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Thallium

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Thallium

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THALLIUM

Thallium (Tl) is a chemical element that belongs to group III of the periodic system, with an atomic weight of 204.37. Natural thallium consists of two stable isotopes with the mass numbers of 203 (29.5%) and 205 (70.5%). Natural radio-isotopes Tl^{206} , Tl^{208} and Tl^{210} with the respective half-lives of 4.19 min., 4.79 min., 3.1 min. and 1.32 min. occur in nature among decomposition products of the radioactive series of uranium, thorium and actinium. Of the artificial thallium isotopes, Tl^{204} is the most important single nuclide with a half-life of 3.56 years [1, 2, 3, 4].

Thallium is a silvery white metal with a greyish shade. Thallium may be uni- or trivalent, the univalent form being the most stable one [2, 3].

Thallium is considered to be one among dispersed elements. It has been found as a negligible admixture in various rocks, soils, the ashes of many coals, some plant species, water of some seas and mineral springs. Thallium is dispersed among various minerals of other elements. The smallest thallium content is found in ultrabasic rocks, an average $6 \cdot 10^{-6}\%$. Basic and medium rocks contain from $1.3 \cdot 10^{-5}$ to $1.5 \cdot 10^{-5}\%$. In acid rocks thallium is present in quantities from $1 \cdot 10^{-4}$ to $3.5 \cdot 10^{-4}\%$. Natural minerals of thallium proper are very rarely found but in enters, as an isomorphic impurity, into a great number of other minerals and mineral salts where it partially replaces basic minerals in the crystals of their compounds [1, 3, 5].

Among the various thallium compounds the most ones most widely used are sulfide (as well as oxysulfide), halide salts (chloride, bromide, iodide), sulfate, carbonate, acetate, and malonate-formate [3, 6, 7].

Melting point: 303°C [1, 2, 3, 7]

Density: at 20°C is 11.85 g/cm^3

at 306.5°C — 11.289 g/cm^3

at 330.0°C — 11.259 g/cm^3

Boiling point: 1457°C .

At the pressure of 1 mm of mercury column the boiling point for thallium is 833°C .

Relative vapour density: at 825°C — 1 mm of Hg

983°C — 10 mm of Hg

1103°C — 40 mm of Hg

1196° C — 100 mm of Hg
1274° C — 200 mm of Hg
1364° C — 400 mm of Hg
1457° C — 760 mm of Hg [1, 2, 3, 7].

Thallium is not soluble in water and alkali water solutions [1, 2, 3, 7].

It dissolves satisfactorily in 25% sulfuric acid at 90° C. In hydrochloric acid it dissolves very slowly because of the formation on its surface of a film of thallium chloride. In nitric acid thallium dissolves readily, forming a univalent metal salt [1].

Thallium carbonate readily dissolves in water at the rate of 5.23 g/100 g at 18° C and 27.2 g/100 g at 100° C. Thallium malonate-formate is miscible with water in whatever proportions. Thallium sulfate has a water solubility of 4.87 g/100 g at 20° C and 18.45/100 g at 100° C. Thallium acetate dissolves in water as well. Thallium chloride is water-soluble to 0.32 g/100 g at 20° C and 2.38 g/100 g at 100° C; for thallium bromide it is 0.05 g/100 g at 25° C and 0.25 g/100 g at 68° C; for thallium iodide the respective solubility figures are 0.0064 g/100 g at 20° C and 0.12 g/100 g at 100° C. [6]. Thallium oxide is not soluble in water [6].

PRODUCTION PROCESS(ES)

There are several methods to obtain thallium now in use in the USSR [1, 5, 6, 7, 8].

Basic feedstocks for thallium production are the dusts and sublimates that are by-products of polymetallic raw material processing. Besides, thallium is extracted from subproducts and wastes of metallurgical production plants (lead-zinc, copper-melting and sulfuric-acid producing facilities) [1, 5, 8].

The process of thallium extraction from varied and chemically complex raw materials (whose basic components are zinc, cadmium, copper, lead, iron and others) consists, on the whole, of its decomposition with thallium transfer into solution, production of thallium concentrate, purification of the concentrate from metal impurities and, finally, obtaining thallium of various degrees of purity. Sometimes preliminary enrichment of the initial products with the production of secondary sublimates by roasting (oxidizing, reducing with coal, or chlorinating with sodium chloride) is applied. Thallium is extracted from the feedstock by acidic or water leaching sometimes with addition of soda. Some kinds of raw materials (for example those containing sulphides) are sometimes subjected to preliminary oxidizing roasting. Sulfatization with concentrated sulphuric acid in the fluidized bed (with the supply of compressed air) at 300—350° C that has been

used recently, accelerates the process of feedstock decomposition and provides for the extraction of all valuable components therefrom [1, 5, 8].

