from both species. Hydrides were trapped on a liquid N_2 GC cold trap which was subsequently gradually heated to separate the hydrides according to their boiling point for analysis by AAS. The authors used the method to determine As species in water, urine and cultured cells. They identified $methylarsenic^{III}$ species in the urine of individuals who had consumed water contaminated with inorganic As.

1.9.4 Beryllium. Apostoli and Schaller[116] investigated *whether urinary Be determination was a suitable biological indicator for assessing occupational exposures to Be and Be compounds*. The authors investigated the relationship between air Be concentrations and urinary Be levels for a group of workers employed in electric steel plants and copper alloy foundries. The median air Be levels ranged from 0.03 to 0.12 μg m^{-3} in the steel plants and were 0.27 μg m^{-3} and 0.31 μg m^{-3}, respectively, in the furnace and casting areas of the alloy plant. Urine Be levels ranged between 0.12 and 0.15 μg l^{-1} for workers exposed to levels of Be around the threshold limit value for inhalable dust of 0.2 μg m^{-3}. They established a positive correlation between external (air) and internal (urine) exposure measures but considered that there was still insufficient data for a biological exposure index to be set for Be in urine.

Duckett *et al.*[117] used SIMS to localise *Be in histological sections* of pulmonary tissue from rats with Be-induced granulomatous pneumonitis. They observed that Be passed through the vascular wall into pulmonary tissue where it was phagocytosed by macrophages.

1.9.5 Bismuth. Barbosa *et al.*[118] *described a method for the determination of Bi in whole blood and urine using ETAAS*. The method used a pyrolytically coated integrated platform tube coated with a tungsten–rhodium mixture, which acted as a permanent chemical modifier and improved furnace tube lifetime by 80%. Urine samples were diluted 1 + 1 v/v and blood samples 1 + 4 v/v with 1% HNO_3–0.2% Triton X-100. Twenty microlitre volumes were injected into the modified tube with a 10 μl volume of Rh. Reported LODs were 3 μg l^{-1} and 8 μg l^{-1} for urine and blood, respectively. Moyano *et al.*[119] described a method for the determination of Bi in urine using FI-HG-ICP-OES with on-line pre-concentration. Bismuth was concentrated by complexation with quinolin-8-ol on an amberlite anion exchange column and eluted with HNO_3. An LOD of 0.02 μg l^{-1} was reported for Bi pre-concentrated from a 100 μl sample volume.

Phillips *et al.*[120] examined the *safety aspects of colloidal bismuth subcitrate* (CBS) quadruple therapy for heliobacter pylori. They used ICP-MS to determine blood Bi levels in 34 patients receiving CBS quadruple therapy. Whole blood Bi levels were determined before and 24 h after treatment. Three patients had levels within the "alarm level" for blood Bi of 50–100 μg l^{-1}. The authors advised that caution should be exercised in prescribing CBS with gastric suppression and that alternative Bi preparations should be investigated.

1.9.6 Boron. Hiratsuka *et al.*[121] developed an ICP-AES method to determine B in blood and tissue of hamsters administered the *p*-, *m*- and *o*-isomers of the neutron capture therapeutic agent boronophenylalanine, in order to study the *biodistribution of the different isomers*. They determined the order of uptake in melanoma cells was *p*-isomer > *m*-isomer > *o*-isomer at all time points measured and that the peak B concentration in melanoma tissue occurred 2 h post administration.

Pavanetto and colleagues[122] studied the *efficacy of different stablilized liposomes for the delivery of boronophenylalanine to hepatic metastases in rats*. Conventional liposomes were

composed of phosphatidylcholine-cholesterol (1 : 1v/v) whilst "stealth" liposomes also contained polyethyleneglycol (PEG), in which the drug was encapsulated as a complex with fructose. Following administration of the liposomes, tissue concentrations of B were determined by ICP-MS and histological analysis with α-spectroscopy was used to visualise the distribution of B in the liver. The PEG liposomes accumulated B in metastatic tissue at therapeutic concentrations (>30 μg g^{-1}) and the authors considered that PEG liposomes should be further explored for enhanced drug delivery to tumour sites.

1.9.7 Cadmium. Liva and colleagues[123] *combined ultrasonic slurry generation and FI with CV-AAS to quantitatively determine Cd in biological and environmental samples*. The authors established the optimum conditions for slurry formation of different sample matrices. Slurry formation with 6 mol l^{-1} HCl and addition of KCN as a masking agent for interfering ions achieved quantitative extraction and determination of Cd in a variety of environmental matrices using direct calibration. Biological matrices, however, required standard additions calibration for quantitative determination. Results obtained for a variety of CRMs were in good agreement with certified values.

Crews *et al.*[124] described studies in which the stable ^{106}Cd isotope was used to examine dietary Cd uptake. Porridge was prepared from wheat intrinsically labelled with ^{106}Cd and eaten by adult and child volunteers. Faecal collections from volunteers were analysed for Cd species using ICP-MS, to determine the unabsorbed fraction. The results indicated that dietary absorption of Cd could be greater than the 5% figure generally quoted. Van Cauwenbergh *et al.*[125] investigated daily dietary Cd intake in the Belgian population using a duplicate portion sampling strategy. Diet samples were microwave digested and the Cd content determined by AAS. A mean daily intake of 23.1 μg was estimated, which was similar to values reported for other countries. The Japanese group of Watanabe and co-workers[126–129] presented the findings of a series of long term studies examining exposures to Cd and Pb in urban populations of Japan and South-East Asia. They reported the findings of a survey on changes in the intensity of exposure to Cd by comparing the recent situation with that of over 15 years ago. Over the period 1991–1997, they determined Cd concentrations in duplicate diet samples, blood and urine samples from over 500 non-smoking women using ICP-MS. Mean values for dietary Cd intake, blood Cd and urine Cd were 25.5 μg per day, 1.9 μg l^{-1} and 4.39 μg g^{-1} creatinine, respectively, which represented a 32% reduction in dietary intake and 450% reduction in blood Cd levels compared with the situation 15 years previously. Nevertheless, these values were still considered high compared with levels in European populations. The authors established that Cd intake was almost entirely through the dietary route and that 40% came from rice. The group examined the relationship between blood Cd and urine Cd in women from South-East Asia. A significant correlation was observed between blood Cd and urine Cd when blood Cd levels were greater than 1 μg l^{-1}. They also investigated whether current levels of Cd exposure in the Japanese population were associated with kidney dysfunction, again measuring Cd in dietary samples, blood and urine using ICP-MS after acid digestion of samples. Urine samples were also analysed for a number of low M_r proteins indicative of renal tubular damage. The authors established a borderline significance for evidence of kidney damage, which suggested that the margin of safety for the Japanese population is small.

1.9.8 Calcium. *Several groups determined the concentrations of Ca in biological tissues and fluids in relation to different medical conditions or in toxicological studies*. Kosch *et al.*[130] used AAS to determine the intracellular and membrane Ca concentrations in erythrocytes of women with pre-eclampsia in order to clarify the role of Ca in the pathogenesis of this condition. Plasma Ca levels were significantly lower in pre-eclamptic women (1.96 mmol l^{-1}) compared with controls (2.43 mmol l^{-1}), whereas membrane Ca levels were significantly increased. The findings led the authors to hypothesise that altered membrane ion transport may be an important factor in pre-eclampsia. Choong *et al.*[131] investigated Ca encrustation on ureteric stents. They developed and validated a model to determine *in vitro* encrustation on various polymers and compared the results with *in vivo* implantation of these polymers in the bladders of rats. The level of encrustation was determined by measurement of Ca using AAS.

Tateyama *et al.*[132] determined Ca in artery, vein, cartilage and bone autopsy samples using MIP-ICP-AES. They noted that as Ca accumulation increased in the aorta it also increased in the femoral artery, intervertebral disk and cruciate ligament but did not increase in veins. Freeman and colleagues[133] investigated skeletal *Ca metabolism* by administration of ^{41}Ca and ^{45}Ca tracers to volunteers and determination of the tracers in urine using AMS. They reported excellent diurnal stability and considered the method to be suitable for assessment of *anti*-resorptive osteoporosis treatment and clinical monitoring. Nagano *et al.*[134] used AAS to determine Ca concentrations in testes of mice treated with i.v. injections of rare earth elements. No significant biochemical changes or changes in testicular weight were noted following injection, but testicular Ca concentrations were significantly increased. The authors considered that the Ca accumulation may be significant in the toxic action of rare earth metals.

1.9.9 Chromium. Gunton *et al.*[135] used ETAAS to determine serum Cr levels in a group of women who had abnormal glucose challenge test results in the third trimester of pregnancy. The researchers also undertook a number of clinical chemistry tests and found no difference in plasma glucose, lipid or insulin concentrations or calculated insulin resistance between women with "normal" plasma Cr levels and those with low plasma Cr levels ($<$ or $=$ 3 nmol l^{-1}). They argued *that plasma Cr levels during pregnancy do not correlate with glucose intolerance or insulin resistance nor accurately reflect body stores of Cr in late pregnancy*. Thez considered a better method for assessing body Cr stores was required to investigate the role of Cr in pregnancy.

Alimonti *et al.*[23] established reference concentration ranges for urine Cr, Ni and V in a population of healthy children living in urban areas of Rome. Urine element concentrations were quantitatively determined by sector field ICP-MS with minimal sample pre-treatment to avoid potential contamination sources. Log transformed data were normally distributed for all three elements. The calculated reference ranges were 0.07–0.76 μg g^{-1} creatinine for Cr, 0.2–1.23 μg g^{-1} creatinine for Ni and 0.02–0.22 μg g^{-1} creatinine for V.

1.9.10 Cobalt. Benkhedda *et al.*[10] developed a method for the quantitative determination of Co in natural waters and biological samples by FI-ETAAS, using a knotted reactor cell for on-line pre-concentration of the analyte. Cobalt was pre-concentrated onto the inner walls of a PTFE knotted reactor by sorption of the ion pair formed between the negatively charged cobalt-nitroso-R-salt complex and tetrabutylammonium counter ion. The authors reported an enrichment factor of 15 and an LOD of 5 ng l^{-1}. To validate the method, the authors determined Co concentration in several biological CRMs. The analytical results obtained were in good agreement with the certified values for Co. Schaffer *et al.*[66] presented the results of *investigations on the release of Co and Cr from metal hip implants*. They used ETAAS to determine blood and urine Co and Cr levels in a group of patients following total hip replacement surgery. Post operative levels of both Co and Cr were significantly elevated in hip replacement patients

compared with controls and more than 40% of the patients exceeded German Expositionaquivalente fur Krebserzeugende Arbeitsstoffe (EKA) threshold values for Co in blood and Co or Cr in urine. The authors identified a need for long term studies on the toxicological risks of metal implants.

1.9.11 Copper. *The role of Cu in a number of diseases has been investigated during this review period.* Almeida and Lima[136] developed a single method for the determination of Cu in both serum and urine matrices using ETAAS with Zeeman-effect background correction. Serum samples were diluted 1 + 24 v/v with distilled H_2O and urine samples were analysed without a dilution step. An LOD of 0.98 $\mu g\ l^{-1}$ was reported for both matrices. The same workers also described a method for quantitative determination of Cu in urine using FAAS. Following wet digestion of urine with H_2O_2, Cu was pre-concentrated by FI using a polyamine ion exchange column. With a starting volume of 5 ml of urine, an LOD of 1 $\mu g\ l^{-1}$ was reported. The results obtained by this method were in good agreement with those obtained using the ETAAS method. Mondal *et al.*[137] also developed a method employing pre-concentration for the determination of Cu and Zn in biological samples by AAS. Samples were digested by microwave heating. Both Cu and Zn were pre-concentrated by solid phase extraction on an imidazolylazo resin. The authors described optimum conditions for extraction and desorption of the metal ions.

Ford[138] examined the *relationship between serum Cu and coronary heart disease* in US adults using data obtained from the National Health and Nutrition Survey (1976–1992). Serum Cu was determined by AAS. Age adjusted serum Cu levels were determined to be about 5% higher in subjects who had died from heart disease than those who had not, which was in agreement with other prospective studies that had identified elevated serum Cu to be associated with cardiovascular disease. Mansoor and colleagues[139] examined the relationship between plasma Cu and homocysteine in peripheral vascular disease. Plasma concentrations of Cu and other trace elements were determined using TXRF. Plasma homocysteine was determined by HPLC. A positive correlation between plasma Cu and homocysteine was observed for patients with peripheral vascular disease but not in healthy control subjects. Hatano *et al.*[140] investigated the relationship between Cu and hepatic damage caused by hepatitis C infection. Levels of Cu and other trace elements were determined in needle biopsy samples of liver from patients with hepatic fibroses using PIXE. Serum Cu levels were determined using ETAAS. The results showed that liver Cu levels increased with progression of fibrosis, whereas Fe and Zn showed no correlation with progression of disease. The authors hypothesised that Cu may contribute to hepatic injury through oxidative stress caused by an excess of the metal. Yilmaz *et al.*[141] used AAS to determine concentrations of serum Cu and Zn in individuals from Southern Turkey with chronic renal failure undergoing haemodialysis. Both Cu and Zn were significantly lower in the haemodialysis patients compared with healthy controls, although serum Cu levels in dialysis patients were still within the normal reference range. The authors recommended that chronic renal failure patients undergoing dialysis should receive Zn supplementation.

1.9.12 Gallium. Research has reported Ga to inhibit osteoclastic resorption, which often occurs following dental trauma and if not treated can lead to tooth loss. *Preliminary studies on the potential use of Ga to prevent tooth loss* were described by Ghazi *et al.*[37] The group used LA-ICP-MS to study the diffusion of $Ga(NO_3)_3$ in human root dentine. Teeth roots were cleaned, shaped, sealed with cyanoacrylate cement and the root canal space filled with a buffered aqueous solution of $Ga(NO_3)_3$. Following an incubation period, longitudinal sections of the root were cut and fixed to the sampling stage of a Nd-YAG laser ablation unit. The sample was ablated across the thickness of the root dentine to quantitatively determine ^{43}Ca, ^{69}Ga and ^{71}Ga by ICP-MS. Concentrations of Ga were highest adjacent to the root canal space. The levels declined across the root dentine layer but increased again at the external boundary of the root dentine layer. The lowest levels of Ga determined in root dentine were above the 10^{-4} M concentration found to inhibit osteoclastic resorption, which led the authors to propose that treatment with $Ga(NO_3)_3$ should undergo clinical trials.

1.9.13 Gold. Messerschmidt *et al.*[62] developed a method for the *determination of ultra-trace levels of Au and Pd in urine using TXRF.* Both elements were co-precipitated with Hg, which was subsequently completely removed by evaporation, leaving the two elements to be measured by TXRF without interferences. Recoveries of Au and Pd from spiked urine samples were $>95\%$ and LODs of 2.0 $ng\ l^{-1}$ and 2.5 $ng\ l^{-1}$ were reported for Au and Pd, respectively. The method was used to investigate urinary levels of Au and Pd in non-exposed and occupationally exposed populations.

1.9.14 Indium. In a study to examine the toxic effects of In on prenatal bone development in rats, Ungvary and co-workers[142,143] determined In levels in maternal and fetal blood, liver, kidney, skull and femur by AAS, following daily oral administration of In to pregnant rats. Indium concentrations were observed to increase significantly in blood and tissues of the mother 4 h after administration of In. Raised In levels were also found in blood, soft tissues, skull and femur of the fetus 4 h after administration. Levels of In continued to rise in fetal bone tissues over the following 24 h period, indicating accumulation in bone tissue. Histological examination of the bone tissue *indicated a specific toxic effect of In on bones developing by chondrogenic ossification.*

1.9.15 Iodine. In order *to assess residual renal function and efficiency of haemodialysis*, Sterner *et al.*[144] used XRF to determine I in serum and urine of patients administered two different urographic iodine contrast media (iohexol and iodixanol) between consecutive haemodialysis sessions. Volunteers received injections of the contrast medium, immediately following a hemodialysis session. Blood and urine samples were taken over the following two days, including both the start and end of the next dialysis session and I concentration determined by XRF. Dialysis elimination of both media was similar to urea and good correlation was reported for body clearance and renal clearance of the media. The authors concluded that a single injection of the contrast medium, immediately after dialysis, followed by measurement of blood I at the start of the next dialysis session gave a good estimate of residual renal function. A further blood I measurement at the end of this second dialysis gave a good estimate of dialysis efficiency.

1.9.16 Iron. A *method for the quantitative determination of Fe in serum ferritin was described* by Nielsen *et al.*[145] Following immunoprecipitation of ferritin, the Fe content of the precipitated protein was determined by AAS. The method was used to study patients with normal and increased body Fe stores. In a different approach to investigating Fe overload, Farquharson *et al.*[56] used K-shell XRF to determine skin concentrations of Fe. The authors wished to examine whether a correlation could be established between the concentrations of Fe in the skin and liver so that skin measurement could be used as a non-invasive method for monitoring chelation therapy in Fe overload. A strong correlation ($r = 0.86$) was demonstrated suggesting that the measurement of skin Fe levels may have potential for monitoring treatment of haemachromatosis and

β-thalassaemia. Skin concentrations of Fe were also investigated by Leveque *et al.*.[146] This group developed a microdialysis technique for collection of Fe from human dermis, which was quantitatively determined by AAS.

Milman *et al.*[59] used *XRF to determine liver Fe* concentrations in autopsy samples from urbanised Greenland Inuit and urban Danes. The median liver Fe content in Inuit was 17.23 mmol kg^{-1} and 16.51 mmol kg^{-1} in urban Danes. The authors observed significant correlations between age and liver Fe in both populations. They found that young and middle aged Inuit had smaller Fe stores than Danes, whilst elderly Inuit had larger Fe stores than their Danish counterparts.

1.9.17 Lead. Considerable continued interest in Pb has again led to a wealth of articles on the determination of this element in biological materials. Matousek and Powell[147] developed a method for the *determination of Pb in urine and blood by ETAAS with in situ electrodeposition of Pb onto the graphite tube*. Following dilution of blood samples (1 + 3 v/v) with 0.1 M HCl and acidification of urine with 1% HNO_3, Pb was electrodeposited onto a previously deposited Pd modifier surface to separate the analyte from the sample matrix prior to atomisation. The Pd modifier surface was renewed after each measurement cycle. The method was validated by the determination of Pb in blood and urine CRMs. Lima *et al.*[148] described a method for determination of Pb in biological samples using slurry sampling and ETAAS. A tungsten–rhodium coating of the graphite tube was used as a permanent chemical modifier and this coating remained stable for approximately 300 analyses of 20 μl volumes of 1.5% m/v slurries. The authors compared results obtained by this method with those obtained by an alternative ETAAS method that employed acid digestion and a Pd–$Mg(NO_3)_2$ chemical modifier. Manton *et al.*[149] used ID-TIMS for the quantitative determination of Pb in serum. Whole blood Pb was also determined using ETAAS. The authors established a linear relationship between blood Pb and serum Pb, given by the equation $y = 0.003 + 0.00241x$ where y = serum Pb and x = blood Pb. The relationship was linear for blood Pb concentrations up to 60 μg l^{-1} and serum Pb represented 0.24% of the total blood Pb, which was lower than previously reported values (0.32%–0.35%). Encinar *et al.*[150] evaluated the performance of Q-ICP-MS, double focusing ICP-MS and multi-collector ICP-MS for the quantitative determination of Pb isotopes in biological matrices. Accurate results were obtained with all instrument types. Roberts *et al.*[151] described a simple method for the determination of Pb in whole blood by ICP-MS. Blood samples were simply diluted 1 + 9 v/v with 0.1% HNO_3–0.1% Triton X-100. The method was used to investigate the potential of blood Pb determinations as a biomarker to measure bone resorption in patients with skeletal metastases. Campbell and Toribara[92] investigated the measurement of hair root Pb as a non-invasive technique for Pb toxicity screening in children. Hair root Pb was determined using XRF. The authors found no significant difference in the elemental count between hair root samples from children with low blood Pb levels ($\sim$1 μg dl^{-1}) and those with highly elevated levels (50 μg dl^{-1}) and concluded that hair root measurements were not a suitable screening tool.

The *relationship between Pb levels in biological fluids and hypertension was investigated by several groups*. Kosch *et al.*[152] determined intracellular Pb concentrations in lymphocytes of patients with essential hypertension using ETAAS. They noted that one sub-group of hypertensive patients had markedly increased levels of intracellular Pb, which they hypothesised may play a pathogenic role. Cheng *et al.*[54] determined bone Pb using K-shell XRF and blood Pb using AAS in a group of over 800 volunteers in order to examine the relationships between bone and blood Pb levels and hypertension. In subjects with no history of hypertension, a positive relationship between bone Pb and systolic blood pressure was identified. In another study of former organolead workers, Schwartz *et al.*[153] found that blood Pb was a predictor of systolic and diastolic blood pressure and hypertension status in men aged over 58.

