# Trace Elements in Human Tissue

## 1. A SEMI-QUANTITATIVE SPECTROGRAPHIC SURVEY

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It is now known that the human body contains, in addition to the major mineral cation constituents—sodium, potassium, magnesium, calcium and iron—another group of elements, whose quantitative levels are uncertain and whose functions are not completely understood. The term 'trace element' is usually applied to this group which, in extremely small quantities, is known to play a vital part in the metabolism of plants and animals. In this paper, however, the term trace element will be extended to include all those metals present in minute amounts in tissue, irrespective of metabolic function.

The realization of the essential function of these minor constituents in plant and animal growth has prompted more attention to their evaluation in recent years. Stiles (1946) has reviewed much of the literature on trace elements in plants and animals and the significance of these substances in relation to nutrition. The toxicological importance of certain metals has also stimulated research on this subject for health reasons, and methods have been devised for establishing the levels of many elements in plant, animal and food materials. This aspect of the subject has been comprehensively reviewed by Monier-Williams (1949).

Considerably less attention, however, has been devoted to the analysis of trace elements in animal and human tissues than to those of plants. Previous research on this subject has been reviewed by Smith, Yeager, Kaufman, Hovorka & Kinney (1951), Kehoe, Cholak & Story (1940*b*) and Davis & Loosli (1954).

With the advent of large-scale atomic-energy programmes in many countries and the use of radioactive substances in reactors, in research and as weapons, a new significance has been given to trace elements in living materials. It is inevitable that there will be a small escape of fission products and of materials with neutron-induced radioactivity into air and water supplies as a result of these programmes. In order to evaluate the hazard due to the metabolism of these substances it is necessary to obtain an estimate of the levels of the various stable elements which occur in the human body. This information has not been available hitherto except for the major constituents. The semi-quantitative spectrographic survey described has been carried out on behalf of the Medical Research Council's Committee on Protection against Ionizing Radiation in order to provide this information in respect of the stable trace elements normally present in the human body.

Comprehensive surveys have also been carried out recently by Tipton, Foland, Bobb & McCorkle (1953), Tipton, Steiner, Foland, Mueller & Stanley (1954), Butt, Nusbaum, Gilmour & Didio (1954) and Koch, Smith, Shimp & Connor (1956).

The present survey has been carried out with an emphasis on minimum manipulation before analysis. This seemed justified in a preliminary survey, even at the expense of sensitivity, in order to avoid the risk of contamination associated with chemical concentration methods.

## EXPERIMENTAL

### *Reagents*

*Hydrochloric acid.* The Polaritan Grade (Hopkin and Williams Ltd.) was redistilled in all-quartz apparatus. The middle fraction was collected and stored in a stoppered polythene bottle.

*Nitric acid.* A.R. grade $HNO_3$ was redistilled in all-quartz apparatus. The constant-boiling-mixture distillate was stored in a stoppered polythene bottle.

*Acetone.* A.R. grade was redistilled from a Pyrex apparatus. The middle fraction was collected and stored in a polythene bottle.

*Distilled water.* Water distilled from a Manesty 00BE still was redistilled from Pyrex glass and collected and stored in a polythene aspirator.

*Chemicals for standard mixtures.* Specpure (Johnson, Matthey and Co. Ltd.) chemicals were used or the metal oxide was prepared by dissolving H.S. grade (Johnson, Matthey) metal in purified $HNO_3$ in dishes of silica or platinum and heating to form the oxide.

*Carbon electrodes.* (Supplied by Charles H. Champion and Co. Ltd.; 5 mm. × 200 mm. solid pure.) Spectrographic examination of these electrodes under the conditions described below showed them to be free from the trace elements under investigation with the exception of boron (strong lines) and copper (weak lines).