To produce thallium concentrate, it is precipitated from solutions, depending on the adopted technological flowchart, in the form of chloride, iodide, sulfide, chromate, bichromate or (after preliminary thallium oxidization with permanganate or persulfate) in the form of hydroxide. Thallium electrolytic precipitation on zinc is a fairly widespread method of its extraction. Thallium extraction with zinc amalgam is also practised. Recently it has been proposed to extract and concentrate thallium by methods of extraction and ion exchange. Further treatment of chemical thallium concentrates is based on the different solubilities of thallium compounds and its associated metals as well as other physico-chemical properties of the elements being separated. Purification consists usually of a number of operations, most often of sequential precipitation of various hardly soluble compounds (after the solution of the primary thallium concentrate). Sulfide thallium concentrate is treated with sulfuric acid solution, whereupon thallium gets precipitated (for additional purification) in the form of chloride. The chloride concentrate of thallium is sulfatized with concentrated sulfuric acid at 300-400°C, the sulfate product (after grinding with addition of water) is treated with calcined soda solution to precipitate cadmium zinc and iron carbonates, while thallium remains in the solution. Thallium is isolated from the treated solutions after acidification with sulfuric acid by electrolytic precipitation on zinc in the form of a spongy metal.

If a solution contains lead, thallium precipitation may be in the form of PbSO_4 or PbSO_4 . The separation of metals with an amalgam method of thallium extraction is achieved by anodic oxidation of the amalgam in various electrolytes, thus sequentially separating out first zinc, cadmium and lead and then thallium, by its precipitation on the cathode in the sponge form. The thallic sponge is washed, briquetted and remelted under an alkali (or charcoal) layer [1, 2, 5].

Metallic high-purity thallium that meets the requirements of semiconductor engineering is produced through combining chemical (alkali refinement with addition of KNO_3 or NaNO_3 oxidizers), electrochemical (anodic solution of thallium with subsequent precipitation on the cathode) and crystallization refinery methods (zone refining or pulling from the melt). Amalgam refinement of thallium and other methods have been proposed also. To prevent oxidation in storage, metallic thallium slabs are kept hermetically sealed under a layer of boiled distilled water or by coating their surface with paraffin or varnish. Thallium compounds are obtained mostly from metallic thallium after additional refining if necessary [1, 2, 5].

To reach a high degree of purity, metallic thallium is remelted fourfold in vacuum, with the melted thallium poured into a new clean vessel during the process. After each remelting contaminations and oxides stayed behind in large quantities on the walls of primary vessel. According to data of spectral analysis, purified thallium contained $4.27 \cdot 10^{-3}\%$ of lead, $3.18 \cdot 10^{-3}\%$ of copper, $1.4 \cdot 10^{-3}\%$ of cadmium and $1.12 \cdot 10^{-3}\%$ of nickel [1, 2, 5].

In the USSR metallic thallium is produced in three grades:

1. «Ch», with the following permissible contents of impurities in weight %: iron — $1 \cdot 10^{-3}$, lead — $1 \cdot 10^{-2}$, copper, cadmium and zinc — $3 \cdot 10^{-3}$, and a thallium content at least 99.96%;

2. «Tl-O» — impurities: copper — $5 \cdot 10^{-5}$; silver, gallium, indium, cadmium, and tin — $1 \cdot 10^{-4}$; iron, aluminium, vanadium, manganese, molybdenum, tantalum, niobium and chromium $3 \cdot 10^{-4}$;

3. «Tl-00» — impurities: copper and nickel — $2 \cdot 10^{-5}$, mercury — $4 \cdot 10^{-5}$, arsenic, silver, gallium, zinc, cadmium, iron, tin and lead — $1 \cdot 10^{-4}$; aluminium, vanadium, germanium, calcium, silicon, manganese, magnesium, molybdenum, niobium, titanium and chromium — $3 \cdot 10^{-4}$ [7].