Two groups reported very interesting studies on the *influence of aminolevulinic acid dehydratase (ALAD) polymorphism on levels of Pb in blood and bone*. Hu *et al.*[154] determined blood Pb using ETAAS and bone Pb by XRF in over 700 non-occupationally exposed men. They observed that individuals with the ALAD-1 allele had cortical bone Pb levels approximately 2.55 μg g^{-1} higher than those with the ALAD-2 variant allele. They also observed that the ALAD-2 variant allele was also associated with higher blood Pb levels when trabecular bone Pb levels exceeded 60 μg g^{-1}. They hypothesised that the variant allele modified Pb kinetics by increasing mobilisation of Pb from trabecular bone. Schwartz *et al.*[155] examined the relationship between bone Pb, blood Pb and ALAD polymorphism in a large group of lead workers and a non-exposed population. They also established that individuals with the variant allele had higher blood Pb levels but found no difference in tibia Pb levels. Like Hu and colleagues, they concluded that the variant ALAD gene modifies Pb toxicokinetics. The same group also established that the variant allele of the vitamin D receptor also modified Pb kinetics.[156]

Todd and colleagues presented a comprehensive series of papers on factors influencing the accuracy and reproducibility of *in vivo* bone Pb measurements by XRF.[157,158] They *established that the bone Pb value and its uncertainty increased towards the ends of the tibia* which they considered to be associated with the more trabecular composition of the tibia ends.[49] The group addressed the problem of contamination of phantom calibration sources used for the determination of bone Pb and proposed a refinement to the current calibration methods to eliminate underestimation of bone Pb levels.[47] They also established that a synthetic apatite matrix was a more representative calibration phantom than plaster of Paris for bone Pb measurements.[46]

Brown and colleagues[159] examined environmental factors contributing to blood and bone Pb of women from Mexico City who had recently given birth. They established that age, cumulative use of lead-glazed pottery and the period spent in the city were the major predictors of high bone Pb. Mean blood Pb and tibia Pb concentrations were 9.5 μg dl^{-1} and 10.2 μg g^{-1}, respectively, which were significantly higher than values for women in the United States. They *considered that bone Pb stores may pose a threat to women of reproductive age* long after Pb exposure had declined. In a related study, Hernandez-Avila *et al.*[160] investigated the impact of menopause on bone Pb mobilisation in women from Mexico City. They found an inverted U-shaped relationship between age and blood Pb with highest blood Pb levels in women aged between 48 and 57 years. They concluded that bone Pb was re-mobilised at menopause and could constitute an important exposure source.

1.9.18 Magnesium. There has been *continued interest this review period in the role of Mg in various pathological conditions*. Batista *et al.*[161] used a variety of analytical techniques including SEC, AAS, P-NMR and ion-selective electrodes to examine the distribution of Mg in plasma. The plasma Mg distribution was determined to be approximately 26% protein bound, 14% complexed with low M_r anions and 40% ionised. Abarca *et al.*[162] described a rapid method for the determination of Mg in multivitamin preparations using FAAS in which samples were simply dissolved in an acid solution. An LOD of 3.8 μg g^{-1} was reported and recoveries of Mg spiked placebo samples was 98.9–100.8%. Omu *et al.*[163] determined levels of Mg in serum and semen using AAS. Serum and seminal Mg levels were determined in a group of men with normal sperm parameters and a group suffering from premature ejaculation.

Significantly lower levels of Mg were observed in the semen of men with premature ejaculation. The authors hypothesised that the reduced Mg levels caused vasoconstriction from increased intracellular Ca levels which could lead to premature emission or ejaculation. Sievers *et al.*[164] undertook longitudinal studies of Mg balance in premature infants. Concentrations of Mg in infant formulas and in urine and faecal samples were determined by FAAS. Significantly higher levels of Mg retention were observed in premature infants fed infant formula compared with term infants and the authors cautioned against excessive supply of formula containing raised Mg levels to preterm infants. Andrasi *et al.*[165] reported the results of studies on the determination of Mg in brain regions of Alzheimer's disease subjects. The authors used ICP-AES, ICP-MS and INAA to determine concentrations of Mg in samples of tissue from 10 regions of normal and diseased brains. They observed that in all brain regions studied, Mg levels were significantly decreased in Alzheimer's disease. Kisters *et al.*[166] determined Mg in serum, erythrocytes and urine of healthy subjects and patients with diabetes mellitus using AAS. A hypomagnesemia was observed in diabetics both for serum (0.73 mmol l^{-1} *versus* 0.83 mmol l^{-1}) and erythrocytes (1.34 mmol l^{-1} *versus* 1.84 mmol l^{-1}). Koneke *et al.*[167] also used AAS to determine Mg in plasma of patients with hyperthyreosis. They reported that this condition was also associated with a mild Mg deficiency.

1.9.19 Manganese. Two research groups reported studies on the *determination of Mn in blood or tissues of rats and mice following administration of Mn compounds*. Chaki *et al.*[168] used AAS to determine Mn concentrations in blood and brain tissue of rats receiving total parenteral nutrition (TPN) with an elevated trace element content. The authors also used magnetic resonance imaging to examine signal hyperintensity in the brain. Immediately following cessation of TPN treatment, elevated levels of Mn in both blood and brain were determined and signal hyperintensity was observed in selected brain regions. A positive correlation was established between signal intensity in relevant brain sites and blood Mn concentration. Zheng *et al.*[169] compared the toxicokinetics of $MnCl_2$ and methylcyclopentadienylmanganesetricarbonyl (MMT) in rats. Following a single i.v. or oral dose of $MnCl_2$ or a single oral dose of MMT, plasma Mn concentrations were quantitatively determined by AAS. Following i.v. administration of $MnCl_2$, Mn was rapidly cleared from the blood with a half-life of 1.8 h and after oral administration, Mn rapidly appeared in the systemic circulation. With oral administration of MMT a delayed elimination half-life of 55.1 h was observed. Clearance of Mn from rats given MMT was 37-fold less than those given $MnCl_2$ and a gender difference in clearance rates was observed. The authors concluded that Mn derived from MMT was likely to accumulate in the body following repeated exposures.

Two groups reported the findings of *population studies on Mn levels in biological fluids and tissues*. Diaz *et al.*[170] used ETAAS to determine serum Mn concentrations in a representative sample (368 individuals) of Canary Islanders. A reference range of 0.19–3.33 μg l^{-1} was determined. Mean serum Mn levels were higher in individuals from Fuerteventura, which the authors attributed to differences in both environmental levels of Mn and dietary habits compared with the rest of the Islands. The authors also noted that serum Mn levels tended to decrease with increasing alcohol consumption and that sportsmen had higher Mn levels than other groups. The findings of a study by Fortoul *et al.*,[171] which determined concentrations of Mn in lung autopsy samples from Mexico city residents, led the authors to conclude that Mn exposure *via* air did not pose a health hazard to residents of Mexico City

1.9.20 Mercury. Two reviews on the determination of Hg in biological matrices have been published in this ASU review period. Harrington[172] presented a comprehensive review of speciation of Hg using HPLC. Cano-Pavon *et al.*[173] *presented a comparative review of non-chromatographic, LC and GC methods for the determination of Hg species in biological samples*.

Chen and Chou[174] developed a modified T-piece device to overcome an identified problem of *insufficient reaction time in a commercial HG system* used for the determination of Hg in biological samples. The introduction of the T-piece, which combined sample and reductant streams, increased the reaction time between sample and reagent to achieve complete release of Hg vapour for determination by AAS. The modified system gave accurate results for a variety of biological CRMs.

Jeffry and Barry[175] compared different *sample digestion mixtures for the determination of Hg in biological samples* using closed vessel microwave digestion with FI-CVAAS. They observed that digestion of reference materials, having a low Hg content (<0.05 μg g^{-1}), with HNO_3–HCl–H_2O_2 gave markedly elevated values compared with the certified value. They hypothesised that the high results were due to interference from NO_x species absorbing close to the Hg absorption wavelength. Addition of sulfamic acid to the digest prior to FI-CVAAS overcame the interference and gave results in agreement with certified values. Tu *et al.*[176] described a rapid simple method for the determination of methylmercury in biological samples using GC-MIP-AES and GC-ICP-MS. Samples were leached with acid and then derivatised and extracted *in situ* with $NaEt_4B$ and nonane. The nonane phase was injected into a gas chromatograph coupled to either MIP-AES or ICP-MS for determination of Hg. Recoveries of Hg in the nonane phase were greater than 90% and reported LODs were 4.4 ng g^{-1} with MIP-AES and 2.6 ng g^{-1} with ICP-MS. Two groups described methods for the determination of Hg in biological matrices by XRF. O'Meara *et al.*[177] optimised polarisation, filtration and X-ray tube voltage parameters for the *in vivo* determination of Hg in kidney using polarised XRF. Toribara[87] reported a study on the determination of Hg in single hair strands using linear scanning XRF. The technique was used to establish the circumstances surrounding a fatal exposure to dimethyl Hg.

Vahter *et al.*[178] presented the findings of a longitudinal study of *exposure to inorganic and organic mercury* in pregnant and lactating women. Inorganic and organic Hg were determined in maternal and cord blood using alkaline reduction and CVAAS. Total Hg in urine was determined using ICP-MS. The authors noted that blood methylmercury decreased during pregnancy due to a reduced intake of fish. Cord blood methylmercury levels were almost twice maternal blood levels, which the authors considered to reflect earlier maternal exposure before pregnancy. Maternal blood Hg (median level = 0.37 μg l^{-1}) and urine Hg (median level = 1.6 μg l^{-1}) were highly correlated and were both associated with the number of amalgam fillings. Warfvinge[179] examined the distribution of Hg in brains of neonatal and adult squirrel monkeys following exposure to Hg vapour. Brain Hg concentrations were determined using CVAAS and Hg distribution in brain sections examined by autometallographic silver enhancement. Accumulation of Hg in the cerebellum after exposure to Hg vapour was similar to the distribution pattern following exposure to methylmercury.

1.9.21 Molybdenum. Sievers and colleagues[180] used both AAS and sector field ICP-MS to determine Mo in samples of Mo-supplemented phenylalanine-restricted infant formula and plasma samples from infants with phenylketonuria. The authors observed that Mo intake and retention of Mo in infants on the supplemented diet were 18 times higher than those of breast fed infants, which was reflected in the plasma Mo levels. At 4 months the median plasma Mo level in breast fed infants was <0.02 μg l^{-1} compared with 2.5 μg l^{-1} for

infants with phenylketonuria, whilst at 12 months there was no statistically significant difference between the groups. The authors recommended that the present practice of Mo supplementation in such diets be revised.

1.9.22 Nickel. Wang and Hansen[12] described a *novel sample introduction technique for the quantitative determination of Ni in biological samples by FI-ETAAS with on-line preconcentration*. A micro-column, connected to an integrated FI system, was loaded with a defined volume of a cation exchange resin. A metered volume of sample solution was injected onto the column and the entire column contents (beads and injected solution) transported with 30 μl of carrier directly into the tube of the electrothermal atomizer. The ensuing thermal treatment and atomization was performed in parallel with the preconcentration of the following sample. With this approach, the authors reported an enrichment factor of 72.1, an LOD of 9 ng l^{-1} and a sampling frequency of 12 h^{-1}. The method was validated by determining concentrations of Ni in CRMs and a human urine sample. Kocadereli *et al.*[67] also used ETAAS to determined salivary concentrations of Cr and Ni in patients with fixed orthodontic appliances. Samples of stimulated saliva were collected from groups of volunteers immediately prior to fitting of a dental appliance and subsequently one week, one month and two months post fitting. Corresponding saliva samples were also collected from a control group with no fitted dental appliances. The researchers observed large individual variations in the concentrations of salivary Cr and Ni but found no significant difference in mean values between the group with fitted appliances and the control group. They concluded that the fitting of orthodontic appliances did not significantly affect salivary Cr and Ni levels.

Oliveira *et al.*[181] determined urine Ni levels using ETAAS to assess workers' exposure to $NiSO_4$ in a Brazilian galvanising plant. Urine samples were taken before and after workshifts on five successive days. On each day levels of Ni in workplace air were also monitored by personal sampling. Low to moderate exposure to Ni was identified in all work areas investigated. Air Ni levels ranged from 2.8 to 116.7 μg m^{-3} and corresponding urine Ni levels ranged from 3.5 to 43.2 μg g^{-1} creatinine. Significant differences between pre- and post-shift urine Ni levels were observed on each of the workdays. A *good correlation ($r = 0.96$) between urine Ni and air Ni levels was reported*, which further supports the well established case for urine Ni measurements being a reliable indicator of internal dose following occupational exposure to soluble Ni compounds.

1.9.23 Palladium. An *indirect method for the quantitative determination of Catopril (KPL) in pharmaceutical preparations by AAS was described* by El Reis *et al.*.[182] Catopril was reacted with an excess of Pd^{II} to form KPL–Pd^{II} complexes which were separated from unreacted Pd ions by ion exchange chromatography. The unreacted Pd^{II} was retained on a cationic ion exchange column whilst the KPL–Pd complexes were eluted. Palladium in the eluate was quantitatively determined by AAS.

1.9.24 Platinum. Work on Pt in this review period has focused *on environmental exposures and pharmacokinetics of Pt based anti-cancer agents*. Zimmermann *et al.*[183] compared sector-field ICP-MS with adsorptive cathodic stripping voltammetry for the quantitative determination of ultratrace levels of Pt in biological samples. Samples were microwave digested with HNO_3–H_2O_2 for determination by ICP-MS and high-pressure ashing was used for determination by voltammetry. For a 300 mg tissue sample, an LOD of 200 pg g^{-1} was reported for ICP-MS which was 20 times less sensitive than the ASV method. The authors obtained almost identical results with both techniques for analysis of samples with Pt levels above 1 ng g^{-1}. They determined tissue levels of Pt between 0.1 and 2.3 ng g^{-1} in the tissues analysed. Caroli and colleagues[184] determined Pt and platinum group metals (PGMs) in urine using sector field ICP-MS after UV irradiation of samples. They examined levels of PGMs in urine from children living in urban areas of Rome. Urine concentrations of the metals ranged from 0.9 ng g^{-1} creatinine for Pt to 8.5 ng g^{-1} creatinine for Rh. Concentrations of the metals were strongly associated with traffic density.

Morrison *et al.*[185] used sector field ICP-MS to determine Pt in plasma ultrafiltrate, plasma and whole blood from *patients administered the novel anti-cancer drug oxaliplatin*. A standard nebuliser was used for analysis of blood and plasma whilst ultrafiltrate was analysed using a USN. A second group, Massari *et al.*,[186] used ETAAS to determine Pt in the same biological matrices for pharmacokinetic studies of oxaliplatin. They identified that oxaliplatin was rapidly and extensively bound to erythrocytes (40%) and plasma proteins (33%). Vouillamoz-Lorenz *et al.*[187] developed a method for the determination of Pt in biological fluids using ETAAS. Urine samples were diluted with 10% HCl whilst plasma samples required the addition of 5% Triton-X100, as a chemical modifier, to the furnace platform prior to injection of the plasma sample. Reported LOQs were 50 ng ml^{-1}, 10 ng ml^{-1} and 5 ng ml^{-1} for urine, plasma and ultrafiltrate, respectively. The method was used to determine levels of Pt in samples from patients administered the oral Pt drug JM216.

Two groups described methods for the *determination of platinum in biological matrices using XRF*. Greaves *et al.*[188] used XRF to determine Pt in both serum and urine from paediatric patients treated with Pt drugs. Kadhim *et al.*[57] developed a method for *in vivo* quantitative determination of Pt in kidneys of patients receiving Pt drugs. A polarised X-ray beam from a radiotherapy unit was used to produce emission of characteristic X-rays from Pt in the kidneys, which was derived from carboplatin and its analogues.

1.9.25 Potassium. Haag *et al.*[189] presented the findings of an *important comprehensive study to assess the accuracy of serum K determinations in clinical chemistry laboratories* across Canada. A reference FAES method was used to assign target values to external quality assurance test samples distributed to Canadian laboratories. A total of 503 laboratories reported over 900 individual results. Clinically significant bias of $>1.6\%$ was found in almost 50% of reporting laboratories. A positive bias was most frequently observed at low concentrations (<3.5 mmol l^{-1}) whilst a negative bias was noted at high K concentrations (>5.1 mmol l^{-1}). The authors concluded that the inaccuracy of test results and lack of standardisation adversely affected the establishment of reference values and critical limits which had an adverse effect on medical decisions.

1.9.26 Rare earth elements. Chen *et al.*[190] described a method for the *determination of REEs in human plasma using ICP-MS*. The researchers examined three sample pre-treatments: dilution with 1% HNO_3, digestion with HNO_3–H_2O_2 and digestion with HNO_3–$HClO_4$. They considered simple dilution with HNO_3 to be fully satisfactory for quantitative analysis. An In internal standard was added to diluted samples to correct for matrix suppression effects and instrumental sensitivity drift. Reported LODs ranged from 0.7 ng l^{-1} for Eu to 5.4 ng l^{-1} for Gd.

Kubota *et al.*[191] studied the "*in vitro*" cytotoxicity of Gd in rat and mouse alveolar macrophages. Intracellular concentrations of Gd were determined using ICP-MS. The results showed a marked species difference in cytotoxicity of colloidal Gd to alveolar macrophages. Rat macrophage viability was compromised by Gd concentrations above 3 μM whereas mouse cells were resistant to Gd exposures up to 1000 μM. Lu *et al.*[192] examined the speciation of La in rat liver, using ultrafiltration and gel exclusion chromatography with quantitative

determination of La by ICP-MS. Liver La was associated with a soluble protein fraction having a $M_r > 60000$ and six elution peaks containing La were resolved by chromatography. Normann and colleagues[193] developed a method for quantitative determination of Gd in serum, faeces and peritoneal dialysate by ICP-OES in order to study the *pharmacokinetics of the contrast medium gadodiamide*. They reported that LOQs for Gd in serum, dialysate and faeces were 6.5 nmol l^{-1}, 1.6 nmol l^{-1} and 11 nmol g^{-1}, respectively, and the method was sufficiently sensitive to determine faecal Gd levels less than 0.1% of a clinical dose of the contrast medium.

1.9.27 Rubidium. Following concerns over imbalances of trace elements in dialysis patients, Canavese *et al.*[194] used both ETAAS and NAA to study Rb levels in uraemic patients. Serum concentration of Rb were quantitatively determined in a group of patients undergoing chronic haemodialysis (HD) by ETAAS, whilst NAA was used to quantitatively determine Rb levels in biopsy or autopsy samples from 20 HD patients. The researchers found significantly lower serum Rb levels in HD patients compared with controls (304 μg l^{-1} *versus* 350 μg l^{-1}). Tissue Rb levels were also lower in HD patients, particularly brain tissue (2250 ng g^{-1} *versus* 5490 ng g^{-1}). The results led the authors to conclude that *Rb deficiency could occur in dialysis patients and that further work was needed to clarify the role of both pre-dialysis factors, such as diet, and dialysis procedures in the development of Rb deficiency*. They considered the findings particularly important as Rb may have a neurobehavioural role in humans.

1.9.28 Selenium. Interest in Se speciation continues to attract the *development of methods to determine the Se species in different biological matrices*. Kobayashi *et al.*[195] presented the findings of a study on Se metabolism in rats following an i.v. injection of ^{82}Se enriched selenate and selenite. Concentrations and distribution of ^{82}Se enriched species in serum, urine, liver and kidney were determined using HPLC-ICP-MS. The authors determined that selenate and selenite were metabolised differently in the bloodstream. Selenate was taken up by the liver less efficiently than selenite, which was taken up by the liver following reduction to selenide in erythrocytes.

Several groups described methods for speciation of selenium using ICP-MS. Pelaez *et al.*[98] compared two derivatisation procedures for the determination of selenomethionine (SeMet) in nutritional supplements using GC-ICP-MS. Esterification and acylation were either carried out simultaneously with ethylchloroformate–ethanol or sequentially using propan-2-ol esterification and acylation with trifluoracetic acid anhydride. Derivatives were extracted into $CHCl_3$ and injected into the gas chromatograph. The authors selected the two-stage method for the determination of SeMet in parenteral solutions. Gammelgaard *et al.*[196] determined Se species in urine using cation exchange chromatography coupled with ICP-MS and CE-ICP-MS. Urine samples were extracted with a crown ether to remove Na and K ions. With oxalic acid or ammonium formate eluents, five Se containing species were separated. Two of the species were identified as SeMet and trimethylselenonium ion (TMSI), but the remaining three remained unidentified. Marchante-Gayon *et al.*[26] evaluated the analytical performance of ICP-MS with a hexapole reaction cell for the determination of Se species in human urine. Selenium species were separated using reverse-phase and ion-pair HPLC. Following administration of a Se nutritional supplement to 8 volunteers, TMSI was determined in the urine of 3 subjects as a major component, but in all cases the main urinary Se species was not identified. Cao *et al.*[197] also used reverse-phase HPLC to separate Se species from a urine sample prior to determination using ICP-MS and characterisation by ES tandem MS-MS. Six distinct Se species were separated and the first two fractions identified as SeMet and selenocystamine.