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### *Preparation of standards for spectrography*

*Soft tissue.* All standards and samples of tissue ash were ground in agate mortars with the precautions against contamination described below. A series of synthetic standards were prepared, based approximately on 'standard man' (Recommendations of the International Commission on Radiological Protection), and similar to those prepared by Tipton *et al.* (1953). The basis for the soft-tissue standards consisted of a mixture of the major inorganic components of soft tissue, i.e. $KH_2PO_4$, NaCl, MgO, $CaCO_3$ and $Fe_2O_3$. This basis or matrix of the major constituents, which were not estimated spectrographically, was common to all the soft-tissue standards. It was found to be free from spectrum lines of the trace elements under investigation.

A mixture containing 100 mg. of each metal was prepared from the following compounds: $AgNO_3$, $Al_2O_3$, $HAuCl_4$, $H_3BO_3$, $BaCO_3$, $Bi_2O_3$, CdO, $Co_3O_4$, $Cr_2O_3$, CuO, $Li_2CO_3$, $Mn_3O_4$, $MoO_3$, NiO, $Nb_2O_5$, PbO, RbCl, $SiO_2$, $SnO_2$, $SrCO_3$, $TiO_2$, $V_2O_5$, ZnO, $ZrO_2$. By dilution with the mixture of major soft-tissue constituents described above, standards were prepared, containing 1000, 400, 200, 100, 40, 20, 10, 4, 2, 1 p.p.m. of each metallic element.

*Bone standard.* Calcium phosphate as a basis or matrix for the bone standard was prepared from 'specpure' $CaCO_3$, purified HCl and A.R. grade $(NH_4)_2HPO_4$. The calcium phosphate was examined spectrographically and found to be free from lines of the trace elements under investigation.

### *Tissue specimens*

An endeavour was made to obtain tissue specimens from persons as near normal as possible [cases from instantaneous accidental death found to be free from evidence of gross organic disease at autopsies performed at various hospitals in the British Isles (see acknowledgements)], since little is known about the relationship between disease and trace-element distribution (cf. Olson, Heggen, Edwards & Gorham, 1954). For purposes of comparison, samples were collected from children and from infants dying in the neonatal period. Samples were also obtained from cadavers with evidence of disease.

In an attempt to determine the influence of local geology on the distribution of trace elements, some specimens were collected from people who had lived in the north-east of Scotland (Old Red Sandstone) and in the Cornish peninsula (granite), but insufficient specimens were available to make a significant comparison. Information about age, sex, occupation, diagnosis and cause of death, duration of disease and details of medication with metals was recorded as routine at autopsy.

A special effort was made to obtain samples which had had minimum contact with the dissection knife. The specimens were placed in polythene bags in a waxed container and transported to the laboratory immediately. After refrigeration at $-15°$ until hardened, the tissues were dissected with a quartz knife, a portion being selected from the centre of the specimen. Tissue surfaces, possibly contaminated at the autopsy by instruments, dust or body fluids, were thus eliminated. Samples dried in dishes of fused silica at 100° for 12–15 hr. were weighed, transferred to a muffle furnace and ashed at 500° for 12–15 hr. or until a white ash was obtained. To eliminate contamination from the roof of the muffle furnace, a Vitreosil (silica) lining was fitted. The greatest care was exercised at all stages in order to reduce contamination from atmospheric particles. Filtration of the air supplied to the laboratory through Vokes filters was unsatisfactory because the amount of dust in the air entering was so high as to cause rapid exhaustion of these filters. The supply of air under pressure to the laboratory was blocked off and manipulation of the ash was carried out in a portable 'dry box' constructed of Perspex. This was maintained at a slight positive pressure, by passing in compressed air filtered through a column of glass wool 12 in. high. Spatulas ground from Perspex rod were used for scraping the ash on to glazed paper (Teledeltos paper, free from the trace elements under investigation; supplied by the courtesy of Wiggins Teape and Alex Pirie Sales Ltd.). The ash was then stored in polythene containers.

### *Spectrographic method*

A semi-quantitative procedure using the cathode-layer d.c. arc was employed. Estimation of the trace elements was based on visual comparison of suitable selected spectral lines with corresponding ones on a standard plate prepared by examination of mixtures of known trace-element concentration.