In the USSR the following of the thallium compounds are produced: thallium nitrate, lower bromide, lower hydrate, hydroxide, lower iodide, malonic formate (Clerichi liquid), formate, oxide, lower oleate, lower carbonate lower sulfate, lower stearate, lower acetate, monosubstituted lower phosphate, lower chloride, silver iodide, and lower silver nitrate. All compounds that are commercially produced go with the «Ch» label that means «extremely pure» [7].

USE

At present thallium and its compounds find very wide application in semiconductor and electrical engineering to produce selenium-rectifier stacks. Application of small thallium quantities makes it possible to cut on the consumption of costly materials such as pure selenium, bismuth, cadmium and others and manufacture rectifiers with a reverse voltage up to 40 V (in ordinary selenium rectifiers — up to 30 V) [2, 3, 5, 6].

Thallium is used for the production of photoresisters, highly sensitive photocells, new kinds of semiconductor glasslike materials with widely varying conductance properties, photoconductivity, and others. Metallic thallium, in alloy with other materials, is used for the production of phototriodes with sensitivity in the infra-red spectral region as well as for alloying germanium, silicon and cadmium compounds to impart acceptor properties to them [2, 3].

In nuclear engineering thallium compounds find application as activators of luminescent alkali-halide crystals or for stabili-

zation of the luminescence process in various models of scintillation counters [3].

In electronics, metallic thallium is used for grading spectral instruments involved in quality control of films and negatives and for evaluation of X-ray photoprints in medical diagnosis. One other application is in manufacture of discharge and fluorescent non-electrode sunlamps [3].

In instrument engineering a radioactive isotope of thallium, T^{204} , is used as a continually operating generator of γ — radiation in various instruments for studying and monitoring technological processes [3].

In optics, artificially grown crystals TlB_2 and TlJ come for use prisms and lenses in infrared spectroscopy, infrared achromatic lenses and lense components for microscope objectives in the infrared part of the spectrum [3].

Thallium is also used for making thermocouples. Thallium alloys possess good antifrictional properties and high resistance against corrosion as compared with silver-lead or copper-lead alloys. This is the reason why they are widely used in bearing alloys, aluminum bearings, coats for underground pipelines facing, manufacturing insoluble anodes, electric contacts and special safety fuses [3].

Thallium malonic formate (Clerichi liquid) is widely applied in mineralogic analyses and geologic and mineralogic investigations of rocks and ores [2, 3, 9].

Thallium sulfonate, carbonate and acetate enter into rodenticide poisons to control rodents. Thallium acetate is an integral part of a depilatory, now being applied in medicine and animal husbandry. Thallium salts used as fuel antidetonators in internal combustion engines. Finally, thallium and its compounds are employed as catalysts in various chemical reactions and processes [3].

PATHWAYS INTO THE ENVIRONMENT

During the process of metallic thallium production air working-room air pollution with thallium aerosol is possible. In metallic thallium melting, release of thallium oxide vapours into the air is often observed because their pressure is higher than of thallium vapour itself. As this happens thallium concentration in the air may run up to $0.026-0.1 \text{ mg/m}^3$ and even as high as $0.12-0.18 \text{ mg/m}^3$. Besides that, thallium chloride aerosol may be formed, its formation preceded by a reaction between thallium and chlorine, an admixture constituent of technical alkali [5, 8].

An increase in the concentration of thallium oxide aerosols in air comes from its pouring when the maximum concentration of thallium aerosol reached 17.4 mg/m^3 and the minimum content 13.5 mg/m^3 [5, 8].

While producing thallic salts, thallium gets into the air in the form of dust at concentrations from 0.028 to 0.136 mg/m³; in packaging its concentration grows to 0.163-0.354 mg/m³ [5].

Production atmosphere become contaminated with thallium-containing aerosols during monocrystal manufacture when its concentration at the time of unloading monocrystals and the next 30 minutes exceeds maximum allowable concentration (MAC) [10].

In thallium crystal lapping, thallium concentration in the air varies from 0.036 to 0.0072 mg/m³ [5].

It was found that at facilities producing thallium formic malonate (Clerichi liquid), the processes of metallic thallium solution, evaporation and filtration give out a thallium air content of 0.0038 to 0.0111 mg/m³ [9].

The production of metallic thallium, as well as its various salts, monocrystals and crystalline systems was accompanied by air contamination in the production environment equal to 0.0038—0.0066 mg/m³. In some operations of a periodic character like e. g. furnace cleaning, as well as in emergencies like explosion of the ampoules thallium concentrations in air may reach high levels. Thallium is released into air in the form of condensation and desintegration aerosols [9].