Li and colleagues[198] developed a method for the quantitative determination of *total selenium in serum* using FI-HG-AAS. Serum samples were digested by microwave heating and selenate was reduced to selenite. The reported LOD was 0.3 μg l^{-1} and the results of analysis of serum CRMs were in good agreement with the certified values. The authors used the method to determine dietary Se status in Austrian and Slovenian populations and, in particular, Se status in Slovenian mothers and newborn infants.[199] The mean serum Se concentration of mothers at the time of birth was 62 μg l^{-1}, whilst the umbilical cord serum concentration was 34 μg l^{-1} (55% of the maternal value). A significant correlation was determined between maternal serum Se and umbilical cord Se levels but no correlation between maternal serum Se and colostrum Se levels was observed. The authors concluded that the dietary Se status for pregnant women in Slovenia was borderline. Several other groups have presented the results of studies on Se status of selected populations. Trzcinka-Ochocka *et al.*[200] examined Se status in children and adults from a non-polluted and a contaminated region of Poland. Whole blood Se concentrations were determined using ETAAS with a copper acetate–$Mg(NO_3)_2$ chemical modifier. Mean blood Se concentrations in adults and children from the unpolluted region were 54.8 μg l^{-1} and 43.8 μg l^{-1}, respectively, and these levels were not significantly different from levels determined in the individuals from the contaminated region. Romero *et al.*[201] determined serum Se concentrations in 395 individuals from the Canary Islands using HG-AAS. The mean serum Se concentration was 74.7 μg l^{-1} and 22 adults (7%) had serum levels below 45 μg l^{-1}, a level at which an increased risk of cardiovascular disease and cancer has been reported. Children below 14 years of age had serum Se levels significantly lower than the remainder of the group. Al-Awadi and Srikumar[202] investigated the relationship between plasma Se levels and human milk Se levels in lactating Kuwaiti mothers. Milk and plasma Se was determined using AAS. They identified SeMet as the major chemical form of Se in milk. Barrera *et al.*[86] determined Se levels in hair of mothers and infants using ETAAS. Hair samples were digested with HNO_3–H_2O_2 and diluted with H_2O. A Pd chemical modifier was injected with the sample to achieve complete pyrolysis of the sample at 1200 °C.

Boulyga *et al.*[203] developed a sensitive method for the determination of Se in biological matrices using ICP-MS after acid digestion of the samples. The sensitivity for Se was significantly improved by using a sample introduction system, which combined pneumatic nebulisation with HG in a mini-cyclonic spray chamber. Analytical performance of the method and Se losses during sample preparation were monitored by spiking samples with enriched ^{78}Se prior to digestion. Machado *et al.*[81] described a novel method for the determination of Se in biological matrices using FI-AAS with *electrochemical hydride generation*. The electrolytic cell was composed of two reservoirs, one containing sample and the other electrolytic solution, separated by a Nafion membrane. The generated hydride was transported, in an Ar stream, to a quartz tube in an air–propane flame for determination of Se. The authors reported the optimum conditions for analysis and the accuracy of the method was assessed by analysis of biological CRMs.

1.9.29 Silicon. Van Dyck *et al.*[204] presented the findings of a *large study on serum silicon levels in Belgian adults and children*. Serum Si concentrations were determined using ETAAS. The authors observed that Si concentrations were significantly higher in children and adolescents (1–18 years) than in adults (19–60 years). Highest levels were determined in infants less than 1 year old. The results led the authors to hypothesize that these profiles may suggest Si essentiality in humans. Hauptkorn *et al.*[205] developed a method for the quantitative determination of Si in biological samples by ICP-AES. Samples were prepared using a non-oxidative alkaline procedure with TMAH and

high-pressure microwave digestion. Using a sample mass of 100 mg, an LOD of 2 mg kg^{-1} was achieved. The authors evaluated the method by analysing biological tissue samples spiked with Si and compared the results with those obtained by XRF and solid sampling ETAAS.

There is continued interest in assessing the health risks associated with silicone implants, where silicone may be released into body tissues from ruptures of the implant or gradual diffusion through the implant envelope. Lugowski *et al.*[206] determined both total Si and organic solvent extractable Si (silicone) in body fluids from patients with breast implants and a matched control group, using ETAAS. The mean whole blood Si level in implant patients was 38.8 μg kg^{-1} compared with a mean of 24.2 μg kg^{-1} in controls. Mean levels of Si in breast milk from implant patients was 58.7 μg kg^{-1} compared with 51.1 μg kg^{-1} in control subjects.

1.9.30 Silver. In a study to investigate any *adverse health effects from a novel silver coating applied to mechanical heart valve prostheses*, de la Riviere *et al.*[207] used ETAAS to determine serum Ag levels in patients fitted with the coated valve. Blood Ag levels peaked shortly after surgery and declined gradually during the post-operative period. Average blood Ag levels in the treated patients were consistently below 4 μg l^{-1}.

1.9.31 Strontium. Burguera and colleagues[208] described a *rapid FAAS method for the determination of Sr in digested bone samples*. The authors established optimum conditions to minimise interferences from the major matrix components Ca, K, Mg, Na and P. A "Y" piece was connected to the nebuliser for simultaneous introduction and on-line mixing of ionisation or releasing buffers with solutions of standards and samples. They recommended an N_2O–C_2H_2 flame, due to improved sensitivity and precision compared with an air–C_2H_2 flame, and reported an LOD of 0.015 mg l^{-1} and a precision of 0.5% RSD with the N_2O–C_2H_2 flame. The FAAS method was evaluated by comparison with an ETAAS method. The authors also examined different digestion methods for the bone samples and achieved complete digestion of the bone matrix using concentrated HNO_3 with sonication or microwave digestion.

1.9.32 Thallium. Galvan-Arzate *et al.*[209] determined Tl in rat brain by AAS in a study to examine the distribution of Tl and toxic manifestations arising from subchronic administration of sublethal doses of thallous acetate. Higher concentrations of Tl were determined in total brain tissue of rats given a 1.6 mg kg^{-1} dose compared with those given half this dose. However no differences in the regional distribution of Tl was observed between the two dose groups. Lipid peroxidation, as a marker of oxidative stress, was determined by the measurement of lipid fluorescent products. The authors observed a significant increase of lipid peroxidation in just two regions of the brain from the rats treated with 0.8 mg kg^{-1} Tl and in all brain regions of the rats treated with the higher dose. They *concluded that oxidative events in susceptible brain regions are associated with exposure to sublethal levels of Tl.*

1.9.33 Tin. In a forensic investigation of a poisoning incident in China, Jiang *et al.*[210,211] determined organotin species in a variety of biological tissues and fluids. *Organotin species were identified and quantitatively determined by GC with flame photometric detection, GC-MS and ICP-MS*. For the determination of Sn species by GC, the biological samples were digested with $CuSO_4$–KBr–H_2SO_4, extracted with 0.1% tropolone in cyclohexane and derivatised with an n-pentyl Grignard reagent. Organotin concentrations in various body organs ranged from 0.1 to 1.93 μg g^{-1} (wet weight). Results of analysis identified both dimethyl Sn and trimethyl Sn as the main species associated with the poisoning incident.

1.9.34 Titanium. *Improved mechanical properties, biocompatibility and corrosion resistance of Ti–Al–V alloys has led to an increase in their use for spinal implants*. Villarraga and colleagues[212] examined the release of Ti from cervical spine plates in a canine model, using AES to determine Ti concentrations in tissues surrounding the implants. They determined highest levels of Ti in tissue samples closest to the screw–plate interfaces. The authors also developed a computational model to simulate different metal release mechanisms, and postulated that the release of Ti was due to fretting and wear at the screw–plate interfaces and by dissolution of the oxide layer and diffusion of Ti ions at the centre of the plate.

1.9.35 Tungsten. To study the pharmacokinetics of W, Poucheret *et al.*[213] *used ICP-AES to determine W in plasma from rats and dogs administered W compounds*. With simple dilution of the plasma samples, an LOQ of 100 ng ml^{-1} was reported, with an analytical precision of 17% RSD at this concentration. The method could quantitatively determine plasma W concentrations up to 90 μg ml^{-1}.

1.9.36 Uranides. Baglan and colleagues[214] investigated the *determination of Th in urine by ICP-MS for biological monitoring of individual occupational exposure to Th*. They established that a simple 100-fold dilution of urine was satisfactory for quantitative determination of ^{232}Th concentrations below 1 mBq l^{-1} and a 20-fold dilution suitable for determination of levels below 0.06 mBq l^{-1}. (The reviewers were confused by these units.)

1.9.37 Vanadium. In a *comprehensive study of V contamination in intravenously administered drugs and solutions*, Heinemann and Vogt[99] used ETAAS to quantitatively determine V in 51 intravenous solutions and drug preparations and six components of a multi-trace element solution. They found highest levels of V in albumin solutions, which had V concentrations exceeding 600 μg l^{-1}. Significantly elevated V levels of 14.3 μg l^{-1} and 122 μg l^{-1} were also determined in two heparin preparations.

Vanadocenes (cyclopentadienyl complexes of V) have been identified as a *potential new class of contraceptive agent* due to their potent inhibitory effect on sperm motility. D'Cruz and Uckun[215] investigated the intravaginal toxicity of gel-microemulsion formulations of two vanadocenes (VDACAC and VDDTC) in rabbits, using AAS to quantitatively determine V levels in selected body fluids and organs following repeated administration of the vanadocenes over 10 consecutive days. No vaginal irritation or inflammation was observed in animals administered a 0.1% concentration of the formulations and only mild irritation was observed at a concentration of 0.25%. For both dose groups, no changes in clinical chemistry profiles were observed, neither was V incorporated into body fluids or tissues at levels above 1 μg g^{-1}. The authors concluded that repeated administration of VDACAC and VDDTC at levels up to 2000 times greater than their spermicidal EC50 value did not cause marked vaginal irritation or systemic absorption of V in the rabbit model.

Kwiatek *et al.*[216] compared PIXE and AAS methods for the quantitative determination of V in blood and tissue samples from rats administered a V supplemented diet. For both analytical methods, samples were mineralised and V extracted with APDC. No statistically significant differences were observed between tissue levels of V determined by the two techniques.

1.9.38 Zinc. Chia *et al.*[217] examined the relationship between blood and semen Zn concentrations and sperm quality in fertile and infertile men. Blood and semen Zn concentrations were determined using AAS. The geometric mean seminal Zn

level was significantly lower in the infertile group compared with the fertile group (183.6 mg l^{-1} *versus* 274.6 mg l^{-1}) whereas no significant difference in blood Zn levels was observed between the groups. Semen Zn concentration was also positively correlated with sperm density, motility and viability. Nicolis *et al.*[218] investigated the *use of hair as a diagnostic tool for monitoring patients on parenteral nutrition*. The authors determined Zn concentrations along single strands of hair using SR-XRF. The authors determined significant fluctuations in hair Zn with time, based on analysis of successive segments of hair, which led them to argue that the method was a suitable monitoring tool to validate adequate Zn supplementation for patients on parenteral nutrition. Rulon *et al.*[219] determined Zn concentrations in post mortem serum and brain samples from Alzheimer's disease (AD) subjects using FAAS and INAA, respectively. A statistically significant increase in serum Zn levels was found in AD subjects compared with controls (136.4 μg dl^{-1} *versus* 71.1 μg dl^{-1}) but no significant difference between AD subjects and controls were found for Zn concentrations in four brain regions (amygdala, hippocampus, cerebellum and temporal gyri). Majewska and colleagues[220] determined Zn concentrations in whole blood and thyroid tissue of women patients with various thyroid diseases. Zinc concentrations in both blood and thyroid tissue were determined using TXRF. Of the disease states investigated, Zn concentrations were lowest in tissue samples from patients with thyroid cancer (23.1 μg g^{-1}) and highest in tissues from patients with Graves disease (41.7 μg g^{-1}) whereas in blood samples the opposite result was found.

Griffin and colleagues[221] developed a six compartment pharmacokinetic model for Zn metabolism in children using data obtained from stable isotope determinations of Zn in biological fluids and excreta. Seven healthy female volunteers were given an oral dose of ^{67}Zn enriched tracer. Blood, urine and faeces samples were collected for 6 days following administration and Zn isotopes determined using TIMS. Using the model, the authors noted that body weight corrected Zn compartments were significantly greater in children than in adults.

2 Analysis of foods and beverages

This section draws attention to papers that describe *novel developments for the measurement of major and trace elements in individual foods and beverages and in whole diets*. We also summarise reports that document typical concentrations in selected food types. Table 1 presents the essential points of these and other papers.

Little by way of formal *review articles* has been seen. The comprehensive 2001 Atomic Spectrometry Update cited almost 200 papers published in 1999–2000[1] while properties and applications, toxicity, measurement and daily dietary intake of Be were reviewed.[222]

Problems associated with *contamination* were highlighted in one paper[223] where release of 15 elements from six devices for milling and grinding wheat was measured. None of those investigated was completely contaminant-free.

Two papers were seen where differences between *organic and non-organic foods* were investgated. Kidney Cd concentrations were significantly higher in pigs fed with organic feed compared with those conventionally fed; 91.6 and 84.0 μg kg^{-1}, respectively.[224] This was despite the feed having lower levels of Cd. The authors noted, however, that the vitamin–mineral supplements given to the organic pigs contained much greater amounts of Cd and that Cd in the manure was also greater, indicating larger total ingestion of the metal. Rasmussen *et al.* reported that I was lower in organic than in non-organic milk.[225]

2.1 Sampling and sample preconcentration

It is well known that *Cd is not evenly distributed throughout the kidney*. In a study involving microwave digestion and ETAAS, it was shown that variations are less dramatic in porcine compared with bovine kidney and that freezing the sample caused some redistribution of the Cd.[226] The authors confirmed that a well designed sampling method is necessary.

2.1.1 Extraction. In a very simple procedure, Se was *directly extracted* from coconut milk and coconut water into a mixture of tertiary amines, for measurement by ETAAS. Sample decomposition and contamination were avoided and recovery at 99.5–102.3% was excellent.[227] Extraction of species of As, Sb, Se and Te from fish was achieved using CH_3OH–H_2O.[228] The species were separated and detected by HPLC and ICP-MS as part of a stability study. Some conversion of Sb^{III}, Sb^{V} and selenomethionine to new species occurred on extraction and further transformations took place during storage at −20 °C but not at 3 °C. The same extraction medium was used by a different group who achieved quantitative extraction of As from oyster tissue using microwave heating at 40 W for 5 min.[100] An LOD of 2.3 ng l^{-1} for Be in drinking water was obtained with a method that took 100 ml of sample and formed a chelate of Be with acetylacetone.[229] The chelate was collected on a Sep-Pak cartridge and eluted with 2 ml CH_3OH for ETAAS. Fe^{III} was measured in wine as a thiocyanate complex extracted into IBMK.[230] Concentrations of 0.10–6.00 mg l^{-1} were measured by FI-FAAS. Total Fe was also determined. In an indirect method, I in milk was combined with Hg and 2,2′-dipyridyl. The ion pair thus formed was extracted into IBMK and the Hg measured by ETAAS.[231] An *in vitro* study demonstrated that phytate has a negative influence on Zn bioavailability from infant foods. Samples were simply subjected to a dialysis procedure prior to analysis by FAAS.[232] Other papers report extraction of As, Cu, Fe and Hg from samples using various acids and/or solvents at different heating conditions (see Table 1).

2.1.2 Digestion. *Comparative studies of digestion procedures* are regularly reported and four were seen in this review year. To measure Fe in wine, digestion with HNO_3–H_2SO_4 was preferred[233] while for Fe and Zn in wheat, microwave heating gave the best response.[234] ETAAS was used for the determinations in both of these studies whereas ICP-AES was employed for multielement analysis of various foods (see Table 1). Microwave digestion was generally preferred but for certain elements, *e.g.*, Al, poor results were obtained unless special steps were included.[235,236]

In an elaborate investigation, Bermejo-Barrera *et al.*[6] sought to determine optimum conditions of acid concentration and volume, sample size, microwave power and exposure time for the *preparation of seafood products* for many elements. Appropriate procedures for measuring different elements by AAS were recommended and applied to CRMs, with good accuracy.

An unusual application involved the measurement of *As in sugar by ETAAS* with *in situ* digestion. An 8% m/v solution in 0.2% v/v HNO_3 was sampled and the high C content was removed by introducing air during a 40 s pyrolysis step at 600 °C.[237]

Sweileh constructed a novel FI system, which accepted *powdered multi-vitamin tablets* into an acid solution, which was passed through a heating coil to an anion exchange column where Cu and Zn were retained. After a column wash the analytes were eluted with dilute HNO_3 for determination by AAS. Accurate and precise results were claimed.[97] Digestion solutions typically contain HNO_3, $HClO_4$, H_2SO_4 and H_2O_2

in various combinations but more vigorous oxidising agents, V_2O_5 for Al[238–240] and HF for Sn[241] have been reported.

Alkaline digestion with Na_2CO_3–NaOH was employed to prepare infant formulas for determination of I^-,[242] while Se was measured by ETAAS in mussel and wheat samples after TMAH digestion.[243]

In a comparison of trypsin and pancreatin for the *enzymatic digestion* of baby foods, good results were obtained for the subsequent speciation of As using trypsin but there was poor separation of DMA and AB with pancreatin treated specimens.[244]

2.1.3 Preconcentration. Most of the reports on *preconcentration* involve analysis of drinking waters or other beverages. Use of FI systems and on-line collection onto a column of a suitable solid phase predominate. A novel arrangement for Pb used a minicolumn packed with polyurethane foam loaded with 2-(2-benzothiazolylazo)-2-*p*-cresol. Trapped Pb was eluted with 0.1 M HCl with detection by FAAS. The LOD was 1 μg l^{-1}; scope for increasing the sensitivity was available.[245] Most studies used FAAS or ICP-MS for detection at ng l^{-1} concentrations, although the eluted analyte was collected into an analyser cup for measurement of As[246] and Co[247] by ETAAS. Use of the knotted reactor for concentration of the Co-nitroso-R salt complex is reported yet again.[10] Somewhat similar in principle was an FI system, which involved precipitation of Cd as an ion pair between tetraiodocadmate and quinine.[248] The precipitate was then dissolved with C_2H_5OH for determination by FAAS. A sample volume of 15 ml was taken and a concentration up to 32-fold was achieved. Separation and concentration by precipitation was employed to again determine Cd in drinking water. Using Fe^{III} hexamethylenedithiocarbamate a colloid precipitate was formed and analysed by FAAS or ETAAS.[249] Simple evaporative procedures were reported with *in situ* concentration of large sample volumes of beer within the graphite furnace,[250] or applied to a thin layer or paper chromatographic media[251] where a stream of hot air permitted a concentration factor of 200 within 20–30 min.

2.2 Speciation

Examples of *separation of inorganic species* predominate in this period with publications referring to Al, As, Br, Cr, Fe, Hg, I and Se. Most of the technical details relating to separations were similar to those reported previously although some of the applications were novel. Developments for the speciation of As and Se are described in the sections on individual elements below.

Al in drinking water was separated into particulate, exchangeable, non-exchangeable inorganic and non-exchangeable organic species by filtration and ion-exchange. Exchangeable and non-exchangeable inorganic Al were the main forms and changes occurring by boiling the water were reported.[252] The anion exchange separation of bromate and bromide in drinking water[253,254] also removed polyatomic ions at *m*/*z* values of 79 and 81 which eluted before and after the bromate.[253] Cr^{VI} in infant formula was similarly isolated by ion exchange, for measurement by ETAAS.[255] I in milk was speciated by SEC[256] and by IC[257] and the measurements made by ICP-MS. Chemical isolation by extraction of a complex formed with thiocyanate into IBMK was used to determine Fe^{III} in wines.[230]

SEC with ICP-AES for detection was employed for the separation of complexes and multi-element analysis of breast milk[17] and tea.[258] Well established procedures involving *ion exchange HPLC* and ICP-MS were similarly used to examine samples of water and fish.[228,259]

2.3 Applications using hydride generation

In over half of the papers reviewed for this section AFS was used for the eventual measurement, to take advantage of the lower detection limits afforded by this technique. A number of food types were investigated, usually for *As or Se but other hydride forming elements, including Pb*, were also determined. A range of foods available in Ireland were analysed to compare dietary intakes of Se with that of other countries.[260] Only one report[81] made use of a system for electrochemical HG. A Nafion membrane separated the sample and electrolyte and conditions such as flow rates, applied current, *etc.*, were optimized. An air–liquid petroleum gas (LPG) flame heated the quartz atomization cell. For the determination of Se, the LOD was 10 μg l^{-1}.