*Apparatus.* Spectrograph, Hilger Medium Quartz; spectrograph slit, 10 $\mu$; photographic plate, Kodak IIN, backed, 10 in. × 4 in. or 10 in. × 2 in. as required; distance of source from (*a*) masking screen, 26 cm., (*b*) slit of spectrograph, 100 cm.; arc gap, 8 mm.; mask gap, 3 mm.; electrodes: lower, cathode, carbon (see below); upper, anode, carbon rod; current, 9 A d.c. at 200 V; exposure times, 3 min.

*Sample form and electrode loading.* The ground tissue-ash or standard was mixed with an equal quantity of spectrographically pure carbon by grinding in an agate mortar. The mixture was tamped into a hole $\frac{1}{32}$ in. in diameter, 12 mm. deep, in the special carbon electrodes (Slatter & Stitch, 1955, 1956), by the techniques of Mitchell (1948). The electrodes were cut from the carbon rod supplied by Champion and Co. on a machine tool made for this purpose (Slatter & Stitch, 1955, 1956).

*Procedure.* An image of the discharge arc was focused on the masking screen of a Bausch and Lomb optical head, and light from the anode was masked by adjusting the screen. The light from the cathode layer was focused on the slit of the spectrograph. To use the benefits of a 3 min. exposure (averaging of random variation in emission due to variation of electric current, air currents, etc., differential volatilization of elements and reduction of timing errors), an adjustable rotating light sector was constructed. This was placed immediately in front of the slit of the spectrograph. A 30° opening passing one-twelfth of the total light was selected as giving a satisfactory exposure.

*Photographic processing.* The Kodak IIN plates were developed for 4 min. with rocking in Kodak D 19 b developer in total darkness, placed in a 2% acetic acid for 30 sec., fixed in Fixol (Johnson and Sons Ltd., Hendon, London, N.W. 4) (diluted 1:3) and washed in tap water for 30 min. and rinsed with distilled water.

*Evaluation of plate.* The intensity of the spectral lines was compared visually with the corresponding lines on the standard plate. This was carried out in a Judd Lewis Comparator or, preferably, a projection comparator.

*Reproducibility of method.* With each series of samples analysed, a standard mixture of trace elements was exposed on the spectrographic plate. The intensity of the spectral lines of the trace elements from this standard was checked against those of the original standard plate. The results for a number of such determinations are shown in Table 1.

Table 1. *Reproducibility of spectrographic method*

Soft-tissue standards were examined with separate photographic plates over a period of 2 years. Concentration of various elements was estimated in terms of an original standard plate: (*a*) range, (*b*) 'mean', (*c*) number of determinations.

| Standard concn. (p.p.m.) | | Element | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Al | Au | Cd | Mn | Mo | Cu | Ti |
| 20 | (*a*) | 20–40 | — | 20–40 | 10–30 | — | 15–40 | — |
| | (*b*) | 27 | — | 23·7 | 16·3 | — | 25 | — |
| | (*c*) | 8 | — | 8 | 8 | — | 8 | — |
| 100 | (*a*) | 100–150 | 70–150 | 40–150 | 70–200 | 70–150 | 70–100 | 70–200 |
| | (*b*) | 116·7 | 89·4 | 97·8 | 98·9 | 103·3 | 93·3 | 117·2 |
| | (*c*) | 18 | 18 | 18 | 18 | 18 | 18 | 18 |
| 200 | (*a*) | 200–300 | 150–200 | 150–200 | 200–300 | 200–200 | 100–200 | 200–400 |
| | (*b*) | 250 | 175 | 175 | 250 | 200 | 150 | 300 |
| | (*c*) | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 400 | (*a*) | 400–400 | 300–400 | 200–300 | 300–700 | 400–400 | 300–400 | 400–400 |
| | (*b*) | 400 | 350 | 250 | 500 | 400 | 350 | 400 |
| | (*c*) | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