Considerable contamination of equipment surfaces, walls and nearby object with thallium concentrations in the range of 0.25 to 12500.0 m/m³ was established [9].

Thallium may be present in the waste waters of chemical, varnish and paint and glass producing plants and factories [13].

CONCENTRATIONS

Average concentration of thallium in the earth's crust is $3 \cdot 10^{-4}\%$ [1, 3, 5]. Thallium is part of most polymetallic ores but in many of them its content never exceeds ten thousandth fragments of percent. In considerable amounts thallium is found in some ore deposits in the Altai region (USSR): Beryozovo (up to 0.004%), Nikolayev (0.0025%), and others. The ores of the Tekeley deposit are more rich, with up to 0.005% Tl. In some areas of the Central Kazakhstan manganese deposit the ores contain up to 0.01% thallium.

According to the Geological Science Institute, USSR, thallium often occurs in zinc-copper pyrites in the Ural region where it is commonly bound up with sphalerites. In the Altai region, depending on the character of the source, thallium is associated with pyrite, sphalerite and galenite [1].

Thallium often presents itself among lead and polymetallic deposits (in galenites) in the Urals, Altai, Kazakhstan, Tadjikistan, Trans-Baikal and Far East region.

Thallium, a frequent associated mineral of lithium, potassium,

rubidium and cesium, isomorphically replaces alkali metals in aluminosilicates, alums and chlorides. The basic thallium collectors among silicates are soda-potash feldspars and micas. Thallium was also found in some Soviet arsenic deposits — in realgar and orpiment [1, 2].

Thallium is found in large amounts in plant products and water sources [1].

In the regions around thallium deposits its content in ground water reaches 2.7 mg/l [14].

In ground water of the Angaro-Lena artesian basin a considerable accumulation of thallium has been discovered. The highest thallium content is observed in highly concentrated brines of calcium-chloride type, enriched with potassium and rubidium. Thallium content is at the level of 0.02 to 2.76 mg/l [15].

An appreciable thallium content occurred in the humus layers of oak and beech woods [1].

Thallium is also found in sea water from which it crystallizes out with potassium compounds [1, 15].

BIOCONCENTRATIONS /CLEARANCE TIME/ MAMMALIAN METABOLITES

Test animals were injected with 20 mc of Tl^{204} and then the time of its retention in tissues and target organs was determined with the scintillation counters SBS-1, Mark-II in a dioxane scintillator or the automatic scintillation counter «Gamma» [16].

Unlike zinc, nickel and barium, thallium is retained longer in blood plasma that seems to suggest its more pronounced cumulative properties. Thallium is characterised by great tropism to gonads and its content after 24 hours amounted to 1.04% of the total amount of injected isotope. After 72 hours thallium was found in sperm. Thallium possesses great tropism in relation to cerebral tissue [16].

In an experiment on laboratory animals applying radioactive tracer method, thallium-204 accumulation in organs and tissues 1, 3, 6, 12, 18, 24, and 72 hours after a single intragastric administration of a readily soluble thallium compound was studied. Organs and tissues, according to the degree of tropism of thallium isotope to them, are arranged as follows: kidneys testes > liver > spleen > prostate > brain > fur. The same distribution was revealed by analysis of the degree of organs' vulnerability in terms of morphological (histological, histoenzymatic, histochemical) parameters on the 20th day of thallium intoxication. Thus the most sensitive «target organs» on exposure to thallium are kidneys and tests, thus suggesting the metal's nephrotoxicity [17].

Thallium stores up in intercellular liquid, combines with aminoacids and builds up in bones as phosphate. Thallium-204

rapidly disappears from blood and distributes itself among the organs, concentrating mainly in kidneys and salivary glands. With gradual redistribution its deposition takes place in bones and hair. Normal concentration of thallium in the hair is 10^{-3} mg% and in the urine — 10^{-6} mg% [6].

Standard thallium concentration in human urine as determined by the mass-spectrographic method is $0.13 \cdot 10^{-3}$ to $1.69 \cdot 10^{-3}$ mcg/g [12].

After extensive feeding for 30 days to cats and rats various organs (muscles, liver, kidneys) of the sheep which received before thallium acetate at 16 mg/kg during 8 and 14 days, no noticeable toxic effect was found out [18].