Exceptional LODs may be achieved by using *vapour generation coupled to ETAAS*. Matusiewicz and Mikolajczak used HG and CV to determine As, Sb, Se, Sn and Hg in beer.[250] The hydrides were formed and transported by gas flow to a Pd-treated graphite furnace where they were retained by adsorption. When trapping was complete the furnace was heated to atomize the analyte. Using a 10 ml sample the LODs were 28, 21, 10, 50 and 90 ng l^{-1}, respectively.

Other reports include work where *total analyte concentrations* were measured or where species were separated by on-line HPLC (see Table 1).

2.4 Applications using flame atomic absorption and emission spectrometry

Costa *et al.* reported on the measurement of Cu, Fe, Mn and Zn in Portuguese wines by *FI-FAAS*.[261] Sample volumes were selected to allow determinations in ranges between 0.25 and 15.00 mg l^{-1}. Sweet wines from the Canary Islands, Spain, were classified according to the concentrations of Ca, Cu, Fe, K, Mg and Na measured by FAAS.[262] Lower concentrations of Cu[263] and of Fe^{III} [230] were determined using on-line separation techniques. On-line preconcentration methods were developed to measure Cd in mussels,[248] Pb in seafoods,[245] and Cu[263] and Pb[264] in water, with determination by FAAS. Impressive enhancement factors (up to 340 times) were reported using these rapid procedures.

Phosphate in foods was determined by forming the bismuth phosphomolybdate complex, extraction into IBMK and measurement of Bi by FAAS. The LOD was 0.008 μg l^{-1}.[265]

After a simulated gastro-intestinal digestion, infant foods with added phytate were dialysed and the fraction containing *low molecular weight Zn species* measured by FAAS to assess bioavailability.[232]

A methane–air flame was investigated for the measurement of *Rb in water by FAES*. Flame composition, observation height and spectral bandpass were optimized and an LOD of 2.3 μg l^{-1} was obtained.[266]

2.5 Applications using electrothermal atomic absorption spectrometry

A few interesting developments have been seen in this review period. On-line preconcentration[10,247] and furnace trapping of hydride species[250] were described above. *Matrix modification* continues to be a fruitful topic for further investigation. A combination of W + Pd + tartaric acid was used by Acar *et al.* to stabilise Pb for the successful analysis of Turkish cookies.[267] Recovery was 99% and the LOD was 1.2 μg l^{-1}. Samples of mussels from coastal areas of Japan were lyophilised and digested using HNO_3, HF and $HClO_4$ and the residue dissolved in HNO_3. This solution was then analysed for Sn, with Ni added as modifier.[241]

Various "*difficult*" *sample matrices* were effectively analysed. An La modifier was used for the measurement of P in vegetable oil, with results in the range of 10–790 mg kg^{-1}.[268] Wheat

prepared in various ways to produce acidic slurries were taken for measurement of Fe and Zn and a modifier containing $Al(SO_4)_3$ improved the signal shape and the stability of the slurry.[234] Two reports referred to the analysis of sugar, one for the measurement of seven elements, the second for As. Both employed a Pd modifier with air ashing and one included ascorbate with the Pd.[237,269] The volatility of Hg and I makes these elements difficult to measure by ETAAS but three papers appeared in this period. Samples of baby foods and seafoods were prepared as slurries and suspended in 0.1% Triton X-100–3% HNO_3–2% $KMnO_4$–4% $AgNO_3$ for determination of Hg.[270] Iodine in milk and baby formulae was indirectly measured by forming an ion pair with Hg^{II} and 2,2′-dipyridyl, which was extracted into IBMK. A maximum ash temperature of 150 °C was possible with Pd in IBMK as the modifier.[231] Analysis of CRMs showed that both procedures gave acceptable results and data from the analysis of real samples were given. In the third paper the I^- in infant foods was again indirectly measured, this time by precipitation with Ag, redissolution in a cyanide solution and determination of the Ag by ETAAS.[242] Details of the temperature programme and chemical modifiers were given and the LOD was 3.1 μg g^{-1}. Preparation of samples as slurries featured in other work involving Al in typical foods consumed in Spain,[238] and Cd in seafoods.[271] Supporting media containing 10% C_2H_5OH–5% H_2O_2–0.5% HNO_3 or 0.1% Triton X-100–5% H_2O_2–0.5% HNO_3 were used to prepare slurries of baby foods for measuring Al and Cr, respectively.[272] Aqueous calibration was possible as there was no matrix effect and LODs were 50 and 4 pg for Al and Cr.

2.6 Applications using inductively coupled plasma mass spectrometry

A quick glance at the papers seen in this review indicate that *more than half of those using ICP-MS were concerned with measurements of just a single analyte*. Furthermore, in two-thirds of the publications ICP-MS was presented merely as the analytical technique for a specific application, with no new instrumental or methodological development. In one innovative piece of work a new miniature cyclonic spray chamber and a concentric glass nebuliser designed for low sample uptake, were used to measure I in foods.[273] With the low sampling rate nebulizer wash out was accelerated compared with other systems. Sample digestion using only HNO_3 was achieved under pressure within a sealed container at 230 °C. Ethanol in wine is reported to impose a matrix effect when samples are aspirated using a conventional nebuliser, requiring use of an internal standard. A microconcentric nebulizer with a membrane desolvator (MCN 6000) eliminated the interference.[274] Specimens with high Ca contents suppress the Pb signal causing erroneously low results or failure to detect the presence of this metal. Sector field ICP-MS however is not subject to this interference and was used to measure Pb in calcium supplements at concentrations down to 0.6 μg g^{-1} which was suitable to meet the legislative requirements set by safety authorities.[94] Work to show that this technique may be employed for multielement analyis of milk fractions[275] and tomatoes[276] was reported but no obvious advantages in terms of simplicity, freedom from interferences, sensitivity, *etc.*, were claimed.

Measurement of a *single isotope or of isotopic ratios* provides useful information to identify the source, or to follow the fate, of an element. Barbaste *et al.*[277] compared different mass analysers and found that the precision achieved with TOF or sector field MS was far superior when compared with Q-MS for the determination of $^{206}Pb:^{207}Pb$, $^{208}Pb:^{206}Pb$ and $^{206}Pb:^{204}Pb$ ratios in wine. The Pb isotopic ratios in wine have been thought to be specific for the region of origin but long-term changes in ratios were reported as a consequence of discharges into the atmosphere from industry and petrol additives during the last 50 years.[278] An alternative to Pb isotopic ratios for this purpose may be afforded by $^{87}Sr:^{86}Sr$.[279] Wine samples were diluted in H_2O and submitted to a two-step cation exchange separation, which also removed interference from Rb. Eluted fractions were evaporated, taken into HNO_3 and sampled at the mass spectrometer. Precision was better than 0.3% RSD. Intestinal absorption of Cd was investigated in human volunteers following ingestion of porridge containing flour intrinsically labelled with ^{106}Cd.[124] It was suggested that absorption may be greater than previously stated.

Using *chromatography to eliminate interferences* was a feature of several papers including that of Creed and Brockhoff[253] who determined bromate in drinking water. Br^-, brominated haloacetic acids and ions at *m*/*z* 79 and 81 (speculated as possibly being PO_3^+, $H_2PO_3^+$, HSO_3^+) were all removed by IC using a PA-100 column. Bromate was measured with an LOD of 0.3 ng g^{-1}. A similar analytical arrangement was described for measuring several halogen and arsenic ions in drinking water.[259] The chromatographic system incorporated an anion micro-membrane suppresser that removed Na^+, K^+ and other ions, which can cause polyatomic interferences and produce instability within the ICP.

Electrothermal vaporization requires little sample preparation prior to introduction into the plasma and can obviate the need even for dilution, which may introduce contamination. Multielement analysis of honey[280] and vegetable oil[281] were accomplished by ETV-ICP-MS.

Unusual applications for which ICP-MS was used include measuring the bioaccumulation of ^{137}Cs and ^{40}K in mushrooms[282] and Mo in diets prepared for infants with phenyketonuria.[180]

2.7 Applications using other analytical techniques

Inductively coupled plasma-atomic emission spectrometry is a well established technique and is widely used for *multielement analysis of foods and beverages*. Several papers were seen in which the technique was employed for measuring trace and major elements, or as a detector following chromatographic separation of complexes (Table 1). However, none of these publications included any novel analytical innovations.

A simple, rapid procedure was reported in which *methylmercury* was extracted from fish by a 5 min leach in acid. Sodium tetraethylborate and nonane at pH 7.0 were then added and after 40 min, assisted by ultrasonication, ethylation and extraction had occurred. More than 90% of the methylmercury was recovered in the nonane phase, which was analysed by GC with MIP-AES or ICP-MS for detection. The LODs for Hg were 4.4 and 2.6 ng g^{-1}, respectively.[176]

Concentrations of Cs and Se in mushrooms,[283] and of 12 elements in rice[284] were determined with essentially no sample preparation using *XRF*. The influence of stages of lactation on trace elements and minerals in human milk of Nigerian women were investigated using PIXE.[285]

2.8 Developments in individual elements

2.8.1 Arsenic. Speciation features prominently, as ever, and while most papers describe procedures for effective separation there was also concern with the stability following extraction from fish with methanol–water. Mixtures of As^{III}, As^V, AB, MMA, DMA and phenylarsonic acid were stored at 3 °C and at −20 °C for up to 30 days. No losses or instability of the As species were reported although problems with Sb and Se were noted.[228] Measurements were by ICP-MS. Suner *et al.* investigated the separation of *As species in seafoods*.[101] They later developed their procedure so that extracted samples were applied to a cation exchange column. Eluent at the void volume was run onto an anion exchange column to separate As^{III}, As^V,

MMA, DMA and AB, which were measured by HG-AAS after on-line thermo-oxidation. Arsenic species retained on the cation exchange column (AC, TMAO and TMI) were then separated, oxidised and detected by AFS.[286] Separation of seven species, from tuna fish, on a single column was achieved by Nakazato *et al.*[113] These workers employed an ion exclusion column packed with a carboxylated methacrylate resin. The mobile phase was 0.35 mM Na_2SO_4 at pH 3.8 and ICP-MS was used for detection. Good separation of As^{III}, As^{V}, MMA, DMA, TMAO, and AC or TMI was obtained and the ArCl interference on ^{75}As was removed by the chromatographic separation. Other procedures for speciation of As using chromatography and ICP-MS were reported for samples of oyster,[100,287] rice,[288] carrots[289] and baby foods,[244] all papers featured work to ensure that quantitative extraction was achieved.

Drinking water with high As concentrations may be treated with Fe to form precipitates. As this occurs the natural As^{III} and As^{V} distribution alters so that investigation of the original water is impaired. Addition of EDTA to the water maintained As in solution for speciation and measurement by IC and ICP-MS.[290] A simple *differentiation of As^{III} and As^{V}* in beer was described based on treatment with or without KI.[291] Recoveries of As^{III} and As^{V} were 95% and 96%, respectively.

Total As was measured in flour by ETAAS following a preconcentration procedure. After digestion the *As was precipitated by adding an Ag solution*. The Ag_3AsO_4 was dissolved in a small volume of 6 M NH_4OH and taken for analysis with an LOD of 0.3 ng ml^{-1}, a 20 fold improvement.[246]

2.8.2 Cadmium. Interest in the measurement of *Cd in foods* appears to have increased during this period. In a number of papers ETAAS was used to measure the metal in seafoods, meat products and drinking water samples (see Table 1), and also for the quantitation of Cd-containing species in spinach and radish after separation by SEC.[292] Flame AAS was seen to be suitable when some form of preconcentration was included[248,249] or with atom trapping.[293] In an interesting study from Japan, dietary intakes of Cd were measured in duplicate diets collected in 1977–1981 and again in 1991–1997. Samples were homogenised, wet ashed and analysed by ICP-MS. Significant reductions in intake and in blood Cd concentrations were observed.[129]

2.8.3 Lead. A preconcentration procedure with on-line sample enrichment on a functionalised polyurethane foam column and FAAS, giving an LOD of 1 μg l^{-1} was described earlier.[245] An *unusual chemical modifier*, W + Pd + tartaric acid, was favoured for measuring Pb in cookies by ETAAS[267] but the more recognisable mixture of $NH_4H_2PO_4$ + $Mg(NO_3)_2$ was used when Cd and Pb were determined simultaneously in a number of foodstuffs.[294] The compromise ash and atomize temperatures were 750 and 1600 °C and results for both elements were acceptable when recovery tests and analysis of CRMs were undertaken.

Although Pb can be measured with a *HG technique* this is not usually the method of choice due to limitations of sensitivity. One report, however, noted that HG-AAS gave a wide analytical range with good precision and accuracy.[295] Measurement of Pb in a calcium medium and of Pb isotopes, by ICP-MS was reviewed in section 2.6.

2.8.4 Mercury. A simple selective reduction procedure using $SnCl_2$ followed by $NaBH_4$ was used to determine Hg^{II} and methylmercury separately, by CVAAS. Results were verified by analysis of a CRM.[296] Measurement of methylmercury alone, by GC-MIP-MS or GC-ICP-MS[176] has been described above as has a procedure to determine Hg by ETAAS.[270] *Mercury in fish* from rivers contaminated as a consequence of gold mining activities[297] and in mushrooms growing in non-polluted areas,[298] was determined by conventional CVAAS.

2.8.5 Selenium. *Selenium continues to be the element that attracts the greatest interest* when judged by the number of published papers. Typical concentrations in Irish foods were measured by HG-AAS.[260] Unlike As there is less concern with speciation although an appreciable amount of work, all involving chromatography, was presented. Selenium, as in yeast and garlic, may provide protection against cancer and Ip *et al.* identified the major species in these foods as selenomethionine and γ-glutamyl-Se-methylselenocysteine, respectively.[299] Selenate-supplemented fertilisers are added to the soil in some areas to improve the Se content of crops. It was shown that when incorporated into cereals the major fraction was selenomethionine.[300] Aqueous extraction of the sample was not particularly effective but with enzymatic hydrolysis 80–95% of the total Se was recovered. In two other studies Se in mushrooms, measured by AF, was present in an unidentified compound[301] while in breast milk selenomethionine was the main form.[202]

Capillary electrophoresis has been developing rapidly in recent years. Separation of six Se species was demonstrated and the technique applied to the analysis of a nutritional supplement.[302] Extraction of Se compounds from nutritional formulas proves to be a particular challenge and two studies concentrated on this aspect. For the analysis of yeast-based supplements microwave heating with HCl or enzymatic treatment with proteinase K were equally effective.[303] Esterification of seleno-amino acids and acylation with trifluoroacetic acid anhydride, was the approach adopted for GC-ICP-MS.[98] For the measurement of Se^{IV} in drinking water sodium tetraethylborate was added to form the ethane-1,1′-selenobis complex which was measured by GC-MS.[304]

2.9 Single and multielement analysis of foods

A few *food types* feature in much of the published work (see Table 1). The following sections present some of the items of special interest that relate to particular food items.

2.9.1 Human milk and infant formulas. Several of the publications reviewed this year attempt to define the typical concentrations of a particular element or a group of elements. However, *the composition of human milk and of formulas is difficult to characterise*. It has been known for several decades that temporal changes occur both during a nursing session and longer-term over days-weeks-months. A further study used PIXE to show this in Nigerian women.[285] Silvestre *et al.*[69] studied the effects of factors such as maternal age and smoking habits, left and right breast on Cu, Fe and Zn concentrations, and a number of influences were discerned. The technique of SEC and ultrasonic nebulization ICP-MS was adopted to determine the concentrations and protein binding of six elements in human milk.[17] In addition, effects of maternal age and residential area were investigated. An *in vitro* investigation using continuous-flow dialysis was undertaken to assess the bioavailability of Ca, Fe and Zn from infant foods. These metals were highly available from human milk while thickening agents added to formulas can inhibit their availability.[305] The influence of phytate in infant foods on Zn bioavailability was studied *in vitro*.[232] The concentrations of 18 elements in three different infant formulas were compared and while most were equivalent in all three, there were some exceptions noted.[306]

There is considerable current interest in infant exposure to Hg during pregnancy and from human milk, where the maternal dietary intakes are high. Samples of human milk

and other specimen types were analysed for Hg by AAS and significant associations with Hg in the maternal diet were reported.[307] Other studies of *toxic elements in infant foods* included comparison of enzymic extraction prior to As speciation[244] and measurement of Al and Cr in slurried samples.[272]

2.9.2 Fish and seafoods. Given the large amounts and the chemical forms of As in seafoods it is not surprising that many of the papers address the issue of As speciation, as was discussed in section 2.8.1. Use of *metallic mercury to extract gold*, leading to contamination of rivers, prompted studies of the concentration and speciation of Hg in edible fish.[297] Concentrations that were well in excess of the WHO limit were measured in some species. Various methodological developments concerned with procedures for sample digestion and/or extraction, were reported. Preconcentration of Cd by on-line continuous precipitation–dissolution FIA and FAAS was described and applied to the analysis of mussels.[248] An equally elaborate on-line system for preconcentration of Pb in seafoods involved the use of a minicolumn packed with functionalised polyurethane foam[245] (see section 2.1.3).

2.9.3 Milk and dairy products. In the production of white *cheese, milk* passes through stages of cheese curd, and preripened cheese to the final product. The concentrations of As, Cd and Pb were found to increase enormously as milk was transformed into curd, but remained similar thereafter. There was no Hg detected in any of the samples.[308] Concentrations of eight elements were measured in yoghurt from the main producers in Spain.[309] The same authors investigated the effects of adding different fruits on the mineral composition[310] and reported some large differences associated with wild berry, pineapple and peach. The potential for using sector field ICP-MS to measure minerals in human, cow and formula milks was reported.[275]

2.9.4 Water. Analysis of *drinking and bottled water* provides the topic with the largest number of papers in this review year. Somewhat surprisingly, most are reports of single element measurements. In an unusual piece of work concentrations of Rb were determined by FAES using an air–CH_4 flame.[266] The LOD was 2.3 μg l^{-1}. Apart from more straightforward presentations of an element in water from a particular source other analytical papers describe systems for analyte preconcentration, usually involving on-line FIA (see Table 1).

The European drinking water *maximum admissible levels* do not apply to mineral waters and an examination of bottled waters provided some startling results. In a study in which 66 elements were measured in 56 different waters from throughout Europe, it was found that only 15 would meet the drinking water regulations.[311] In a similar Japanese study 22 elements were determined in 170 samples of bottled water. As in the European study some regionally associated variations were seen. None of the results exceeded the Japanese standards for mineral water but four samples would not have satisfied the maximum drinking water levels in Japan.[312]

2.9.5 Wheat and flour. Innovative analytical applications included a paper in which sample preparation was achieved using TMAH digestion. Results for measurement of Se were compared with an acid digestion procedure.[243] An elaborate system to isolate and preconcentrate As for measurement by ETAAS was discussed above (section 2.8.1).[246] Preparative methods (in acid at room temperature, acid at 60 °C, acid and microwave heating, dry ashing) were compared[234] and only the microwave approach produced clear solutions and consistent results for Fe and Zn measured by ETAAS. Solutions produced by wet ashing were analysed for Co using an FI system, which included on-line pre-concentration prior to ETAAS. The concentrations of Co reflected the *area where the wheat was grown* and the amount of bran in the milled wheat.[247] Other studies also demonstrated the regional variations and correlations between elements in soil and in the wheat.[313,314] Following supplementation of soil *via* selenite added to fertiliser it was seen that enhanced incorporation of Se occurred. Speciation using HPLC-ICP-MS demonstrated that a major part of the Se taken into wheat was converted into selenomethionine.[300] Flour and bread prepared in Ireland contained slightly more Se than similar foods in the UK but much less than those in North America.[260]

2.9.6 Wines and beers. What were described as *simple and rapid procedures* were reported including one method where no pretreatment was carried out and no chemical modifier was used for measuring Cu, Mn and Pb by ETAAS.[315] Recoveries were of the order of 85–125% suggesting that simplicity may not equate with accuracy. Indeed, a matrix effect attributed to ethanol was observed when wines were analysed by ICP-MS and that it was necessary to include an In internal standard.[274] In a systematic study of sample preparation for measurement of Fe in wine, dealcoholization, dry and wet mineralization using different acid mixtures with and without heating were investigated. It was seen that heating with HNO_3–H_2SO_4 gave the best results.[233] Other attempts for simplicity involved FI systems for on-line preconcentration so that FAAS might be employed.[230,261] Several workers proposed that results of multielement analyses or the isotopic ratios (*e.g.*, of Pb or Sr) may be used to authenticate the source of wines.