Table 2. *Spectrum lines employed and corresponding minimum detectable concentration of element*

| Element | Line | Sensitivity (μg./g. of ash) Soft tissue | Bone |
|---|---|---|---|
| Ag | 5209·1 | 100 | 100 |
| Al | 3082·2 | 20 | 20 |
| | 3944·0 | — | — |
| | 3961·5 | — | — |
| Au | 2676·0 | 40 | 40 |
| Be | 3321·3 | 100 | — |
| Bi | 2898·0 | 400 | 1000 |
| Cd | 2288·0 | 20 | 4 |
| | 3261·1 | — | — |
| Co | 2411·6 | 40 | 40 |
| | 2424·9 | — | — |
| Cr | 3005·1 | 40 | 10 |
| | 3015·2 | — | — |
| Cu | 3247·5 | 10 | 10 |
| | 3274·0 | — | — |
| Mn | 2576·1 | 4 | 10 |
| | 2593·7 | — | — |
| Mo | 3132·6 | 20 | 10 |
| Ni | 3414·8 | 40 | 40 |
| Pb | 2833·1 | 100 | 40 |
| Rb | 6206·3 | 10 | — |
| | 6298·3 | — | — |
| Sn | 2421·1 | 100 | 40 |
| | 2429·5 | — | — |
| Ti | 2641·1 | 40 | 40 |
| | 2644·3 | — | — |
| Zr | 2567·6 | 200 | 400 |
| | 2568·9 | — | — |

*Sensitivity of method.* The sensitivity (minimum detectable concentration, expressed as μg./g. of ash) for the elements investigated is given in Table 2 for soft tissue and for bone. It was seldom possible to use the strongest lines of the elements to be determined, because of interference from the lines of iron and other matrix or trace elements. Those lines were selected for use where resolution from the lines of interfering elements was satisfactory or the line of the interfering element was too weak to interfere under the conditions employed.

## RESULTS AND DISCUSSION

It cannot be overemphasized that the results obtained from this survey are only semiquantitative. The figures reported, both for ranges and mean, of the various concentrations of trace elements found are not intended to convey a definite numerical significance: they are orders of magnitude only. Nevertheless, such results show the organs in which certain elements occur and the approximate level of these elements. Comparisons between infants, children and adults have been made, and certain marked differences between these groups are at once apparent. No significant difference between sexes was detected, although Hartman, Laue, Neuberg, Rosenheim & Volmer (1934) reported slight differences between the sexes with respect to trace elements in liver. Similarly no obvious difference was apparent between levels or distribution of the elements in 'normal' adult persons and the specimens of pathological origin, although specific disease groups were not studied.

Aluminium, copper, manganese and rubidium were found regularly in most of the soft tissues examined, but rubidium was not detected in bone. These results are shown in Table 3. For the purpose of calculating a 'mean', values greater than 1000 p.p.m. (expressed as $>1000$ p.p.m.) were given a value of 2000 p.p.m. Values obviously much greater than 1000 p.p.m. were given the symbol $\geqslant 1000$ p.p.m. and 5000 was taken for calculation of the 'mean'. This assumption must be borne in mind in assessing the significance of the 'mean' values reported; they are not absolute values but may be regarded as approximate average levels.

*Aluminium.* There has been much controversy (e.g. McCollum, Rask & Becker, 1928; Kahlenberg & Closs, 1929) as to whether aluminium is a regular and normal constituent of human tissue. These results confirm those of most investigations that aluminium is regularly present.