Thallium rids itself slowly from the body through kidneys and gastrointestinal tract is extensive (up to 1 year) [6, 19].

A patient who drank about 80 ml of 1.15% thallium acetate solution had 1-1.5 months later 3.69% of thallium in the urine and 1.49% in the blood plasma [19].

After a single intramuscular injection of 1 ml of thallium acetic acid solution to a rabbit, an equivalent of 5.37 g of pure metal, thallium elimination took 13 days, with 1.053 mg (23.4%) of thallium excreted with urine and 3.574 mg (66.6%) with feces, giving a total amount of eliminated thallium of 4.827 mg (90%) [38].

When thallium carbonate was introduced into rat stomach a dependence between the dose and intensity of thallium urinary excretion was determined. This linear dependence is observed to the dose of 30 mg/kg, when the elimination curve rises steeply [22].

MAMMALIAN TOXICITY ARRAY

By the general character of its effect, thallium may be classed with the poisons affecting central and peripheral nervous systems, gastrointestinal tract and kidneys. Both univalent and trivalent thallium compounds cause hair shedding that increases with thallium concentration. The effect of thallium on the hair can be explained by disturbed keratin formation in the hair bulbs. Hair shedding seems to result from direct influence by thallium compounds on the follicular machinery or central nervous and endocrine systems [6].

The median-lethal dose of thallium carbonate for subcutaneous injection to adult albino mice is 27 mg/kg. Old animals are more sensitive to injection of the same dose (their mortality was 70%) and preadolescent and pregnant animals are somewhat less sensitive to thallium exposure at the same dose (their mortality was 35%) [20].

The median lethal dose of thallium carbonate for subcutaneous injection to albino rats is 18 mg/kg [20].

The absolutely lethal dose of thallium carbonate for subcutaneous injection is 32 mg/kg for albino mice and 25 mg/kg for albino rats [20].

The median lethal dose of thallium carbonate in intragastric administration to albino mice is 21 (17.4-24.15) mg/kg, and the absolutely lethal dose equals 25 mg/kg [5, 8].

The median lethal dose of thallium carbonate in intragastric administration to albino rats in terms of thallium ion is 15 ± 0.77 mg/kg [5, 8].

The median lethal dose of thallium carbonate (cutaneous application) for albino rats is 117.3 (78.2—156.5) mg/kg. Nasal discharges, dispepsia, growing depression were observed in the tested animals, followed by death on the 2-7th day [22].

The median lethal dose of thallium chloride in intragastric administration to albino mice is 23.7 (21.8—25.76) mg/kg; the absolutely lethal dose is 30 mg/kg [5, 8].

The absolutely lethal dose of thallium iodide in intragastric administration to albino rats is 55 mg/kg and that of thallium bromide — 35 mg/kg. The respective minimum lethal doses are 28 mg/kg and 29 mg/kg [20].

The median lethal dose of thallium sulfate in intragastric administration to albino mice is 23.5 (20.9-26.31) mg/kg and the absolutely lethal dose is 35 mg/kg [5, 8].

The median lethal dose of thallium formic malonate in intragastric administration to albino rats is 18.8 (15.5-22.1) mg/kg or 0.06 micro millimoles; the corresponding epicutaneous exposure is 57.7 (48.2-67.2) mg/kg [9].

In evaluating acute toxicity of thallium chloride, bromide, carbonate, sulfate, nitrate, phosphate, formate, stearate and oleate, it was determined that the clinical picture of animal intoxication is similar for all thallium salts. Starting from the 3-4th day after intoxication, mucous nasal discharge, weight decrease, diarrhea, progressive adynamia, and somnolence were observed. By the 5-6th day animals became flaccid and immobile, and then died. Upon injection of thallium oleate, formate or bromide the skin on external genital organs of male animals became ulcerated. Investigations proved that the test animal species most sensitive to thallium salts are albino mice and rats and that guinea pigs and rats are usually less affected. The LD₅₀ value (in terms of thallium ion) for most compounds is within the limits of 20 to 30 mg/kg [23].

Threshold dose of thallium carbonate in subcutaneous injection is 0.00024 mg/kg (according to modified regeneration of fur integument) [20].

A study of cutaneous-resorptive effect of thallium carbonate found that thallium ion penetrated intact skin rather easily. The rate of skin penetration for mouse tail skin by 2% solution of thallium carbonate (according to calculations) is 0.0025 mg/cm²

per 1 min. Exposure to 2% thallium carbonate solution during 1 hour caused 50% death of the tested animals and 3-hour exposure caused 100% lethality [20].