2.10 Dietary intake studies

Several interesting studies were reported during this year. *Total dietary intakes for adult reference groups* were reporteds for Br and I in the UK,[316] Cd and Si in Belgium,[125,317] Cd and Pb in south-east Asia and Japan,[127,318] I and Sr in Germany,[319,320] Mn in India[321] and for eight elements measured in foods in Thailand.[322] Again using duplicate diet analysis, the intake of Cd by women in Japan was found to have fallen by 32% between 1981 and 1997 although it is still high compared with other countries.[129] Rice was seen to be the major source of the Cd. Dietary intakes of Cu by the same individuals showed considerable variation when measured on six different occasions throughout one year[323] and it was suggested that short term investigations will give very misleading data. Intakes in infants and children also featured with analyses of breast milk and infant formulas[164,306] and total diets.[324]

2.11 Reference materials and collaborative trials

A panel of RMs of relevance to *radiological protection*, including a Total Diet and a Typical Diet were prepared by NIST and evaluated by seven laboratories. Caesium, I, Sr, Th, and U were measured by various techniques including ICP-MS.[82]

A series of reports were published by the *AOAC International*, of a collaborative study, in which up to 16 laboratories participated on related projects.[325–327] Samples of different food types were sent to each participant for measurement of up to five elements by AAS. The reports examined results achieved after microwave digestion, results after dry ashing and As results after microwave digestion. Agreement between laboratories for each of the analyses was presented as the relative standard deviations.

3.0 Conclusions

It has been apparent in recent Updates that a newer set of problems is emerging in the clinical trace element field relating to the use of newer materials and techniques in medicine and surgery.

One important issue is the breakdown of surgically-implanted metal prostheses. It is clear that the use of Co–Cr alloy prostheses results in release of Co and Cr into the surrounding tissue and into the circulation.[65,66] Brodner *et al.*[65] recommended that, because of the build-up of these elements in blood serum, they should not be inserted into patients with chronic renal failure. From the study by Kocadereli *et al.*,[67] the release of Cr and Ni from fixed orthodontic appliances into saliva is not significant over the first two months. The search for alloys with improved corrosion resistance involves other metals which also need examining for their potential toxicity. Alloys of Ti–Al–V have been developed for spinal implants and Villarraga *et al.*[212] examined the release of Ti in a canine model. Release of Ag from a silver coating on mechanical heart valve prostheses into blood was studied by de la Riviere *et al.*[207]

Medical advances in body organ imaging techniques and radiation therapy have resulted in the use of relatively high concentrations of some unusual compounds. In this review year, the pharmacokinetics of release of Gd from the contrast medium gadodiamide[193] and B concentrations in blood and tissues from the neutron capture agent boronophenylalanine[121] have been studied.

A third concern of continuing interest is the release of silicones from silicone breast implants. Lugowski *et al.*[206] demonstrated increased mean whole blood and breast milk Si concentrations in patients with breast implants. However, the range of Si concentrations in controls and patients is considerable with significant overlap such that the measurement of an individual's blood Si concentration would not be suitable for the monitoring of implant leakage.

There were two interesting advances reported that may have future potential. The first is the use of Ga to inhibit osteoclastic resorption of roots of teeth which can lead to tooth loss. An interesting study using LA-ICP-MS[37] showed that diffusion of $Ga(NO_3)_3$ into root dentine was sufficient to get a concentration high enough to be therapeutically useful. Secondly, a non-invasive XRF method of determining skin Fe concentrations[56] seems to have potential for assessing liver Fe concentrations in haemochromatosis and β-thalassaemia.

For the first time reports were seen of investigations involving organically produced foods and it will be of interest to see whether this continues.

Further application of techniques for As speciation featured within the clinical and foods/beverages sections. The most important development was the demonstration of methylated species containing As^{III}, the significance of which is likely to become apparent in the near future. After much interest in capillary electrophoresis in the last few years few examples were found of the recent use of this technique.

Analytically, there have been no discernible new directions. It is interesting, however, to see further developments in low-cost techniques for dissolution of samples and preconcentration using flow injection. It appears that, perhaps as more laboratories replace AAS by ICP-MS, the latter technique is being used for work where just one or two analytes were reported.

Table 1 Analysis of clinical and biological materials, foods and beverages

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Al	Serum	AA;ETA;HPLC	Al speciation after the administration of DFO was studied in serum samples obtained from 6 dialysis patients 44 h after the administration of a single dose of DFO. Both HPLC and ultrafiltration techniques were used to separate different Al species	104
Al	Serum	AA;ETA;L	Low M_r complexes of Al in human serum from 6 CAPD patients were separated by FPLC and identified by ES-MS-MS as Al-phosphate and a mixture of Al-citrate and ternary Al-citrate-phosphate complexes	103
Al	Serum	MS;ICP;L	Binding of Al and Fe to sites on transferrin was investigated	328
Al	Bone	MS;ICP;L	Al was determined in 30 bone samples taken from one patient. Results reported by weight of dry bone had the lowest coefficient of variation as compared with results reported by weight of wet bone, weight of bone-ash and Ca content of bone	329
Al	Foods, beverages	AA;ETA;L	Al was measured in the Spanish diet. Samples were mineralised using HNO_3–V_2O_5	238
Al	Baby foods	AA;ETA;Sl	Untreated foods were prepared in 0.1% w/v Triton X-100. Following homogenisation the slurries were taken for ETAAS yielding LODs of 4 pg. See also Cr, ref. 272	272
Al	Herbs, spices	AA;ETA;L	The same authors as in ref. 238 used the same method to determine Al in 72 samples of 17 herbs and spices regularly consumed by the Spanish population	239
Al	Potable water	-;-;L	Field extraction *via* a variety of chelation columns followed by measurement in the laboratory was used for on-site speciation of: 1) total recoverable; 2) total acid-leachable; 3) total dissolved; 4) dissolved extracted; and 5) dissolved non-extracted Al	330
Al	Tap water	AA;ETA;L	Al speciation in water boiled in an aluminium kettle was investigated	252
As	Cells, urine	AA;Hy;L	As^{III} species were separated exploiting the effect of pH on the generation of arsine. The LODs were 1.1, 1.2, and 6.5 μg As l^{-1} for As^{III}, MMA^{III} and DMA^{III}, respectively. Methylated As^{III} species were detected in urine from environmentally exposed subjects and in human cells exposed *in vitro* to inorganic As^{III}	115
As	Urine	AA;-;IC-HG	Reference values were evaluated for 4 As species (As^{III}; As^{V}; DMA; MMA) in urine from 101 men in northern Germany. The LODs of the analytical method used were: 1.1; 10; 2 and 2 μg l^{-1}, respectively	331
As	Blood, serum, urine	AA;ETA;L	The determination of the total content of As in blood, serum and urine by ETAAS with Zeeman correction is described. Samples were diluted with 0.1% w/v Triton X-100. A mixture of H_2O_2 (15% w/v)–HNO_3 (0.65% w/v)–Ni (0.5% w/v) was used as a chemical modifier. The LOD was 20 pg (2 ng ml^{-1})	332

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
As	Urine	AF;Hy;ion-pair chromatography	Samples were collected after treatment with dimercapto-1-propane sulfonate. In addition to As^{III}, As^{V}, MMA and DMA and a new species (MMA^{III}) was identified	333
As	Urine	MS;ICP;HG	A procedure for the oxidation of As^{III} to As^{V} prior to speciation of As compounds in human urine was investigated, using either Cl_2, MnO_2, H_2O_2 or I_3^-. I_3^- gave the best results	334
As	Urine	MS;-;LC MS;ICP;LC	As species in urine of rats chronically exposed to DMA were identified and quantified by both LC-ES-MS and LC-ICP-MS. LODs in LC-ES-MS were 75–200 pg As, about ten times higher than that of LC-ICP-MS. Three of the five As peaks in urine were identified as DMA, TMAO and TMA. The mechanisms underlying the generation of the unidentified compounds were investigated	335, 336
As	Urine	MS;-;GC	DMA and MMA were determined in urine after a newly developed solid-phase microextraction (SPME). The LODs were 0.12 and 0.29 ng ml^{-1}, for DMA and MMA, respectively	111
As	Urine	MS;ICP;LC-HG	Using an ion exclusion column with carboxylated methacrylate resin and Na_2SO_4 mobile phase, good separation of seven As species was achieved. LODs were 0.016–0.075 ng ml^{-1}	113
As	Urine	MS;ICP;LC	Features influencing separation of As^{III}, As^{V}, AB, DMA and MMA, such as column temperature, eluent molarity, Cl^- and sampling *via* direct nebulization or by HG, were investigated and optimum conditions were recommended	112
As	Urine	MS;ICP;HPLC	Different columns were evaluated for separation of As species and removal of the Cl^- induced polyatomic interference on AB. A silica based cation exchange column was the most effective and AB was measured in a urine CRM	337
As	Urine	MS;ICP;HPLC	Eight species were separated by anion exchange chromatography and identified. Urine samples from subjects drinking contaminated water were analysed without any pre-treatment. Questions concerning As metabolism were raised	338
As	Urine	MS;-;GC	DMA and MMA were determined in human urine samples by GC-MS after derivatisation with thioglycol methylate. The LODs were 0.95 and 0.8 ng ml^{-1}, respectively	339
As	Lung	AA;Hy;L	Reference ranges were determined for As and Se concentrations in lung and hilus tissue from 50 deceased persons. Wide intra- and inter-individual variations were observed	64
As	Biological samples	MS;ICP;HPLC MS;ICP;CE	Methods for separation of As, Cd and Se species were reviewed. The most popular technique was SEC-ICP-MS	340
As	Tissue	MS;ICP;L	The bioavailability of As in gold mine tailings was investigated in mouse pups administered a sample of size-fractionated mine tailings as an aqueous suspension, by oral gavage, providing 4 mg As kg^{-1} body weight. As was determined by ICP-MS in microwave-digested tissue samples collected 1 h after gavage. The LOD was 2 ng As g^{-1} dry weight. Tissue As was significantly higher in exposed pup than in control tissues in the following order: liver > blood > skin > brain > carcass	341
As	Seafood	AA;Hy;HPLC AF;Hy;HPLC	On-line thermo-oxidation and switching between cation and anion columns allowed the separation of 8 As species. The precision of measurement was at worst 12%	286
As	Seafood	AA;ETA;L	8 laboratories participated in a collaborative study of the determination of As in seafood using acid microwave oven digestion and ETAAS. The highest (worst) repeatability and reproducibility RSDs were 17.4 and 24%, respectively	327
As	Seafood, water	AF;Hy;LC	AB, AC, TMAO and TMI were determined using HPLC-thermo-oxidation-HG-AFS.	101
As	Oyster	AF;Hy;HPLC	As species were extracted using a low power microwave procedure. Quantitative extraction of AB, DMA and arsenosugars was obtained at a power of 40 W, and in 5 min, using the extracting agent CH_3OH–H_2O (1 + 1)	100
As	Oyster	MS;ICP;L	HNO_3 + H_2O_2 were used to digest samples in a microwave oven. By varying the applied power it was possible to extract differing quantities of the cationic and ionic species, which were then separated using ion-exchange HPLC and measured by ICP-MS	287
As	Tuna fish, human urine	MS;ICP;HPLC MS;ICP;HG	A robust ion-exclusion LC method was coupled either directly or *via* HG to ICP-MS and used to separate As^{III}, As^{V}, MMA, DMA, AB, AC, TMAO and TMI	113
As	Baby foods	MS;ICP;HPLC	As species—AB, AC, DMA, As^{V}—were determined following extraction using either trypsin or pancreatin, with the former being of most practical use	244
As	Carrots	MS;ICP;HPLC	As was extracted using accelerated solvent extraction and 5 species quantified. Recoveries were in the range 80–102%	289
As	Rice	MS;ICP;L	As^{III}, As^{V}, MMA and DMA were determined following extraction with 2 M trifluoroacetic acid at 100 °C for 6 h. The majority of the As was inorganic, with MMA and DMA accounting for less than 10% of the total	288

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
As	Wheat flour	AA;ETA;L	As^V was precipitated using Ag, dissolved in 6 M NH_4OH, collected in an ETAA spectrometer cuvette and determined using $Pd(NO_3)_2$ as modifier. The LOD was 0.3 ng ml^{-1}	246
As	Sugar	AA;ETA;L	60 μl of sugar solution in 0.2% HNO_3 were pipetted directly into a preheated tube held at 70 °C. By using 5 μg of Pd, a first pyrolysis step at 600 °C and air during the 40 s, large C deposits were avoided. The LOD was 0.08 μg l^{-1}	237
As	Drinking water	AF;Hy;L	As^{III}, total As, Sb^{III}, and total Sb were determined with LODs in the low ppt region	342
As	Drinking water	MS;ICP;L	EDTA treatment was found to stabilise As^{III} and As^V in Fe-rich waters for up to 14 days	290
As	Beer	AF;Hy;L	The LOD was 39 ng l^{-1}	291
Au	Urine	XRF;-;-	Separation and enrichment of Au and Pd from environmental and biological samples was achieved by Au and Pt co-precipitation with Hg, followed by complete evaporation of Hg. The LODs were 2.0 ng l^{-1} for Au and 2.5 ng l^{-1} for Pd	62
Be	Urine	AA;ETA;L	Urine was mixed with 0.2% acetylacetone–2 M ammonium acetate buffer and 0.4% Triton X-100. An LOD of 0.37 μg l^{-1} was obtained and analysis of a CRM gave excellent results	343
Be	Urine	MS;ICP;L	Concentrations of 0.12–0.15 μg l^{-1} were reported following occupational exposure	116
Be	Drinking water	AA;ETA;L	Samples were chelated, preconcentrated on Sep-Pak columns, then eluted using C_2H_5OH and a 20 μl portion introduced into the cuvette of an ET-AA spectrometer. The LOD was 2.3 ng l^{-1}	229
Bi	Blood, urine	AA;ETA;L	W and Rh were used as chemical modifiers. The platform was coated with a mixture of W and Rh and 100 ng Rh were added with each injection. Urine and blood samples were diluted with a solution containing 1.0% v/v HNO_3 + 0.2% Triton X-100. The LODs were 3.3 μg l^{-1} (urine) and 8.4 μg l^{-1} (blood)	118
Bi	Urine, river sediments	AA;ETA;IC	A sequential system for the on-line ion exchange separation and preconcentration of metal ions was developed. Samples were loaded onto SP Sephadex C-25 cation exchange resin, eluted with diluted HNO_3 and transported *via* air segmentation into the graphite tube for quantification	13
Bi	Urine	AE;ICP;FI-HG	On-line preconcentration at pH 4.5 was achieved using a quinolin-8-ol and Amberlite XAD-7 column. The complex was eluted by HNO_3. With 100 ml urine the LOD was 0.02 ng ml^{-1}	119
Br	Drinking water	MS;ICP;L	Bromate was separated from interfering ions on a PA-100 column in combination with a 5 mM HNO_3 + 25 mM NH_4NO_3 mobile phase and determined using ID–ICP-MS	253
Br	Drinking water	MS;ICP;FI	FI with an on-line anion exchange column was used to determine bromate and bromide, with the LOD for the former being 0.13 μg l^{-1} for a 500 μl injection	254
Br	Foods, beverages	MS;ICP;L	Br and I were determined in 20 UK food groups, sampled in 1997	316
Ca	Urine	AMS;-;-	It was shown that ^{41}Ca may be used to investigate skeletal Ca metabolism in situations such as osteoporosis and during treatment for bone disease	133
Ca	Infant formula, human milk	AA;-;L	Formula is sometimes thickened to prevent regurgitation. The results of a study of Ca, Fe and Zn in thickened formulas were described. The results showed that thickening with non-digestible fibre, such as locust bean gum, reduced bioavailability	305
Ca	Human milk, infant formula	AA;-;L	An *in vitro* method for determining Ca, Fe and Zn bioavailability was claimed to offer results in agreement with those obtained by *in vivo* studies, but with greater efficiency and lower costs	73
Ca	Cow's milk	AA;F;L	Samples were digested using HNO_3–$HClO_4$, 4 + 1	344
Ca	Cheese, dental plaque	AA;F;L	A study, using 16 adult volunteers, suggested that cheese-containing meals increase plaque calcium concentration and thus probably protect against dental caries	345
Ca	Chinese foods	AA;-;L	Ca and Fe levels were measured over a 6 week *post-partum* period in special Chinese foods such as "ginger vinegar soup". This soup was found to contain levels of Fe normally associated with high Fe foods	346
Cd	Blood	MS;ICP;L	An ID procedure was developed for the certification of RMs. Two digestion methods were evaluated and the method also included anion exchange chromatography to remove interferences from Cl, Mo and Na. The LOD was 0.005 ng g^{-1}	347
Cd	Blood, urine, food	MS;ICP;L	Two papers on the results of a comprehensive study of non-occupational exposure to Cd and Pb, conducted between 1991 and 1998, in 11 major South-Eastern Asian cities. The first paper concentrated on urban populations, the second on female intakes	127, 318
Cd	Blood, urine, food	MS;ICP;L	A study of 607 Japanese women showed blood and urine Cd results could be used as biomarkers of environmental exposure to Cd, but that urine Pb results were not reliable enough to replace blood Pb in assessing environmental exposure	128

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Cd	Blood, urine, food	MS;ICP;L	Cd levels in a survey conducted in Japan over the period 1991–1997 were compared with those found in a similar survey conducted in 1977–1981. Although levels had decreased, they were still high when compared with international values	129
Cd	Liver	AA;F; IC-HPLC	A method was developed to determine the concentration of metallothionein (MT) isoforms. Critical steps in sample preparation, such as MT extraction, MT saturation with Cd and protein separation, were optimized. The LODs were 2.0 μg g^{-1} liver for MT-1 and 1.3 μg g^{-1} liver for MT-2, respectively	348
Cd	Liver cytosol	AE;ICP;HPLC	MTs in extracts from cirrhotic livers were separated by SEC–anion exchange chromatography. Cu, Cd and Zn were determined to calculate the concentrations of the MTs, highest levels were in primary biliary cirrhosis	349
Cd	Metallothionein	MS;ICP;HPLC	The analytical performances of FPLC and anion-exchange chromatography for rabbit liver metallothioneins separations and Cd speciation were compared	350
Cd	Biological samples	MS;ICP;HPLC MS;ICP;CE	See As, ref. 340	340
Cd	Kidney	XRF;-;S	Using a Monte Carlo model, ^{133}Xe was investigated as the excitation photon source for an XRF system for the measurement of Cd concentration in kidney. Cd concentrations of 15–60 μg g^{-1} kidney tissue could be easily detected for distances between the skin and the kidney surface of 30–60 mm	58
Cd	Foodstuffs	AA;ETA;L	Cd and Pb were determined simultaneously using transverse heating, Zeeman-effect background correction and a 0.5% (w/v) $NH_4H_2PO_4$–0.03% (w/v) $Mg(NO_3)_2$ mixture as chemical modifier. Using these conditions the LODs were 0.38 and 9.3 pg for Cd and Pb, respectively	294
Cd	Equine meat	AA;ETA;L	Horse meat is a constituent of the diet in parts of Italy and this study showed that this product accounted for approximately 1% of the Cd intake in this population group	351
Cd	Porcine and bovine kidney	AA;ETA;L AA;F;L	To detect small differences in renal Cd levels between groups, *e.g.*, in the case of biological monitoring of Cd exposure, sampling of the outer cortex was suggested as the optimal method in a detailed study of sub-sampling strategies	226
Cd	Porcine tissues	AA;ETA;L	In an investigation of organically and conventionally reared pigs, the organic animals' kidneys were found to contain significantly higher levels of Cd; this was thought to be due to differences in feed and bioavailability	224
Cd	Seafood	AA;ETA;Sl	A method using platform atomisation, $NH_4H_2PO_4$ modification and Triton X-100 as dispersing agent was reported to give accurate, precise results for a range of samples including tuna and mussels	271
Cd	Durum and soft wheat	AA;ETA;L AA;F;L	Cd, Cu, Pb and Zn were determined in more than 400 samples of Italian wheat	314
Cd	Wheat	MS;ICP;L	Hydroponically grown wheat was intrinsically labelled with ^{106}Cd, made into porridge and fed to human volunteers. ICP-MS analysis of the faeces suggested Cd absorption rates may be higher than previously suspected	124
Cd	Carrot, endive	AA;F;L AA;ETA;L	Samples were collected from 8 gardens in Slovenia at different distances from a power station and Cd, Pb and Zn determined. Although heavy metals were not found in the soil, high levels were found in the edible portions of the vegetables	352
Cd	Radish, spinach	AA;ETA;L	High M_r Cd-containing proteins were characterised as part of a comprehensive study	292
Cd	Vegetable oils	MS;ICP;L	ETV–ICP-MS was used to determine Cd, Pb and Zn at LODs of 0.1, 0.2 and 2.0 ng ml^{-1}, respectively. The sample was introduced as an emulsion of 10% v/v oil–2% v/v Triton X-100–2% v/v H_2O_2–0.4% v/v HNO_3	281
Co	Urine	AA;ETA;L	4-(2-Thiazolylazo)resorcinol was added to urine and the Co-complex was retained on a column of Amberlite XAD-16. Elution was achieved with 1 M HNO_3 in acetone	353
Co	Hip joint wear particles	AA;F;L	Protocols to isolate particles employ treatment with aggressive agents or the use of enzymes. Depending on the procedure followed, extraction of Co or Cr from the particle may occur leading to erroneous results when the composition of the particles is determined. Enzymatic extraction caused the least change	354
Co	Natural waters	AA;ETA;L	An on-line FI–ETAAS method utilising ion-pair sorption on the inner walls of a PTFE knotted reactor was described. An enhancement factor of 15 was obtained for a 60 s loading and the LOD was 5 ng l^{-1}	10