Results obtained for this element must always be regarded with suspicion because of the ubiquitous occurrence of aluminium, as aluminosilicates, in dust. In this survey aluminium was detected in most specimens of soft tissue. The levels detected in bone were regularly very much lower than in soft tissue, and this is taken to indicate that values obtained for soft tissue were real and not resulting from contamination, since both bone and soft tissue suffered identical but minimal hazards of contamination. Most striking is the relatively high concentration of aluminium in adult lung (Fig. 1). This has been observed by other workers (e.g. Tipton *et al.* 1953, 1954; Koch *et al.* 1956). The marked increase in the concentration of this element in lung with age was demonstrated (Fig. 1) and is undoubtedly the result of inhaling large quantities of dust. An accumulation of this element with age is apparent also in liver and kidney (Fig. 1). The value of approximately 500 p.p.m. obtained for liver in this survey is comparable with that reported by Koch *et al.* (1956) (approx. 300 p.p.m.), but is higher than the figure of 62 p.p.m. reported by Tipton *et al.* (1953). Similarly, the value obtained for spleen (approx. 300 p.p.m.) agrees well with the value of 300 p.p.m. reported by Koch *et al.* (1956) and Tipton *et al.* (1954) (approx. 334 p.p.m.), but not with the value of 66 p.p.m. reported semiquantitatively by Tipton *et al.* (1953). The values obtained were generally higher than those reported by Kehoe, Cholak & Story (1940*a*, *b*).

*Cadmium.* The comparatively high levels of cadmium in the kidneys of adults are at once apparent from Fig. 1. Cadmium has been reported in bovine kidney (Malinga, 1941) and in the kidneys of other animals (Klein & Wichmann, 1945), and the concentration of this element in human kidney has been demonstrated by Tipton *et al.* (1953, 1954) and Koch *et al.* (1956).

Fig. 1 reveals that there is a marked difference in the levels of cadmium between the various age groups; the concentration increasing with age. Cadmium was regularly detected in the livers of adults.

*Chromium.* Chromium was not regularly detected in this investigation. The element was measured in specimens of liver (1), heart (1), thymus (2), cartilage (3) and testis (1) of some children. The element was not detected in any of the specimens of lung examined; this does not support

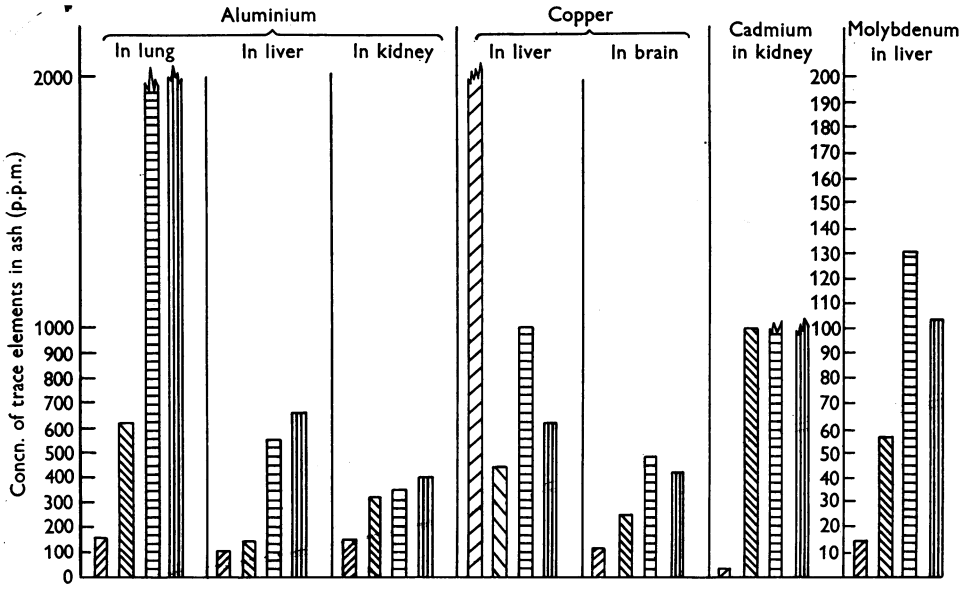


Fig. 1. Influence of age on the concentration of some trace elements in human tissues. ▨, 0–3 months; ▧, 1–12 years; ▤, material from normal adults 19–89 years; ▥, material from pathological adults, 18–89 years: the following diseases are represented in this group; carcinomas of kidney, rectum and bronchus, gastric ulcers, pneumonia, temporal glioma, hypertensive heart failure, coronary atheroma, thrombosis, mitral stenosis and acute stem-cell leukaemia. The values for individual disease groups were not found to differ significantly from those obtained from the normal adults. Broken columns at 1000 and 2000 p.p.m. indicate that calculated approximate average levels exceed these values respectively.

the findings of Ureone & Anders (1950), who reported 45 p.p.m. of chromium, calculated on the fresh tissue (approximately 4500 p.p.m. of ash).