In experiments on rabbits it was determined that thallium carbonate had irritative effect on the mucous coats of eyes (hyperemia, purulent, conjunctivitis, keratoleukoma) and skin (epidermal necrosis, edema and infiltration of dermis) [22].

Neither general nor local fur shedding was observed in response to single epicutaneous exposure of thallium acetate, at concentrations of 6-7 mg/kg for rabbits and 2.5-3.5-5.0 mg/kg for rats. With continued local irritation of skin, zonal fur shedding was observed, due to high accumulation of thallium under the skin as a result of local irritation [2, 5].

Local effects of thallium formic malonate included hyperemia of rat skin and punctate hemorrhage with subsequent formation of scabs. Thallium injection into rabbit conjunctival sac caused blepharospasm and lacrimation, drastic hyperemia and chemosis. Extreme hyperemia of conjunctiva and extensive keratoleukoma were observed 48 hours later. By the end of the 1st week keratoleukoma and conjunctiva swelling had persisted. Thus thallium formic malonate formate has well-expressed irritating effect on skin and mucous membranes [9].

As a result of intragastric administration of thallium carbonate in doses of 2.5 and 5.0 mg/kg, a high cumulative capacity of thallium was arrived at. All animals died after exposure to the total dose of 22.5 mg/kg, in other words, less than the established absolutely lethal dose [18].

Following intragastric administration of thallium carbonate to albino rats for 30 days at 0.8; 0.4 and 0.2 mg/kg pronounced alterations in kidneys, testes, liver and skin of rats were observed [4, 26].

It was determined that intragastric administration of thallium carbonate for 20 days in the following doses: 0.5; 0.05; 0.005; and 0.0005 mg/kg caused fur regeneration to decrease abruptly [21].

After intragastric administration of thallium sulphate to albino rats for 15 days in doses of 0.6 mg/kg and 1.25 mg/kg the following effects were observed: clearly expressed stagnation, passiveness, progressive loss of weight, and decrease of catalase activity by 48%. At the end of the exposure the animals which had been receiving the 1.25 mg/kg dose of thallium showed 53% less hippuric acid elimination than control animals, 6 hours after subcutaneous injection of sodium benzoate dose of 400 mg/kg. Considerable changes in the balance of protein fractions in blood serum were observed. Relative content of albumins was reduced by 38.2% from the initial level and the relative content of globulins increased by 26.3% [5, 8].

Inhalation of thallium iodide and bromide dust (in equal ra-

tios) at a concentration of 0.005 mg/l repeatedly (8-10 times during one month) lowered in the test rats the duration of swimming in cold water (17°C). At daily exposure for 2-3 weeks to thallium iodide-bromide mixture dust in concentrations from 0.0005 to 0.0007 mg/l no external signs of intoxication were noticed while, at the same time, thallium cumulative ability was ascertained. Concentrations of 0.0012-0.0152 mg/l for the same period of exposure caused the death of test animals and a concentration of 0.00038 mg/l when given for 52 days caused no visible indications of poisoning [20].

In a chronic experiment the effect of thallium sulfate given intragastrically to rabbits at 0.35 mg/kg and subcutaneously at 0.35 mg/kg and of thallium carbonate given intragastrically at 0.25 mg/kg were studied. The experiment lasted 6 months. By the 5th month certain changes in the animals' behaviour were noticed: aggressiveness, inhibition and developing paralysis of lower extremities. Considerable changes of the protein-forming function were found that were expressed as disproteinemic shift involving an albumin decrease of 29.3% globuline increase of 40% at the expense of β -fractions, growth of γ -globulins and reduction of the albumin-globulin coefficient by 47%. Certain changes of some enzymatic systems were observed as well, for example: a rapid and steady decrease of alkaline phosphatase by 62-72% and decrease of sulphydryl groups in blood serum down to 35-40 mm in 100 ml (control amount — 70-100 mm). The change in sulphydryl groups suggests that thallium toxicity is based on its chemical affinity to sulphur [5, 8, 24].

With 8-month-long intragastric administration of 0.005 mg/kg of thallium to albino rats, it induced changes of conditioned — reflex activity, SH-groups in blood, content of DNA and ribonucleic acid in spleen, activity of alkaline phosphatase, lactate dehydrogenase, glucose-6-phosphatodehydrogenase and dehydratase of delta-aminolevulinic acid in blood [14].