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Co	Flour fractions	AA;ETA;L	Flour fractions were wet ashed in 0.1 mol l^{-1} HNO_3, and the resulting solution carried by a FI system to a chelation system and then a preconcentration column. The column was flushed using ethanol and the eluent collected in a PTFE autosampler cup. Co was found to be mainly associated with the bran fractions. The milling process did not affect results	247
Cr	Body fluids	AA;-;-	The literature (1983–March 1999) on Cr speciation in liquid matrices was reviewed	355
Cr	Blood, urine	AA;ETA;L	Cr in blood or urine was determined after dilution with water and using NH_4NO_3 as matrix modifier	356
Cr	Urine	MS;ICP;L	Reference concentration ranges (μg g^{-1} creatinine) for Cr (0.07–0.76), Ni (0.20–1.23) and V (0.02–0.22) in urine were estimated for children, aged 6–10, from the urban area of Rome	23
Cr	Hip joint wear particles	AA;F;L	See Co, ref. 354	354
Cr	Infant formula	AA;-;LC	Cr^{VI} was found to be in the range 10–75 ng g^{-1}	255
Cr	Baby foods	AA;ETA;Sl	Samples were treated with 10% v/v C_2H_5OH–5% v/v H_2O_2–0.5% v/v HNO_3, slurried and analysed using ETAAS which yielded an LOD of 50 pg. See also Al, ref. 272	272
Cr	Herbs, spices	AA;ETA;L	Samples were digested using HNO_3–V_2O_5 and Cr determined in 72 samples of 17 herbs and spices. The highest levels found were 1042 μg g^{-1}(dry weight)	357
Cr	Milk, sugar	AA;ETA;L	A fast, direct method using Zeeman-effect ETAAS was described, yielding LODs of 0.13 ng ml^{-1} and 0.23 ng ml^{-1} for cane sugar and milk, respectively	358
Cr	Water	AA;ETA;L Thermal lens spectrometry;-;L	Cr^{VI} was determined directly or on-line following chromatographic separation. Thermal lens spectrometry performed favourably in comparison with ETAAS and offered a lower LOD, 0.1 μg l^{-1}, than ETAAS	359
Cs	Mushrooms	XRF;-;S	Cs and Se were determined in mushrooms following treatment of the fungi with the 2 elements. Cs was found to accumulate within the mushrooms	283
Cu	Serum	MS;ICP;L	After separation of proteins by anion exchange chromatography a solution containing stable isotopes was added to permit an ID analysis	29
Cu	Serum, urine	AA;ETA;L	The method was applied to both urine and diluted (1 + 24) serum samples. Zeeman-effect background correction was used. The LOD was 0.98 μg l^{-1}	136
Cu	Urine	AA;F;L	A polyamine ion exchange column was included in an FI system. Cu was retained from a 5 ml sample to give an LOD of 1 μg l^{-1}. However, H_2O_2 pre-digestion was necessary to achieve accurate results	9
Cu	Biological materials	AA;F;L	Samples were solubilised using microwave heating. Cu and Zn were concentrated by extraction onto polystyrene–divinylbenzene with imidazoylazo functional groups. Parameters to provide optimal performance were investigated	137
Cu	Liver cytosol	AE;ICP;HPLC	See Cd, ref. 349	349
Cu	Human milk	AA;F;L	62 women provided samples from the 2–15th day *post-partum*. Cu, Fe and Zn were determined and the effect of the mother's habits and condition on the results evaluated	69
Cu	Human milk	AA;F;L	The evolution of Cu, Fe and Zn in 144 milk samples from 39 healthy women was analysed from colostrum to the third month *post-partum*	70
Cu	Foods, beverages	MS;ICP;L	The results of a detailed US study using 80 individuals suggested that estimates of the fraction of a population at risk from chronic Cu deficiency or excess Cu intake can be overestimated if based upon short-term measures of intake	323
Cu	Peanuts	AA;F;L	Samples were digested in H_2SO_4–30% H_2O_2	360
Cu	Butter	AA;ETA;L	A rapid method involving simply dissolving the sample in solvent and then direct injection was described for Cu and Fe	361
Cu	Durum and soft wheat	AA;ETA;L AA;F;L	See Cd, ref. 314	314
Cu	Vegetable oils	AA;ETA;L	Cu and Fe were extracted using 10% HNO_3 and the HNO_3 injected directly into the furnace	362
Cu	Vitamin tablets	AA;-;S	Sample powder was placed in a special chamber, then carried by the digestion solution to a thermally heated PVC coil. The analyte metal as the chloro-complex was retained on a coarse-particle (>0.5 mm) anion exchange resin mini-column, the beads held between two plastic screens which allowed insoluble residue to pass through to waste. After a brief column wash, the analyte was eluted with diluted HNO_3 and determined spectrophotometrically or by AAS. Cu, Fe and Zn were determined this way	97
Fe	Serum	MS : ICP;L	See Al, ref. 328	328
Fe	Serum	MS;ICP;L	See Cu, ref. 29	29

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Fe	Liver, serum	AA;-;-	The Fe content of serum ferritin was determined in groups of patients with normal or increased Fe stores by using ferritin immunoprecipitation followed by Fe quantitation. Liver Fe concentrations were measured non-invasively by superconducting quantum interference device (SQUID) biomagnetometry. The diagnostic value of the test in iron overload diseases was assessed	145
Fe	Skin	AA;-;-	A non-invasive procedure, microdialysis, was used to collect sample material, *ex vivo*. Concentrations of 3.6–7.7 μg l^{-1} were obtained and it was concluded that the technique is appropriate for *in vivo* sampling	146
Fe	Skin	XRF;-;S	To assess the validity of skin Fe as a biomarker to monitor treatment in cases of Fe overload, Fe levels in samples of abdominal skin and non-haem Fe concentrations in liver, heart and spleen were determined in Fe loaded rats	56
Fe	Brain	XRF;-;S	Microbeam imaging using SRXRF was carried out in single neurons from patients with Parkinson's disease (PD) and a control subject. Fe accumulated in neuromelanin aggregates in and around the nigral neurons, coprecipitating with Ca, Cu, S, Zn. The Fe intensity inside the melanin pigment granules of a PD case was about one order of magnitude higher than that of the control samples	42
Fe	Human milk	AA;F;L	See Cu, ref. 70	70
Fe	Human milk, infant formula	AA;-;L	See Ca, ref. 73	73
Fe	Human milk	AA;F;L	See Cu, ref. 69	69
Fe	Infant formula, human milk	AA;-;L	See Ca, ref. 305	305
Fe	Flour, milk	AA;F;L	Samples were dry ashed at 600 °C. The method was used to assess Fe intake in pre-school children from the Ivory Coast	363
Fe	Chinese foods	AA;-;L	See Ca, ref. 346	346
Fe	Chicken meat	AA;-;-	This investigation involved the slaughter by shotgun of 60 chickens, removal and then frying of the meat. Fe, Pb and Zn were then determined in the cooked meat and compared with levels from chickens that had been slaughtered without the use of shotgun. Pb levels in the shot birds exceeded recommended concentrations and the authors concluded lead should be replaced with Fe or Zn in shotgun pellets	364
Fe	Cooking utensils, apple sauce, hamburgers	AA;-;-	Preparation of apple sauce in iron cooking utensils reduced consumer acceptability due to discolouration and flavour change. No negative effects were found in hamburger preparation	365
Fe	Peanuts	AA;F;L	See Cu, ref. 360	360
Fe	Butter	AA;ETA;L	See Cu, ref. 361	361
Fe	Vegetable oils	AA;ETA;L	See Cu, ref. 362	362
Fe	Bulgur wheat	AA;ETA;L	$Al_2(SO_4)_3$ was found to be necessary as chemical modifier in a comparison of sample preparation procedures for the measurement of Fe and Zn	234
Fe	Grape juice, wine and other alcoholic beverages	AA;ETA;L	An evaluation of sample preparation procedures concluded that mineralisation using HNO_3–H_2SO_4 yielded the best results	233
Fe	Vitamin tablets	AA;-;S	See Cu, ref. 97	97
Ga	Teeth	MS;ICP;LA	Ga diffusion in human root dentine was investigated by quantitative measurement of Ga in teeth to assess the efficacy of Ga treatment to inhibit osteoclastic activity	37
Gd	Faeces, peritoneal dialysate, serum	AE;ICP;L	A method was developed for the determination of gadodiamide as Gd in biological samples. The limits of quantification in serum and peritoneal dialysate were 6.5 and 1.6 μM Gd, respectively, and in faeces 11 nmol Gd g^{-1} dry weight	193
Hg	Urine	AA;CV;L	Hg excretion after administration of the chelating agent 2,3-dimercaptopropane-1-sulfonate (DMPS) was measured in patients reporting symptoms allegedly caused by exposure to Hg from dental fillings and controls	366
Hg	Cord blood, blood, urine	AF;CV;L MS;ICP;L	Exposure to methylmercury and Hg vapour was assessed in pregnant women and their newborns in Stockholm	178
Hg	Hair	AF;-;-	Hg was determined in samples of hair (approximately 5 mg) collected as part of the National Human Exposure Assessment Survey. With LODs ranging from 4 to 22 μg kg^{-1}, Hg levels could be quantified in 95% of the samples. The mean, median and maximum of the annualised Hg levels in hair were 287, 204, and 3505 μg kg^{-1}, respectively	89
Hg	Hair	XRF;-;S	A scan along a single strand of hair showed peaks that indicated the date at which exposure to dimethylmercury had occurred and the date at which treatment had been administered	87

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Hg	Kidney	XRF;-;S	Instrumental improvements and optimisation of operating conditions were discussed with respect to the *in vivo* determination of Hg in kidney for occupational monitoring in cases of mild to moderate exposure	177
Hg	Food, hair, urine (CRMs)	AA;-;-	The assessment of method uncertainty was described	367
Hg	Environmental samples, biological samples, CRMs	AA;CV;L	A new, rapid technique is described for the determination of total Hg, after the pyrolysis of the sample in a combustion tube at 750 °C under an O_2 atmosphere and Hg collection on a gold amalgamator	368
Hg	Plants, tissues	AA;CV;FI	Three digestion procedures in a closed vessel microwave oven were compared using CRMs	175
Hg	Biological CRMs	AA;CV;S	Samples, without pre-treatment, were pyrolysed at 750 °C in an O_2 atmosphere, collected on a gold trap and analysed using AA with a silicon UV diode detector	368
Hg	Biological CRMs	AA;CV;HPLC	FI–HPLC–CVAAS yielded absolute LODs of 1.7 and 3.4 pg methyl and inorganic Hg	369
Hg	Biological CRMs, fish	MS;ICP;GC AE;MIP;GC	*In situ* ultrasonic assisted derivatisation and extraction using sodium tetraethylborate and nonane, respectively, were used for sample preparation	176
Hg	Water, biological samples	-;-;HPLC	Methods for Hg speciation using HPLC were reviewed	172
Hg	Biological materials	-;-;-	Methods for Hg speciation were reviewed	173
Hg	Babyfood, seafood	AA;ETA;L	Samples were slurried in solutions containing 0.1% Triton X-100–3% v/v HNO_3–2% m/v $KMnO_4$–4% m/v $AgNO_3$, yielding LODs of 59 pg	270
Hg	Fish	AA;CV;L	Hg was determined in fish from a gold mining area in Brazil. The highest reported level was 2250 μg g^{-1}	297
Hg	Fish	AA;CV;L	The LODs for inorganic and methylmercury were 125 and 183 ng g^{-1}, respectively	296
Hg	Mushrooms	AA;CV;L	A study of 13 species of wild edible mushrooms, collected near the Polish town of Augstow was reported. Supposedly an uncontaminated region, but levels up to 2100 ng g^{-1} dry weight were recorded in stalks	298
I	Blood, urine	XRF;-;-	A method to determine residual renal function of HD patients and dialysis efficiency was developed using I-based contrast media (iohexol and iodixanol)	144
I	Human albumin	MS;ICP;L	Optimised conditions were studied for the simultaneous determination of Pt and I in mixtures of diiodo Pt complexes and human albumin to investigate reaction mechanism and kinetics of these potential anticancer drugs	370
I	Infant formula	AA;ETA;L	I^- was determined indirectly. Following alkaline digestion I was precipitated using Ag, then dissolved in cyanide solution prior to measurement of the Ag using ETAAS	242
I	Infant formula, milk	MS;ICP;L	I species were separated using an SEC column with 30 mM Tris buffer as mobile phase. I speciation in cow, goat, human milk and infant formulae, all from different countries was conducted. The whey was found to contain 95% of the I for all of the samples except infant formulae, in which it accounted for 15–50%	256
I	Cows' milk	MS;ICP;HPLC	I species in cows' milk from the Thuringian region of Germany, were determined at LODs of <2 μg l^{-1}	257
I	Milk, beverages	MS;ICP;L	Large geographical (and seasonal) variations in I concentrations were found in different beverages supplying an appreciable part of the I in the Danish diet. Organic milk was found to have a lower I content than non-organic milk	225
I	Dairy foods	MS;ICP;L	In a study of 12 women receiving diets rich in dairy foods, no evidence was found to suggest low availability was a factor influencing the continued high incidences of goitre in Germany	319
I	Foods	MS;ICP;L	See Br, ref. 316	316
I	Biological and nutritional SRMs	MS;ICP;L	Samples were digested in HNO_3 and I measured using ID–ICP-MS, the instrument was equipped with a mini cyclonic spray chamber	273
Mg	Plasma	AA;F;L	The distribution of Mg in plasma was investigated by SEC, AAS, ion selective electrodes and ^{31}P-NMR. Ionized Mg accounted for 60% of total Mg, with the rest bound to plasma proteins (27%) and low M_r compounds (13%)	161
Mg	Plasma	AA;F;L	In 16 hyperthyroid patients plasma Mg was 0.74 ± 0.08 mmol l^{-1} vs 1.01 ± 0.09 mmol l^{-1} in 20 controls	167
Mn	Blood, brain	AA;ETA;L	The correlation between Mn concentration in blood and Mn deposition in brain were investigated using magnetic resonance imaging and measurements of blood and brain Mn in rats which received total parenteral nutrition (TPN) with 10-fold the clinical dose of trace elements for 7 d	168

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Mn	Brain	AA;ETA;L	Mn was determined in mouse brain by ETAAS with D_2 background correction and $Ca(OH)_2$ as a chemical modifier. The LOD was 1.04 pg	371
Mn	Wine	AA;ETA;L	Wine was found to contribute an average of 281 μg d^{-1} to the Mn intake of the French population	372
Mo	Infant formula, plasma	AA;F;L MS;ICP;L	Because formula is heavily supplemented with Mo, Mo intake and retention in infants with phenylketonuria was more than 18 times that of breast-fed infants	180
Ni	Urine	AA;ETA;FI	The FI system included an SP Sephadex C-25 cation exchange column which retained Ni from the sampled solution. A flow of buffer solution then transferred the Sephadex beads with the Ni into the graphite furnace. While the heating programme was in progress, the next sample was trapped on a renewed column. An enrichment factor of 72.1 was reported with an LOD of 9 ng l^{-1}	12
Ni	Urine	MS;ICP;L	See Cr, ref. 23	23
P	Vaccines	AE;ICP;L	P in haemophilus influenzae type b vaccines was directly related to the concentrations of polysaccharide in the preparations	373
P	Cow's milk	AA;F;L	See Ca, ref. 344	344
P	Vegetable oils	AA;ETA;L	Levels were in the range 10–790 mg kg^{-1}	268
P	Foods	AA;F, air–C_2H_2;L	P was determined indirectly as bismuth phosphomolybdate at the Bi 223.06 nm line, with an LOD of 0.008 μg g^{-1}	265
Pb	Blood, urine	AA;ETA;ED	*In situ* electrodeposition was applied to separate Pb from biological matrices after sample acidification. The method was tested on CRMs. For blood analysis, the LOD was 1.5 μg l^{-1} and CV 3.0%	147
Pb	Blood	AA;ETA;L	A method was described for determining blood Pb using continuum-corrected ETAAS	374
Pb	Blood	AA;ETA;L	Three designs of W-filament atomizers were evaluated for use in a previously described system. Best results were obtained with a long wire style that gave a characteristic mass of 200 pg, an LOD of 1–2 μg dl^{-1} and acceptable accuracy and precision	79
Pb	Blood	MS;ICP;L	Samples were diluted 1 + 9 with 0.1% v/v Triton X-100–0.1% v/v HNO_3. The LOD was 0.06 μg l^{-1}. The method was applied in a preliminary clinical investigation to assess the potential of blood Pb as a biomarker of bone resorption	151
Pb	Serum, blood	MS;-;L AA;ETA;L	Serum Pb measured by ID–TIMS was 0.24% of the blood Pb concentration	149
Pb	Blood	MS;ICP;L	Examples were presented of how measurement of $^{207}Pb:^{206}Pb$ and $^{206}Pb:^{204}Pb$ may identify likely sources of exposure within homes	38
Pb	Blood, urine, food	MS;ICP;L	See Cd, ref. 127	127, 318
Pb	Blood, urine, food	MS;ICP;L	See Cd, ref. 128	128
Pb	Blood	AE;ICP;Re cup in torch	Sample, diluted with H_2O and Triton X-100–0.5% HNO_3, was placed into a rhenium cup which was introduced into the torch. The Pb vaporised to give the AE signal. CRMs were analysed and accurate results were given	18
Pb	Biological materials	AA;ETA;Sl	The furnace platform was pre-treated with a W–Rh modifier that was stable for up to 300 measurements. 20 μl slurry containing up 1.5% m/v sample were added to the platform. Furnace lifetime and analytical sensitivity were improved by the modifier	148
Pb	Biological specimens	MS;ICP;L	Measurement uncertainties for the determination of Pb in RMs by ID were calculated for three instruments; Q-MS, double focusing single collector MS and single focusing double collector MS. Accurate results were given by all three	150
Pb	Tooth enamel	MS;ICP;L	Pb in tooth enamel was measured by ICP-MS and TIMS, as a marker of environmental lead exposure. In neolithic samples the Pb was only one order of magnitude less than was found in modern teeth	375
Pb	Bone	XRF;-;S	The performances of two new digital spectroscopy systems were compared with a conventional system for the *in vivo* measurement of bone Pb. Improved precision and LODs were observed. LODs were 1.5–2.5 and 0.5–1.0 μg Pb g^{-1} bone mineral for the two new systems, compared with conventional LODs of 6–10	44
Pb	Bone	XRF;-;S	A combined K- and L-based XRF *in vivo* method was proposed with a ^{109}Cd radiation source and Ge and Si(Li) detectors. It was suggested that a lower LOD is possible	45
Pb	Bone	XRF;-;S	Replicate measurements were made using cadaver legs and, over a prolonged period, on *in vivo* volunteers. Variation in results were 6–50 μg g^{-1} and 6–13 μg g^{-1}, respectively	157
Pb	Bone	XRF;-;S	Repeated measurements were made along the length of the tibia of cadaver legs. Variations of the results and of the measurement uncertainty were obtained depending on the sampling site	49
Pb	Bone, blood	XRF;-;S	Bone Pb and blood Pb were determined in 43 occupationally exposed subjects. The results were used to assess measurement uncertainty of XRF determinations of bone Pb, with particular attention to spatial orientation, and to address factors influencing bone and blood Pb concentrations	53, 376