*Cobalt.* This element was not detected in the tissues examined because the sensitivity for this element was not sufficiently good. Cobalt is now being sought in human soft tissues and bone, by radioactivation analysis.

*Copper.* The widespread occurrence of copper in tissues has been realized for several years. The highest concentrations of this element were observed in the livers of all groups, but especially so in those of foetus and infants. The copper of livers in this group was generally reported as $\gg 1000$ p.p.m., which probably means in excess of 5000 p.p.m. This high content of foetal and infant liver has been reported by several investigators, e.g. Sheldon & Ramage (1931), McElroy & Glass (1950) and Butt *et al.* (1954). It has been reported by Butt *et al.* (1954) that a similar disproportion between adults and the foetus occurs for iron and zinc, but not for manganese or lead.

The values for copper obtained in this survey agree well with those of other workers. Results for liver from adults (800 p.p.m. approx.) are within the range 300–910 $\mu$g./100 g. of fresh tissue reported by Tompsett (1935). The results agree also with those of Kehoe *et al.* (1940*b*), Butt *et al.* (1954) and Tipton *et al.* (1953, 1954). Results for copper in brain might suggest an increase in concentration with age contrasting with the decrease in liver after infancy (Fig. 1). Similarly the results obtained might suggest an increase in the concentration of copper in kidney with age. The values for adult brain are within the range noted by Tompsett (1935) and similar to those found by Bodansky (1921), Kehoe *et al.* (1940*b*) and Koch *et al.* (1956).

Table 3. *Approximate levels of some trace elements in the tissues of adults*

The figures (parts per million of the ashed tissue) given for range and mean are 'orders of magnitude' only.

| | Aluminium | | | Copper | | |
|---|---|---|---|---|---|---|
| Tissue | Range | Mean | No. | Range | Mean | No. |
| Adrenal | 100–>1000 | 950 | 18 | 40–400 | 250 | 18 |
| Bladder | <20–≫1000 | >1000 | 16 | 70–1000 | 250 | 15 |
| Bone | <20–200 | 50 | 14 | <10–70 | 20 | 14 |
| Brain | — | — | — | 70–1000 | 450 | 7 |
| Cartilage | <20–>1000 | 650 | 14 | 40–700 | 175 | 14 |
| Gall bladder | 150–≫1000 | 1000 | 11 | 200–>1000 | 750 | 11 |
| Heart | <20–>1000 | 300 | 24 | 300–>1000 | 700 | 23 |
| Kidney | <20–1000 | 400 | 26 | 150–>1000 | 550 | 26 |
| Lung | 1000–≫1000 | ≫1000 | 24 | 70–400 | 250 | 24 |
| Liver | <20–>1000 | 500 | 25 | 100–>1000 | 800 | 25 |
| Pancreas | 20–>1000 | 600 | 17 | 70–>400 | 200 | 17 |
| Prostate | 100–>1000 | 1000 | 9 | 100–1000 | 250 | 9 |
| Skeletal muscle | <20–>1000 | 550 | 17 | 40–700 | 150 | 18 |
| Skin | 40–≫1000 | 1000 | 18 | 40–>1000 | 300 | 15 |
| Spleen | <20–1000 | 300 | 22 | 40–>1000 | 200 | 23 |
| Subcutaneous fat | 40–≫1000 | >1000 | 20 | 70–700 | 250 | 19 |
| Testis | 20–1000 | 400 | 10 | 70–300 | 150 | 10 |
| Thyroid | 200–>1000 | 800 | 18 | 100–>1000 | 300 | 18 |