The dose of 0.00005 mg/kg caused less obvious shifts and 0.000005 and 0.0000005 mg/kg none at all [14].

Another study focused on the influence of five hardly soluble thallium compounds: iodide, bromide, chloride (amorphous powders) and crystalline thallium halides, that is, a mixture of 42% thallium bromide and 58% thallium iodide or 30% bromide and 70% thallium chloride. With intratracheal administration the compounds listed above, in the form of suspension in physiologic solution, at 0.5 and 5.0 mg doses to rats, the similar processes in lungs were seen to accelerate with the increasing dose and length of the experiment and then slow down gradually in 9-12 months. 3 months after the introduction of the halides small foci of atelectasis and alveolar emphysema came to sight; 6 months later separate bronchiectasia, emphysema and pneumosclerotic foci appeared and 9-12 months later fibrosis, emphysema and atelectasis came

up though not so markedly expressed. Crystalline halides of thallium cause more serious damage of lung tissue than amorphous compounds. Thallium iodide is the most damaging to lung tissue [2, 7].

Toxic affect of 5-sulfa-8-mercaptochinolate of thallium was evaluated according to its ability to decrease oxygen consumption by mast cell suspension from rat peritoneum in the process of oxidizing 10 mM of sodium succinate. At 10^{-6} and 10^{-5} M thallium salt concentration in the solution, the oxygen consumption rate (evaluated according to the rate of its decrease in the solution) went down to 2.66 ± 0.03 and 3.80 ± 0.04 oxygen microatoms per 10^6 cells per minute, against the control figures (only of 5-sulpha-8-mercaptochinolate at the same concentrations) of 3.27 ± 0.03 and 4.44 ± 0.03 respectively [28].

Determination of histamin, discharged by the mast cells in their incubation with the thallium salt of the same concentrations showed a reliable-increase in histamin liberation equal to $34.3 \pm \pm 3.1$ and $31.6 \pm 2.7\%$ (control figure $6.2 \pm 1.9\%$) [28].

Acute thallic intoxications in humans are characterized by damage to central nervous system, kidneys, gastrointestinal tract and skin. It is suggested that striopallidal system is selectively affected as well. Polyneuritis, convulsions, ataxic gait, tremor, anxiety, insomnia, motor pareses, lack of appetite and bloody diarrhea are observed. Intensive hair shedding usually happens after display of obvious signs of polyneuritis. Non-occupational intoxications are often caused by ingestion of grain pre-treated with thallium compounds or by the use of thallium to treat the diseases of the hairy part of the head. Occupational thallium intoxications claim a smaller percentage of the total [6, 29]. The medium lethal dose for man is 6-40 mg/kg [29].

The lethal dose for man is 0.74 g [19].

Thallic intoxication is signaled first by affection of gastrointestinal tract — acute pain, vomiting diarrhea and constipation. Then polyneuritis is developing, accompanied by unbearable pain in extremities and trunk, and pareses. 2-3 weeks later keratinization disorders are observed; there are expressed by considerable skin desquamation and total hair shedding from the head and face. Psychic disorders are observed as well. The dropping hair, when histologically analyzed, exhibit spindle-like inflation of the root part with rich black-pigment deposition there. In 1-2 months transverse white bands appear on the nails. Thallium is easily absorbed in the digestive tract and cases are known of thallium intoxication through skin [19].

Cases of acute occupational intoxication with thallium formic malonate were recorded. Neurologic syndrom was characterised by diffusive lesion of the nervous system with clear indications that the deep hypothalamic regions of brain had been affected; obvious vegetative-vascular disorders with typical crises, sub-

febrile condition, neuro-endocrine disturbances and intensive hair shedding. Hypothalamic involvement was confirmed by electroencephalographic evidence. Besides, there were clear symptoms of polyneuritis borne out by electro-myography. Gastrointestinal — tract affection (vomiting with blood, tarry water stools) was also noted. Sensitization accompanied by histaminemia was quite clear in the clinical symptom. Intoxication was corroborated by the presence of thallium in biomedica and of «thallic spots» in hair bulbs [30].