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Pb	Bone	XRF;-;S	Uncertainty of measurement was similar with samples from children and adults	158
Pb	Bone	XRF;-;S	An anthropometric phantom for calibrating *in vivo* measurements of stable Pb in the human leg was developed, which energy spectrum is indistinguishable from that of the human leg. It provides a realistic calibration standard to be used for intercomparison measurements	48
Pb	Bone	XRF;-;S	Coherent conversion factors (*i.e.*, factors which convert between the matrix of the calibration standards and those of human bone) for plaster of Paris (the present matrix of calibration standards) and a synthetic apatite matrix were compared. Synthetic apatite matrix was more representative of bone mineral than plaster of Paris	46
Pb	Bone	XRF;-;S	Sources of measurement and calibration errors were estimated	47, 377
Pb	Bone	XRF;-;S	The relationships between either bone Pb levels or its variation with time and the cumulative blood Pb index was investigated in a repeated bone Pb survey. Half-lives between 9 and 15 years for the release of Pb from the tibia were estimated by regression models	51
Pb	Bone	XRF;-;S	The variability of K-XRF bone Pb measurements in young subjects was investigated using tibiae from two male cadavers, aged 17 and 20 years	50
Pb	Blood, bone, urine	XRF;-;S	The associations between biomarkers of Pb exposure and polymorphisms in the δ-aminolevulinic acid dehydratase and the vitamin D receptor genes were evaluated in former organolead manufacturing workers	155, 156
Pb	Bone	XRF;-;S	*In vivo* measurements in lead workers were much lower than on a previous occasion. The authors suggest that contamination may occur when investigating lead workers	378
Pb	Bone	XRF;-;S	Longitudinal changes in bone Pb concentration were assessed	52
Pb	Hair roots, blood	XRF;-;S	Pb in the hair root did not correlate with blood Pb concentrations. Analysis of hair roots cannot be used to screen for undue Pb exposure	92
Pb	Foodstuffs	AA;ETA;L	See Cd, ref. 294	294
Pb	Chicken meat	AA;-;-	See Fe, ref. 364	364
Pb	Durum and soft wheat	AA;ETA;L AA;F;L	See Cd, ref. 314	314
Pb	Cookies	AA;ETA;L	W, Pd, W + Pd and W + Pd + tartaric acid (TA) were tested as chemical modifiers in the determination of Pb. The W + Pd + TA modifier mixture was found to be preferable, yielding an LOD of 1.2 μg l^{-1}	267
Pb	Carrot, endive	AA;F;L AA;ETA;L	See Cd, ref. 352	352
Pb	Calcium supplements	MS;ICP;L	High resolution ICP-MS was used to determine Pb in 136 brands of supplements. Two thirds of the samples failed to meet the Californian requirements	94
Pb	Vegetable oils	MS;ICP;L	See Cd, ref. 281	281
Pb	Water	AA;F;L	Chelation preconcentration and the slotted quartz furnace yielded LODs of 1 μg l^{-1}	264
Pb	Wine	MS;ICP;L	The accuracy of the determination of Pb isotope ratios was evaluated using quadrupole, multicollector magnetic sector and TOF analysers for measurement of a range of European wines. The poor sensitivity of TOF necessitated preconcentration. The quadrupole gave poor isotope precision	277
Pb	Wine	MS;ICP;L	Pb isotope ratio analysis showed that the ratios in wine reflected environmental inputs	278
Pd	Urine	MS;ICP;L	Environmental exposure to Pd, Pt and Rh was assessed in 310 children, aged 6–10 years, from Rome (Italy). Urine samples were UV irradiated prior to analysis. The mean concentration values were (ng g^{-1} creatinine) 7.5 ± 5.4 (Pd), 0.9 ± 1.1 (Pt) and 8.5 ± 8.0 (Rh)	184
Pd	Urine	XRF;-;S	See Au, ref. 62	62
Pt	Plasma	AA;ETA;L	A validated method was described for the monitoring of patients treated with cisplatin in a liposomal formulation	379
Pt	Biological fluids	AA;ETA;L	Urine was diluted with 10% HCl, and plasma was mixed with 5% Triton X-100. Ultrafiltrates were preconcentrated onto the graphite platform. Heating programmes were optimised for each matrix. Samples were from patients treated with JM216	187
Pt	Blood, plasma, urine	MS;ICP;HPLC	The fate of oxaliplatin after its i.v. administration was investigated by HPLC-ICP-MS and ESMS. In plasma, Pt was mainly bound to γ-globulins (40%) and albumin (40%). In urine 1 h after infusion, 50% of the total Pt was oxaliplatin. In red blood cells, Pt was bound to haemoglobin (60%) and to low M_r compounds (40%)	380
Pt	Blood, plasma, plasma ultrafiltrate	MS;ICP;L	Standard equipment was used for blood and plasma samples (LOD = 0.1 μg ml^{-1}) while a USN (LOD = 0.001 μg ml^{-1}) was required for the ultrafiltrate. Pharmacokinetic studies following administration of oxaliplatin were reported	185
Pt	Human albumin	MS;ICP;L	See I, ref. 370	370

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Pt	Urine	MS;ICP;L	See Pd, ref. 184	184
Pt	Serum, urine	XRF;-;S	A TXRF procedure was developed for the routine monitoring of plasma and urine Pt levels in paediatric cancer patients undergoing chemotherapy with Pt-containing drugs	188
Pt	Kidneys	XRF;-;S	An *in vivo* XRF method was developed to measure Pt concentrations in the kidneys of patients receiving chemotherapy	57
Rb	Serum	AA;ETA;L	Concentrations in 70 dialysis patients were low compared with 75 control subjects; 304 $\pm$ 81 and 350 $\pm$ 74 μg l^{-1}, respectively. This may be relevant to neurobehavioural activity of uraemic patients	194
Rb	Mineral and well waters	AE;F, CH_4–air;L	Using the 780 nm line the LOD was 2.3 μg l^{-1}. The effect of interfering group I and II atoms was considered	266
Rh	Urine	MS;ICP;L	See Pd, ref. 184	184
Ru	Blood	AA;-;-	The fate of the antimetastatic Ru complex ImH was investigated by measuring blood and organ Ru contents in mice after acute i.v. treatment	381
Ru	Tumour cells	AA;ETA;L	Ru uptake by tumour cells was measured as part of a study on the Ru^{III} complex (NAMI-A). The relationship between cell uptake, cell cycle arrest and cytotoxicity was evaluated	382
Sb	Urine	MS;ICP;HPLC	A PRP-X100 anion exchange column with 20 mM EDTA pH 4.7 as mobile phase was used to separate Sb^{III} from Sb^{V}. $TMSbCl_2$ and Sb^{V} were separated with an ION-120 column and a mobile phase of 2 mM NH_4HCO_3–1 mM tartaric acid pH 8.5. LODs were 8 to 20 ng l^{-1}	109
Sb	Drinking water	AF;Hy;L	See As, ref. 342	342
Se	Serum, foods	AA;Hy;FI	A method was developed for the determination of Se in serum following microwave digestion and reduction of Se^{VI} to Se^{IV}. The LOD was 0.3 μg l^{-1}. The method was applied to the determination of Se in sera of Austrian and Slovenian subjects and for the calculation of dietary intakes	198
Se	Serum	AA;ETA;L	Serum Se was measured in 169 adults and 210 children from Poland. A Cu–Mg mixture was used as a matrix modifier. Mean values were <60 μg l^{-1}	200
Se	Plasma	AA;-;L	Plasma Se and glutathione peroxidase (GSH-Px) activity in blood were estimated in 304 horses. Estimates of Se content from GSH-Px activity values were unsatisfactory when compared with measured values	383
Se	Urine, serum	AA;ETA;L	Samples were diluted with 0.2% HNO_3 and 0.1% Triton X-100 added. The solution was injected into the furnace and a modifier containing Ni^{2+}–Pd–NH_4NO_3–HNO_3 was added. LODs for urine and serum were 4.4 and 21.4 μg l^{-1}, respectively. Evaluation using CRMs was satisfactory	343
Se	Blood (CRM)	AA;F;FI-HG	A new system is described, based on electrochemical HG, FI and AAS, to determine Se in biological materials. The LOD was 10 μg l^{-1}	81
Se	Urine	AA;Hy;LC	Se^{IV}, Se^{VI}, SeMet and selenocysteine were separated using a C_{18} anion exchange column. Conditions for optimum separation were determined and LODs calculated	384
Se	Urine	AA;Hy;HPLC	A method was developed for the separation and quantification of SeMet. The LOD was 1.08 μg l^{-1}	385
Se	Leucocytes	MS;ICP;L	See Cu, ref. 35	35
Se	Serum, water	MS;ICP;ETV	ID was used to improve the performances of a previously described method. The uncertainties for the two methods were calculated according to ISO guidelines	386
Se	Urine	MS;ICP;IC	K and Na were removed by extraction of samples with benzo-15-crown-5-ether, which led to improved speciation compared with unextracted urine. IC separation provided five species, SeMet, TMSI and three unidentified compounds	196
Se	Urine	MS;ICP;HPLC	Urine samples from subjects consuming different nutritional supplements were analysed. The work included an evaluation of nebuliser types and of a hexapole collision and reaction cell	26
Se	Urine	MS;ICP;L	Six species in urine, including SeMet and selenocystamine, were separated by reversed-phase chromatography	197
Se	Kidneys, liver, serum, urine	MS;ICP;HPLC	The metabolic pathways of different Se species (selenite and selenate) were investigated in rats injected ^{82}Se-enriched selenate or selenite	195
Se	Biological samples	MS;ICP;HPLC MS;ICP;CE	See As, ref. 340	340
Se	Lung	AA;Hy;L	See As, ref. 64	64
Se	Hair	AA;ETA;L	Se was determined after digestion with HNO_3 and H_2O_2 using Pd as a chemical modifier. The ashing step was carried out at 1200 °C and atomization at 1900 °C	86
Se	Environmental samples, biological samples	AF;Hy;L	Interferences arising from matrix components (*e.g.*, Co^{2+}, Cu^{2+}, Ni^{2+}) and digestion medium were investigated. Calibration using matrix matched standards or standard additions was recommended	387

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Se	Brain	XRF;-;S	Se concentrations were measured in rat brain with an LOD of 20 ng g^{-1}	388
Se	Mushrooms	XRF;-;S	See Cs, ref. 283	283
Se	Human milk, plasma	AA;-;L	The major form of Se in Kuwaiti mothers' milk was found to be SeMet; this species was not found in cows' milk	202
Se	Cows' milk, infant formula	AA;Hy;L	Over a period of 11 years there was little variation in the Se content of branded cows' milk or infant formula in a Japanese study	389
Se	Foods	AA;Hy;L	An Irish study found that Se levels in breads were lower than the USA and Canada and only marginally higher than the UK	260
Se	Rice and dried fish SRMs	AA;F, air–liquid petroleum gas;FI	Electrochemical HG was used to determine Se in biological samples. 30 samples h^{-1} was the throughput and the LOD was 10 μg l^{-1}	81
Se	Mussels, wheat flour SRM	AA;ETA;L AA;Hy;L	TMAH digestion was compared with acid mineralisation. The use of TMAH in speciation studies was also evaluated	243
Se	Cereals	MS;ICP;HPLC	Laboratory experiments investigated if the addition of selenate to fertilizers could be used to enhance Se content of Austrian cereals. Using enzymatic extraction, which greatly improved recoveries, it was found that the selenate had been incorporated in the plants as SeMet	300
Se	Mushrooms	AF;-;LC	Se in mushrooms was found mainly in low M_R forms	301
Se	Plant tissues	MS;ICP;HG	HNO_3–HF–H_2O_2 with microwave oven heating were used for sample dissolution. A special solution introduction device combined pneumatic nebulization with HG in the thin liquid film on the walls of the minicyclonic spray chamber. The LOD was 0.03 μg g^{-1}	203
Se	Coconut milk, coconut water	AA;ETA;L	Sample treatment involved simple suspension in a mixture (1 + 4 v/v) of tertiary amines. Zeeman-effect ETAAS was used, with Pd as modifier, for measurement. For six samples, the Se concentration in coconut water varied from 6.5 to 21.0 μg l^{-1} and in coconut milk from 24.2 to 25.1 μg l^{-1}	227
Se	Drinking water	MS;GC;L	Se^{IV} was derivatised to ethane 1,1′-selenobis by reaction with sodium tetraethylborate and then extracted using SPME (solid phase microextraction). Measurement was by GC-MS and LODs were in the range 81–166 ng l^{-1}	304
Se	Garlic, yeast	MS;ICP;HPLC	Selenised garlic and yeast were speciatied using HPLC–ES–ICP-MS showing the main forms to be γ-glutamyl-Se-methylselenocysteine (73%) and selenomethionine (85%), respectively. In rat feeding studies, supplementation of Se-garlic in the diet caused a lower total tissue Se accumulation when compared with Se-yeast. Se-garlic was significantly more effective in suppressing the development of premalignant lesions and the formation of adenocarcinomas in the mammary gland of carcinogen-treated rats	299
Se	Yeast-based food supplements	MS;ICP;HPLC	Total Se and selenomethionine were determined in 6 brands of supplements. Total levels conformed to label claims, but species present varied widely, with 1 brand containing all inorganic Se. The paper contained details of method development, with overnight treatment with Proteinase K being particularly effective	303
Se	Dietary supplements	-;-;CE MS;ICP;HPLC	6 species were separated in 8 min using CE, with results in good agreement with those obtained using HPLC–ICP-MS	302
Si	Blood, human milk, tissue	AA;ETA;L	Si levels were measured in patients with silicone implants and controls. Control of Si contamination was achieved using a Class 100 laboratory for sample preparation and washing specimen collection tools and laboratory plasticware	206
Si	Serum	AA;ETA;L	Reference values were obtained for Belgian children and adults, including pregnant women	204
Si	Biological specimens	AE;ICP;L	TMAH was added to samples with microwave heating to effect dissolution. An LOD of 2 mg kg^{-1} was reported	205
Si	Foodstuffs	AA;-:L	Using the duplicate diet method the normal daily Si intake in Belgian adults was found to be 18.6 ± 8.5 mg d^{-1}	317
Sn	Blood, tissue, urine	MS;ICP;-	The distribution of organotin compounds in body fluids and organs were studied in a fatal case victim of poisoning from organotin contaminated food	210, 390
Sn	Shellfish	AA;ETA;L	Samples, 0.5 g, were digested using HNO_3–$HClO_4$–HF, 10 + 5 + 5, evaporated to dryness and the residue redissolved in 3 ml HNO_3. 20 μl were injected into the furnace of a Zeeman-effect ETAA spectrometer along with 5 μl of 20 g l^{-1} Ni as chemical modifier	241
Sn	Lard	MS;ICP;L MS;-;GC	Tri- and dimethyltin in lard were found to be responsible for a poisoning incident in the Jiangxi region of China. Unfortunately limited details were given of how this contamination arose. Blood, urine and organs from those affected were also analysed	211

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Sr	Bone	AA;F, air–C_2H_2;L AA;F, N_2O–C_2H_2;L	The effect of common matrix components and ionization interferences were studied. The effectiveness of a "Y" shaped device, connected to the nebulizer for the simultaneous introduction and on-line mixing of standard solutions or samples digests with releasing agents or ionization buffers, to suppress these effects was assessed by comparison with results obtained by ETAAS. The LODs were 0.030 and 0.015 mg l^{-1}, and the precisions were 1.5% and 0.5% RSD, for the air–C_2H_2 and N_2O–C_2H_2 flames, respectively. The latter flame type was recommended	208
Sr	Bone, soil	MS;ICP;L	An on-line IC procedure was developed to separate Rb and Sr, thus allowing the removal of the isobaric interference affecting the determination of Sr isotope ratios. The use of the shielded torch system and USN enhanced Sr signal intensity by 100-fold	39
Sr	Wine	MS;ICP;L	$^{87}Sr:{}^{86}Sr$ showed promise as a method of fingerprinting wine origin	279
Sr	Foods, beverages	-;-;-	Using the duplicate portion method, Sr intake in 14 towns in Eastern Germany was measured. The average Sr intake was 1.1–4.5 mg d^{-1}	320
Th	Urine	MS;ICP;L	Depending on the level of exposure to ^{232}Th the samples were diluted 20- or 100-fold. Measurements were set up for monitoring occupational exposure to Th	214
Ti	Tissues	AE;ICP;L	Mechanisms contributing to the release of Ti from spinal implants were proposed	212
Tl	Blood, faeces, tissues	AA;ETA;L	In an experiment to determine if dimercapto-1-propansulfonic acid and Prussian blue may be used to treat thallotoxicosis, tissues of Tl-dosed rats were analysed. Some beneficial effects were seen using Prussian blue	391
Tl	Brain	AA;-;-	The concentration of Tl was measured in rat brain regions after subchronic administration of sublethal doses of Tl^{I} acetate	209
V	Intravenous solutions	AA;ETA;L	V was determined in solutions for i.v. administration and in 6 salt components of a multitrace element solution. The highest V concentrations were found in albumin solutions	99
V	Urine	MS;ICP;L	See Cr, ref. 23	23
V	Blood, kidney, liver	PIXE;-;- AA;ETA;L	Samples from animals given V-supplemented diets were analysed by two techniques. Similar results were obtained but the advantage of PIXE was the multielement measurements	216
W	Plasma	AE;ICP;L	The performance of a method for the determination of W in rat and dog plasma was described and compared with the requirements necessary to carry out pharmacokinetic studies. The limit of quantification was 100 ng ml^{-1}	213
Zn	Serum	AA;F;L	Concentrations in 152 healthy subjects aged more than 90 years were 11.97 $\pm$ 2.00 μmol l^{-1}. Lower levels were seen in those living in institutions	78
Zn	Serum	AA;F;L	See Cu, ref. 392	392
Zn	Serum	MS;ICP;L	See Cu, ref. 29	29
Zn	Blood, faeces, urine	MS;-;L	Zn metabolism was investigated in 7 girls using stable Zn isotopes and compartmental modelling techniques with TIMS for measurement	221
Zn	Urine	AA;F;L	Basal urinary Zn : creatinine ratio was investigated as an indicator of dietary Zn intake in healthy women	393
Zn	Liver, serum	AA;ETA;L PIXE;-;S	See Cu, ref. 140	140
Zn	Biological materials	AA;F;L	See Cu, ref. 137	137
Zn	Liver cytosol	AE;ICP;HPLC	See Cd, ref. 349	349
Zn	Proteins	XRF;-;S	The *in situ* analysis of trace elements by SR XRF was described. The distribution of elements in protein bands separated by electrophoresis from human liver cytosolic samples was analysed along the polyacrylamide gel	394
Zn	Infant formula, human milk	AA;-;L	See Ca ref. 305	305
Zn	Human milk, infant formula	AA;-;L	See Ca, ref. 73	73
Zn	Human milk	AA;F;L	See Cu, ref. 69	69
Zn	Human milk	AA;F;L	See Cu, ref. 70	70
Zn	Infant foods	AA;F;L	An *in vitro* method was developed to study the effect of phytate : Zn molar ratio on Zn bioavailability. Availability was lower in soybean-based formula than those based on cows' milk	232
Zn	Chicken meat	AA;-;-	See Fe, ref. 364	364
Zn	Carrot, endive	AA;F;L AA;ETA;L	See Cd, ref. 352	352
Zn	Durum and soft wheat	AA;ETA;L AA;F;L	See Cd, ref. 314	314
Zn	Bulgur wheat	AA;ETA;L	See Fe, ref. 234	234
Zn	Vegetable oils	MS;ICP;L	See Cd, ref. 281	281
Zn	Vitamin tablets	AA;-;S	See Cu, ref. 97	97