| | Manganese | | | Rubidium | | |
|---|---|---|---|---|---|---|
| Tissue | Range | Mean | No. | Range | Mean | No. |
| Adrenal | <4–70 | 35 | 18 | 100–>1000 | 400 | 17 |
| Bladder | <4–70 | 20 | 15 | 70–>1000 | 400 | 14 |
| Bone | <4–20 | 4 | 13 | — | — | — |
| Brain | <4–40 | 15 | 7 | 70–150 | 100 | 6 |
| Cartilage | <4–40 | 4 | 14 | 40–>1000 | 350 | 13 |
| Gall bladder | <4–100 | 40 | 11 | 40–700 | 150 | 10 |
| Heart | <4–20 | 10 | 23 | 40–>1000 | 450 | 23 |
| Kidney | <4–200 | 60 | 26 | 100–>1000 | 550 | 25 |
| Lung | <4–70 | 20 | 24 | 70–>1000 | 500 | 23 |
| Liver | 30–1000 | 150 | 25 | 100–>1000 | 500 | 24 |
| Pancreas | 20–200 | 100 | 17 | 70–>1000 | 400 | 16 |
| Prostate | <4–30 | 10 | 9 | 40–150 | 100 | 8 |
| Skeletal muscle | <4–30 | <4 | 18 | 70–>1000 | 500 | 16 |
| Skin | <4–20 | <4 | 17 | <10–>1000 | 250 | 16 |
| Spleen | <4–300 | 30 | 23 | 40–>1000 | 500 | 22 |
| Subcutaneous fat | <4–40 | 10 | 20 | <10–>1000 | 400 | 20 |
| Testis | <4–20 | 7 | 10 | 70–200 | 100 | 8 |
| Thyroid | <4–70 | 20 | 18 | 40–>1000 | 300 | 17 |

The values obtained are somewhat lower than those reported by Tipton *et al.* (1954).

The values obtained for kidney in the adult group (550 p.p.m.) are higher than those reported by Koch *et al.* (1956; 200–300 p.p.m.) and Kehoe *et al.* (1940*a*). They are in agreement, however, with those obtained by Butt *et al.* (1954: 500 p.p.m. approx.). Similarly the values for copper in adult heart (700 p.p.m.) are slightly higher than reported by other workers but are in agreement with those of Butt *et al.* (1954: 600 p.p.m.).

Values obtained for copper in lung (250 p.p.m. approx.) are somewhat higher than the values (112 p.p.m.) reported by Tipton *et al.* (1953) and Kehoe *et al.* (1940*a*: 110 μg. of metal/100 g. of fresh tissue). Similarly the mean value obtained for spleen (200 p.p.m.) is higher than that reported (83 p.p.m.) by Tipton *et al.* (1953) and Kehoe *et al.* (1940*a*: 85 μg. of metal/100 g. of fresh tissue), but is lower than the figure reported by Tipton *et al.* (1954: 8·67 μg./g. calculated on the fresh substance).

Copper was irregularly detected in bone and at low concentration only. This is in agreement with the results of Tipton *et al.* (1953). Tompsett (1935) reported an average value of 15 p.p.m., which is in agreement with the results given above. Koch *et al.* (1956) quote a single value of approximately 20 p.p.m. for the copper content of bone. Kehoe *et al.* (1940*a*) reported figures of 0·410 mg./100 g. for rib and 1·19 mg./100 g. for long bone, calculated on the fresh substance.

*Lead.* The sensitivity for this element was not good and it was generally detected only in liver. The values obtained for lead in this organ (80 p.p.m.) are in reasonable agreement with those reported by Kehoe *et al.* (1940*a*: 130 p.p.m.). Lead was found in the bones of some adults but not in those of infants or children. It was detected in some specimens of heart, kidney, lung, pancreas and the thymus.

*Manganese.* The results obtained for manganese show the highest concentration to be generally in liver, although relatively high levels were observed in the infant group in thyroid and gall bladder. Insufficient numbers were analysed, however, to draw conclusions. The values obtained in the adult group for liver (approx. 150 p.p.m.), kidney (approx. 60 p.p.m.) and brain (approx. 15 p.p.m.) agree with the results of Reiman & Minot (1920), who reported results of approximately 170, 61 and 35 p.p.m., and with those of Kehoe *et al.* (1940*a*), who reported approximately 205, 60 and 30 p.p.m. respectively.