In pathomorphological studies of a victim killed by acute intoxication with thallium formic malonate the developments observed included onflammation of intestinal mucous membrane, ecchymoses, myocardial edema, atrophic changes of skin and subcutaneous cellulose dystrophic and degenerative changes in parenchymatous organs. Histologic analyses of brain disclosed multiple diapedesic hemorrhages, focal glial proliferation, separate lymphoid perivascular infiltrates, dystrophic changes in neurones; lungs exhibited bronchus epithelium metaplasia and myocardium interstitial productive myocarditis [19].

In chronic occupational intoxications the symptoms develop for a longer period [19].

During examination of 51 people working at production facilities where the work-room air becomes contaminated with thallium in the form of condensation and disintegration aerosols in concentrations from 0.0039 to 0.066 mg/m³ complaints were registered of high erethism (49%), fatiguability (39%), periodic headaches (43%), poor sleep (27%), expressed hyperhidrosis (33%), pain in extremities of uncertain character (19%), accidental pains in the heart area (12%). Some of the employees complained of periodic pains in large intestine and epigastric areas, unstable stools, intensive hair shedding and fragile nails. From the complaints deviations were ascertained objectively, primarily the neurological condition; they were: tremor of fingers (33%), hyperhidrosis (33%), proliferative red dermographism (20%), relief of tendon reflexes (22%), tachycardia (32%), a tendency for vascular hypotonia (25%), etc. The complaints and, accordingly, direct-observation data were attributed to functional changes in the central nervous system and regulatory disorders of the vegetative nervous system. When examining the patients, two were found to have Mayes striae and one had intensive hair shedding.

Employees who had been working in close contact with thallium and its compounds for a long period, had nervous system disorders. With a working experience of 5 years or less cases with nervous disorders accounted for 22% of the examined and with a working experience over 5 years, for 77%. In urine tests, 24% of the examined workers appeared to have thallium in the urine and in repeated tests its content was found to fluctuate over a wide range (0.003-0.56 mg/l). But the amount of thallium in

urine shows no definite correlation with changes in nervous system [12].

Examination of employees at a facility producing monocrystals, where the work-room air may be contaminated with thallium-containing aerosols, identified light functional disorders of central nervous system of an asteno-vegetative type and catarrhal conjunctivitis [10].

Workers directly exposed to thallium had considerable changes of alkaline phosphatase in blood serum — 2.7 ± 0.17 units (control figures — 3.5 ± 0.26), increase of general ATPase activity up to 53.4 ± 3.4 units (control — 41.1 ± 2.3 units) and the activity of Mg ATPase up to 40.3 ± 1.9 units (control — 32.8 ± 2.5 units) and of Na, K-ATPase up to 13.1 ± 0.4 units (control — 8.3 ± 0.3 units). No considerable changes in the activity of transaminase, catalase, carboanhydrase and inorganic pyrophosphatase among the people in the examined and control groups were detected. Thus, prolonged effect of small thallium doses causes changes of activity in the enzymes responsible for phosphorous exchange [10].

SPECIAL TOXICITY STUDIES

Mutagenicity. The effect of thallium carbonate exposure on a cell culture of rat embryonic fibroblasts revealed its ability to provoke unifilar ruptures of DNA (by the method of chromatography with hydroxyapatite. The DNA quantity in the fractions was determined by the amount of label precipitated with 5% trichloroacetic acid on «Sinpor N 4» milliporous filters). Treatment of the cell culture with various concentrations of thallium carbonate was maintained for 24 hours. It was established that the number ruptures that arose in the DNA molecule depended on thallium salt concentration. At $1 \cdot 10^{-6}$ M — $82 \pm 2\%$ of bifilar DNA relative to control; at $1 \cdot 10^{-5}$ M — $73 \pm 2\%$, and at $1 \cdot 10^{-4}$ M — $47 \pm 2\%$ developed ruptures. Postincubation for 24 hours in a growing medium brought partial rehabilitation of the DNA bifilar structure and at the low concentrations of thallium salt, the repair was more distinct [31].

To determine the mutagenicity of thallium carbonate a method of studying survival and mutability of the smallpox vaccine virus in rat fibroblast cells treated with this salt, was applied. The survival rate of the smallpox vaccine virus in the fibroblast cells was assuredly reduced on exposure to thallium carbonate; the number of induced mutations during the experiment was three times the virus spontaneous mutagenesis in the control cells [31].

The yield of chromosomal aberrations in the cell culture exposed to thallium carbonate for 24 hours at a concentration of $1 \cdot 10^{-5}$ M exceeded the spontaneous level approximately sixfold (the number of aberrant cells was 12.29 per 100, against the