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Various	Biological and clinical samples, foods and beverages	-;-;-	The 2001 ASU highlighted a number of recent trends including growth in CE applications and movable reduction bed HG	1
Various	Food, blood	MS;ICP;L	A study of the nutrient intake of 52 women in Bangkok showed that Ca and Fe intakes were deficient in the majority of cases	322
Various (4)	Erythrocytes, plasma	AA;-;L	Post operative changes of Cu, Fe, Mg and Zn were observed in plasma but not erythrocytes of 11 patients undergoing neurosurgery	395
Various (4)	Blood, tissues	AA;F;L AA;ETA;L	Rats subjected to stress by restraint and cold had changes to the concentrations of Mg, Mn and Zn but not of Cu	396
Various (5)	Blood, cells, plasma	AA;ETA;L	Specimens were diluted with HNO_3–Triton X-100. The chemical modifiers and heating programmes were optimized for each sample type and element. Reference ranges for the sample types were presented (Cd, Cr, Cu, Mn, Se)	74
Various (10)	Serum	AE;ICP;L	Serum reference values in 141 healthy Norwegians were determined by a validated method. The effects of gender, age, smoking and oral contraceptives on serum levels of trace elements were investigated (Ba, B, Cd, Cu, Fe, Mn, Li, Se, Sr, Zn)	20
Various (16)	Serum	AE;ICP;L	Digested samples were taken with Yt as internal standard and serum based calibration materials. Detection limits and results with a serum CRM were reported. In real samples, the concentrations for eight elements were too low to measure	19
Various (12)	Serum	MS;ICP;L	Reference values for Al, Cd, Co, Cu, Li, Mn, Mo, Ni, Rb, Sb, Se and Zn in serum of term newborns from Rome (Italy) were reported	397
Various (12)	Plasma	MS;ICP;L	In coxsackievirus B3 (CB3) infection, the myocardium is a target in both humans and mice. The concentrations of 12 trace elements were determined in the myocardium of sham-inoculated controls and infected A/J mice 4 and 7 d postinoculation	33
Various (12)	Blood, plasma	MS;ICP;L	The concentrations of electrolytes and trace elements in blood or plasma were determined in samples from patients with coronary heart disease undergoing percutaneous transluminal coronary angioplasty collected before and after the clinical intervention (Ca, Co, Cs, Cu, Fe, K, Mg, Na, Pb, Rb, Sr, Zn)	30
Various (18)	Serum, synovial fluid	MS;ICP;L	The correlation between trace elements in synovial fluid of osteoarthritic knee joints and blood serum was investigated. The grade of inflammation did not correlate with any elemental concentration determined	31, 32
Various (12)	Plasma	MS;ICP;L	Plasma concentrations of Cd, Co, Cs, Cu, La, Mg, Mo, Pb, Rb, Sr, Tl and Zn were studied in haemodialysed (HD) patients over a 6 month period. Cs, Mg, Mo and Rb were reduced and Cd, Co and Pb increased in HD patients as compared with controls	28
Various (7)	Blood	MS;ICP;L AA;ETA;L	Cd, Cu, Hg, Mn, Pb, Se, Zn were determined in samples from patients with motor neuron disease. Cd was higher than in controls	76
Various (15)	Plasma	MS;ICP;L	REEs were determined in human plasma. The LODs for 15 elements ranged from 0.7 (Eu) to 5.4 (Gd) ng l^{-1}. Three sample preparation methods were compared	190
Various (12)	Plasma, myocardium	MS;ICP;L	Mice were infected with coxsackievirus to determine if the inflammation promotes changes in trace elements. Various decreases and increases were observed in plasma and heart tissue which may be related to the disease process	398
Various (17)	Serum	MS;ICP;L	Yet another study to report reference ranges in human serum ($n = 110$)	24
Various (4)	Urine	AA;ETA;L	Analyte ions were precipitated from 10 ml urine into 1 ml HNO_3. Parameters to affect precipitation were discussed (Cd, Cr, Mn, Pb)	399
Various (4)	Urine	AA;ETA;L	The determination of Al, Cr, Cu and Mn in urine was performed using a simultaneous AA instrument and Pd as the chemical modifier. Using an Ar–H_2 mixture (95 : 5) as the purge gas resulted in smaller and more uniformly distributed Pd particles. The LODs were 0.06 (Al), 0.05 (Cr), 0.08 (Cu) and 0.06 (Mn) μg l^{-1}	63
Various (25)	Urine	MS;ICP;L AA;ETA;L	Urine specimens from patients residing in the United States were used to determine representative ranges for 25 trace elements	22
Various (4)	Urine	MS;ICP;FI	Samples were digested and the solutions taken for on-line preconcentration. LODs were from 0.05 (U) to 2.24 pg ml^{-1} (Te) (Ag, Au, Te, U)	400
Various (7)	Urine	MS;ICP;FI	The method involved on-line dilution (by a factor of 16.5) and internal standardisation with ^{103}Rh. The LODs were 0.30 (As), 0.12 (Cu), 0.09 (Mo), 0.08 (Ni), 0.09 (Pb), 0.45 (Se) and 0.96 (Zn) μg l^{-1}	8
Various (25)	Urine	MS;ICP;L AE;ICP;L	Samples from patients with chronic exposure to As in food and air were analysed. Significant differences from unexposed controls were recorded	401
Various (4)	Semen	AA;-;-	The concentrations of Cd, Cu, Pb and Zn in bovine semen samples, to be used for artificial insemination, were investigated in relation to semen activity	402
Various (4)	Semen, plasma	AA;-;-	Low levels of Mg were seen in men with premature ejaculation (Cu, Mg, Se, Zn)	163

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Various (4)	Bile	AA;-;-	The concentrations of Ca, Mg, Pb and Sr in bile were determined in 119 patients with cholelithiasis and 25 controls	403
Various (13)	CSF	AE;ICP;L	Several elements were determined in CSF from subjects with Alzheimer's disease and controls (Al, Ca, Co, Cr, Cu, Fe, K, Mg, Mn, Na, P, S, Zn)	404
Various (11)	TPN fluids, serum, tissues	MS;ICP;L	Contaminants were identified in different fluids which were then infused to animals to determine the accumulation in tissues and possible pathologies (Al, As, Cd, Cr, Ge, Hg, Mn, Pb, Sn, Sr, V)	405
Various (5)	Saliva	MS;ICP;DIN	Samples of human saliva were mixed with HNO_3, diluted 1 : 4 with water and spiked with enriched isotopes for quantification of Ba, Cd, Cu, Pb and Zn by ID. The LODs were 0.11, 0.03, 0.40, 0.05 and 0.59 μg l^{-1}, respectively, and sample throughput was 30 samples h^{-1}	34
Various (7)	Dialysis fluid, plasma	MS;ICP;L	Changes in Ba, Ca, Cu, Pb, Mg, Sr and Zn concentrations during haemodialysis were monitored by measuring their concentrations in plasma and dialysis fluids before and after passing the artificial kidney	27
Various (5)	Pleural fluid, serum	MS;ICP;L	Samples were collected from 13 patients with emphysaema. Results were compared with fluid from other pulmonary conditions and with the corresponding sera (Cu, Mg, Mn, Rb, Zn)	406
Various (10)	Plasma proteins	XRF;-;-	The distribution of trace elements in plasma proteins from mice treated with cisplatin was determined by SEC-SRXRF (Br, Ca, Cu, Fe, Ni, Pt, S, Se, Sr, Zn)	407
Various (11)	Blood	PIXE;-;S	Br, Ca, Cd, Cl, Cu, Fe, K, P, Rb, S and Zn were measured in samples from hypertensive Nigerians and their controls. Significant differences for seven elements were reported	408
Various (14)	Human milk	PIXE;-;S	The content of Al, Br, Ca, Cl, Cu, Fe, I, K, Mg, Mn, Na, P, Rb and Zn in human breast milk from Nigerian mothers was investigated in relation to stages of lactation and term or pre-term delivery	61, 285
Various	Biological materials	-;-;-	The application of hyphenated techniques to the speciation of elemental forms was comprehensively reviewed	3
Various (6)	Tissue	AA;-;-	Concentrations of Al, Ca, Mg, Zn, Cu and Fe in stomach, kidneys, bone and liver of mice fed various Al compounds in drinking water were determined to evaluate the risk of long-term gastrointestinal Al exposure	409
Various (4)	Tissue	AA;Hy;L	Electrolytic HG using different cathode materials was investigated for analytical applications to the determination of As, Sb, Se and Sn. The LODs were in the range of 0.11–0.13 μg l^{-1} for As and Sb	80
Various (32)	Tissue	MS;ICP;L	Trace element concentrations were measured in liver and kidney (32 elements) and bone (20 elements) of 70 deceased adults from the Czech Republic. Some sex-related significant differences were reported	25
Various (10)	Heart tissue	AE;ICP;L	The content of Ca, Cu, Fe, K, Mg, Mn, Na, P, S and Zn in specialised heart tissue was determined to investigate their relationship with fatal cardiac dysfunction of unknown origin	410
Various (8)	Heart valves, nerves, trachea	AE;ICP;L	In a series of papers the authors examined differences between the named elements in various sample types, and the effects of ageing (Ca, Fe, Mg, Na, P, S, Si, Zn)	14–16
Various (17)	Spinal cord	AE;ICP;L AA;ETA;L AA;CV;L	The concentrations of trace elements in the spinal cord of horses with equine motor neuron disease were compared with those of controls. Cu concentration was significantly higher in horses with equine motor neuron disease than control horses (Al, Ca, Cd, Co, Cr, Cu, Fe, Hg, K, Mg, Mn, Na, Ni, P, Pb, Se, Zn)	75
Various (11)	Brain, erythrocytes	XRF;-;S	The concentrations and distribution of metals were determined in I-deficient rats treated with I and Se (Br, Ca, Cu, Fe, I, K, Mn, Pb, Rb, Se, Zn)	411
Various	Brain	PIXE;-;S	Validation of the technique was reported with details of calibration and LODs given	60
Various	Brain	PIXE;-;S	Normal and Alzheimer's brains were studied. Variations within and between regions of the brain were reported	412
Various (4)	Breast tissue	XRF;-;S	The content of Ca, Cu, Fe and Zn was evaluated in healthy and pathological breast tissue, as a possible diagnostic technique for breast cancer	413
Various	Tissue	PIXE;-;S	The release of trace elements from metallic prosthesis to surrounding soft tissues was confirmed and migration paths investigated	414
Various (6)	Tissues	XRF;-;S	EDXRF was used to investigate the effect of Li administration on trace element profile in control and diabetic rats (Br, Cu, Fe, K, Rb, Zn)	415
Various (7)	Gallstones	AE;ICP;L	Samples were digested with HNO_3 and H_2O_2 by means of focused microwave. The effect of the Ca content on the determination of Co, Cr, Cu, Fe, Mn, Ni and Zn was studied	416
Various (7)	Tooth enamel	AA;F;L AA;ETA;L AE;ICP;L MS;ICP;L	The whole enamel and surface layers of extracted non-carious human teeth from population samples and prehistorical remains were analysed using different techniques (Cu, Fe, Mg, Mn, Pb, Sr, Zn)	77

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Various (6)	Tooth enamel	XRF;-;S	Using a SR probe with a resolution of 100 μm, profiles for Br, Cu, Fe, Pb, Sr and Zn through a tooth were determined. Variations between samples from different regions were thought to be caused by the types of diet	43
Various (8)	Hair	AA;F;L	An assessment of the content of Ca, Cu, Fe, K, Mg, Mn, Na and Zn in the black and gray hairs of the same person in Taiwan revealed significant differences	90
Various (9)	Hair	AA;F;L	Age-, sex- and ethnic group related differences were investigated (Ca, Cu, Fe, K, Mg, Mn, Na, Sr, Zn)	417
Various (6)	Hair, nails, teeth	AA;-;-	The relationship between environmental exposure to Cd and Pb and the levels of the essential elements Ca, Cu, Fe and Zn was investigated	418
Various (6)	Hair	AA; F;L AA;ETA;L	Acid-leaching procedures assisted by ultrasonic energy for the extraction of Ca, Cu, Fe, Mg, Mn and Zn from human hair samples were optimised. Acid concentrations and temperature of the ultrasonic bath were the critical parameters	5
Various (4)	Hair	AA;ETA;L	Samples were dissolved in TMAH. A mixture of Pd and phosphate was used as modifier for Pb analysis, Pd alone for As and Cd determinations, none for Ni. The LODs were 0.4, 0.009, 0.1 and 0.5 μg g^{-1}, respectively, for As, Cd, Ni and Pb. Results agreed with those obtained by using a conventional acid dissolution	7
Various (4)	Hair	AA;ETA;L AE;ICP;L	Age and sex related differences were observed for Cu, Fe, Mn and Zn concentrations in head hair from 418 subjects aged between 6 months and 20 years	85
Various (13)	Hair	AE;ICP;L	The concentrations of Al, Ba, Ca, Cd, Cr, Cu, Fe, Mg, Mn, Ni, Ti, V and Zn were determined in the hair of fox terrier, schnauzer and mini schnauzer dogs. The effect of five washing solutions (deionized water, acetone, methanol, EDTA and Triton X-100) was investigated	419
Various (19)	Hair	AE;ICP;L	Reference values were determined in hair samples of children, aged 3–15 (Al, As, Ca, Cd, Co, Cr, Cu, Fe, Mg, Mn, Mo, Ni, P, Pb, Se, Sr, Ti, V, Zn)	84
Various (13)	Hair	AE;ICP;L	Changes in the concentration of Al, Ba, Ca, Co, Cr, Cu, Fe, Mg, Mn, Ni, Pb, Sr, Zn and other trace elements in human hair of subjects with chronic hepatitis were investigated	420
Various (5)	Hair	AF;Hy;L AF;CV;L	A novel method for the determination of As, Bi, Hg, Sb and Se was developed. Pretreatment included microwave digestion followed by continuous flow vapour generation. Samples were digested in two stages with HNO_3 and H_2O_2 for Hg analysis, whilst for the other elements a common digestion step with HCl and H_2O_2 was used. The LODs were 0.2 ng g^{-1} for Hg and between 2 and 10 ng g^{-1} for the other elements	88
Various (71)	Hair, nails	MS;ICP;L	Concentration ranges and differences related to age, sex and smoking habit were assessed in a sample of urban population from Sweden not occupationally exposed	83
Various (10)	Hair	MS;ICP;L AE;ICP;L	Ca, Co, Cr, Cu, Fe, Mg, Mn, Mo, Ni and Zn were determined in hair samples collected from participants in the expeditions in Antarctica prior to departure and at the end of the period spent at the bases	421
Various (4)	Human milk, plasma	AA;-;L	The Cu, Fe, Mn and Zn status of Kuwaiti breast milk was evaluated	71
Various (60)	Human milk	AE;ICP;L	SEC–USN–ICP-AES was used to speciate Ca, Cu, Fe, Mg, Mn and Zn in human milk from 60 lactating Italian mothers. Different binding patterns were observed, dependant on the protein and low M_R fractions yielded by the chromatographic separation	17
Various	Milk, skimmed milk, whey	MS;ICP;L	Double-focusing ICP-MS was used to determine Al, Ca, Cd, Cr, Cu, Fe, Hg, Mn, Na, Ni, Pb, Se, Sr and Zn in a range of milk and milk-derived samples	275
Various (8)	Skimmed-milk yoghurts	AA;F;L	Following dry ashing at 460 °C, Ca, Cu, Fe, K, Mg, Mn, Na and Zn were determined. A second paper from the same group estimated dietary intakes from yoghurt	309, 310
Various	Water	MS;ICP;L	An interesting coupling of IC with a conductivity detector and ICP-MS allowed determination of bromate, bromide, iodine, iodide, As^{III}, As^{V}, Cl^-, NO_3^- and SO_4^{2-} in drinking water	259
Various (66)	Mineral water	MS;ICP;L AE;ICP;L	56 brands of mineral water from throughout Europe were analysed. Only 15 would fulfil the drinking water regulations for all parameters where action levels are defined. Potentially toxic elements such as Pb appeared higher in waters packaged in glass rather than plastic	311
Various (22)	Bottled water	MS;ICP;L	In a study of 170 samples of bottled water from the Japanese market 4 samples contained elements at more than the maximum levels recommended in the Japanese water quality standard	312
Various (22)	Orange juice	MS;ICP;L	Multivariate analysis was used to discriminate between Australian and Brazilian juices	422

Table 1 Analysis of clinical and biological materials, foods and beverages (*Continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Various	Beer	AA;F;L AE;F;L	Samples were digested using HNO_3–H_2O_2 in a microwave oven. The resulting data were analysed using chemometric procedures to classify 25 beer samples	423
Various (5)	Beer wort	ETA;Hy;L	Hydrides of As, Sb, Se, Sn and Hg vapour, were trapped onto Pd- or Au- (for Hg) pre-treated walls of the graphite cuvette. All LODs were <100 ng l^{-1}	250
Various (12)	Sherry brandies	AA;F;L AA;ETA;L AE;ICP;L AA;Hy;L	A survey of 20 brands showed no elevated levels of potentially toxic elements (Al, As, Ca, Cd, Cu, Fe, K, Mg, Mn, Na, Pb, Zn)	424
Various (11)	Spanish brandy	AA;F;L AA;ETA;L	Brandies were classified using multielement data and chemometrics	425
Various (8)	Tea	AE;ICP;L	Pattern recognition techniques allowed green, black and oolong teas to be differentiated (Al, Ba, Ca, Cu, K, Mg, Mn, Zn)	426
Various	Tea leaves	MS;ICP;HPLC AE;ICP;HPLC	Numerous element–organic molecule complexes were found when SEC was used to speciate black tea leaves	258
Various (8)	Beet sugar	AA;ETA;L	Sucrose crystals were dissolved in 0.1% HNO_3 and As, Cd, Co, Cr, Cu, Pb, and Sn determined using Pd–ascorbic acid as chemical modifier. Zn was determined without modifier	269
Various (19)	Honey	MS;ICP;ETV	LODs of 0.1–0.5 ng g^{-1} were achieved for a wide range of elements of environmental concern	280
Various (12)	Rice	XRF;-;S	Al, Ca, Cu, Fe, K, Mg, Mn, Na, P, Ti, Si and Zn were determined without any form of pre-treatment	284
Various (10)	Sardines	AA;-;-	The elemental content of canned sardines from regions of pacific Mexico was determined as part of a larger study of the nutritional profile of the fish content (Ca, Cd, Cr, Cu, Fe, K, Mg, Na, Pb, Zn)	427
Various	Seafood	AA;F;L AA;ETA;L AA;CV;L	An experimental design process, known as Plackett-Burman 2(7) X 3/32 design, was used to optimise seven factors (HNO_3 concentration, HCl concentration, H_2O_2 concentration, acid solution volume, particle size, microwave power and exposure time to microwave energy)	6
Various (14)	Seafood	AA;ETA;L AA;CV;AA	The Plackett-Burman method was used to optimise ultrasonic bath-assisted extraction (As, Ca, Cd, Co, Cr, Cu, Fe, Hg, Mg, Mn, Pb, Se, Zn)	428
Various	Fish	AE;ICP;L	HNO_3 wet-ashing by Parr bomb digestion, HNO_3 wet-ashing by microwave digestion, TMAH–HNO_3 wet digestion, and dry-ashing were compared. The microwave oven method gave the best results	236
Various (22)	Harp seal tissues	MS;ICP;L	Levels of nutrient and harmful elements in young Harp Seal blubber, liver, kidney and muscle were reported	429
Various (10)	Flour	AE;laser;S	A novel technique, known as laser-induced breakdown spectroscopy was used to directly determine Al, Cd, Cr, Cu, K, Mg, Mn, Pb, Rb and Sr at LODs of <18 μg g^{-1}. All of the RSDs were in the range 2–10%	430
REE (15)	Wheat	MS;ICP;L	REEs were determined in 60 wheat varieties	431
Various	Soft wheat, Durum wheat	MS;ICP;L	A study of six different homogenisers showed that all contributed contamination to the analysis of Al, As, Cd, Co, Cr, Cu, Fe, Mn, Mo, Ni, Pb, Se, Sn, V and Zn	223
Various	Olive oil	AA;F;L AA;ETA;L	Following digestion using HNO_3–V_2O_5 Ca and Mg were determined using FAAS and Cr, Mn, Se and Zn by ETAAS	240
Various (5)	Foodstuffs, CRMs	AA;F;L MS;ICP;L	A pair of papers describing methods to determine Cd, Cu, Fe, Pb and Zn using microwave digestion and dry ashing respectively. The microwave method was adopted as official first action by AOAC International	325, 326
Various (4)	Bovine liver and apple leaf SRMs	-;-;L	IR generated by tungsten lamps was proposed as an aid to rapid sample decomposition. Total preparation times were 5 min for dilute acid solutions (Cu, Fe, Mn, Zn)	4
Various (13)	Food SRMs	AE;ICP;L	5 digestion procedures were compared including dry ashing at 500 °C, wet digestion with HNO_3–$HClO_4$, microwave digestion with HNO_3, microwave digestion with HNO_3–H_2O_2, and microwave digestion with HNO_3–H_2O–THF. The last method gave the best recoveries for Al, B, Ca, Cu, Fe, K, Mg, Mn, Na, P, S, Sr and Zn in 7 food SRMs	235
Various (5)	SRMs	MS;ICP;L	The results of a study, involving 7 laboratories, to improve reference values for Cs, I, Sr, Th and U were reported	82
Various (4)	Fish, soil, urine and water SRMs	MS;ICP;HPLC	The stability of As, Sb, Se and Tl species in the named SRMs under different storage regimes and during different extraction procedures was investigated	228
Various	Biological samples, environmental samples	AA;ETA;L AA;Hy;L AA;CV;L	ETA and vapour generation techniques for AA and their hyphenation were reviewed and compared. Optimal application fields were defined	2

[a]Hy indicates hydride and S, L, G and Sl signify solid, liquid, gaseous or slurry introduction, respectively. Other abbreviations are listed elsewhere.

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