The concentration of manganese in brain appears to be somewhat lower in the infant and child than in the adult.

*Molybdenum.* This element was regularly detected in liver and kidney only. In liver, mean levels of about 120 p.p.m. were found in the adult, but values were some ten times less than this in the infant and half this value in the children 1–12 years old. This increase in concentration of molybdenum with age is of interest especially since this element is now known to be an essential cofactor of the xanthine oxidase system (Richert & Westerfield, 1953; De Renzo *et al.* 1953).

The values obtained for adult liver agree well with those reported by Butt *et al.* (1954: approx 141 p.p.m.) and Tipton *et al.* (1954: approx. 160 p.p.m.) but are higher than the mean figures earlier reported by Tipton *et al.* (1953: 12 p.p.m.) and by Koch *et al.* (1956: approx. 55 p.p.m.).

*Nickel.* This was detected in only two tissues in this survey, kidney (one specimen) and cartilage (one specimen). Nickel has been reported by some workers as regularly occurring in human tissues; that it was not generally detected in this survey was due presumably to the poor sensitivity (40 p.p.m.) for this element. Bertrand & Macheboeuf (1925) reported, however, that human and animal organs contained, as a rule, far less nickel than cobalt.

*Rubidium.* The accuracy for the determination of this element was poor. Nevertheless it was possible to demonstrate the widespread occurrence of rubidium at a comparatively high level in all the tissues examined except bone. This is in agreement with the results of Sheldon & Ramage (1931), who reported the widespread occurrence of rudibium in soft tissue and the absence of the element from bone. Of interest in connexion with the low values found for the infant group is the fact reported by Sheldon & Ramage (1931) that the only individual without rubidium was a 10 weeks' foetus.

The occurrence of rubidium in animal-eye lenses was reported by Sizeland (1952), and it was pointed out that the ratio of this element to the potassium present in the tissue was similar to the ratio of the natural abundances of these elements reported by Goldschmidt (1937).

*Silver.* This element was infrequently detected and only at comparatively low concentration. It was found in the lungs of three adults and in the aorta of one. Sheldon & Ramage 1931 detected faint traces of silver in five specimens of lung, but these workers found silver in every specimen of thyroid and tonsil, in 47% of the livers, 44% of the suprarenals and 36% of the lungs of eight individuals examined.

Similar irregularity of silver in biological material has been noted by Kehoe *et al.* (1940*b*), Dutoit & Zbinden (1930), Newell & McCollum (1931) and later workers.

*Strontium and barium.* These elements were not reported in the present survey, because the method was not sufficiently sensitive to detect them regu-

larly. Studies with radioactivation analysis (Sowden & Stitch, 1956, 1957) have, however, established the levels of both these elements in human bone.

*Titanium.* Titanium appeared more frequently and at a higher level in the lung of adults than in infants or children. The values obtained for adult lung (250 p.p.m.) agree well with the mean of 204 p.p.m. reported by Tipton *et al.* (1953). Titanium was also detected frequently in the skin and subcutaneous fat of adults. In this respect titanium follows aluminium, the highest levels of which were found in these situations.

## SUMMARY

1. A method is described for the semiquantitative analysis of some trace elements in human soft tissue and bone, by cathode-layer arc spectrography.

2. Results are presented for the distribution of aluminium, cadmium, copper, manganese, molybdenum, lead and rubidium. Chromium, nickel, silver and titanium were detected infrequently in some organs.

3. Accumulation of some elements in certain organs was observed; relatively high concentrations of cadmium in kidney, copper and molybdenum in liver and aluminium in lung were observed regularly.

4. A comparison of the distribution and concentration of certain elements in the tissues of various age groups is presented and discussed. The concentrations of cadmium in kidney, of molybdenum in liver, of copper in brain and of aluminium in lung were shown to increase with age. In contrast the concentration of copper in liver was shown to decrease rapidly after birth.

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