

THE HAZARDS OF MERCURY VAPOR

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(Die Gefährlichkeit des Quecksilberdampfes)

When I decide to tell a wider audience everything about personal troubles, which in themselves do not concern others and therefore should not be worth publishing, it is because of an intense wish to spare others, who have anything to do with metallic mercury, the very bad experiences which have destroyed a major part of my life and to very emphatically warn against the volatile metal. I can freely tell about it today since it is fortunately enough in the past and a terminated matter.

The insidious dangers of mercury are not sufficiently known and are too little noticed just in the places where people are especially threatened, that is in the chemical and physical laboratories.

For nearly 25 years I experienced symptoms, in the beginning only weak and occasional, in time increasing up to being unbearable and which caused me to doubt if I could continue my scientific work. The cause was not known to me or to any of many excellent doctors I visited to ask for advice. It was considered possible that my problems were caused by an especially narrow nasal passage and an unusual sensitivity of the nasal mucosa. My nose was therefore treated for decades by etching, burning, massage, electricity and bloody operations. Without results! Two years ago something happened - a few of my collaborators fell ill with similar symptoms - and it was revealed that the cause was an insidious mercury intoxication. Because of my chemical work; the study of volatile compounds with vacuum technique using vessels with mercury, mercury pumps, manometers and valves, I was for 25 years in constant contact with mercury.

It is not possible to doubt the casual connection since all symptoms, even if not yet completely, have disappeared (and a short time ago clearly reappeared when I for some time worked in mercury-containing air because of a mishap with the ventilation of my laboratory) when I, for two years have protected myself from inhalation of mercury vapor.

I will give an account of my symptoms and how they developed with time. They agree, even in detail, with all insidious mercury vapor poisonings, something my collaborators and other chemists could confirm. They were and are, largely unknowingly, victims of mercury vapor poisoning and do not know the source of their troubles. Many essential symptoms have, until now, not been sufficiently described and the insidious mercury vapor poisoning has not received the attention it deserves.

The matter started with me as periodically occurring light headaches and weak dizziness which increased with the years to continuous, nervous unrest and irritability, to a pressure on my head which made thinking difficult, to ever increasing headache, finally almost continuous and tormenting (mostly over the eyes), to intense vertigo which was connected with troubles of vision (dim and double vision). Soon also the upper airways were affected; in the beginning light an occasional nasal catarrh, then permanently tight nose, later almost continuous catarrhs of the olfactory mucosa with often bloody mucus production and crust formation, violent throat inflammations and pains in my ears connected with impaired hearing and smell (for some substances like hydrogen cyanide it remained), distaste for tobacco smoke.

In the last years before the cause was recognized, other symptoms appeared: salivation, sour-stale taste in my mouth, eye inflammation, inflammation of the oral mucosa, vesicles and sensitive and ulcerating spots on my tongue, gums, gingiva, insides of lips and cheeks, redness of gums and slight bleeding during toothbrushing, toothache, withdrawal of gingiva from teeth and the appearance of pockets, occasional loose, single teeth. The mouth and teeth changes occurred late with me (the peak of these symptoms did not occur until months after the poisoning had been discovered) since I from childhood had been careful with my mouth hygiene (for instance every evening prolonged rinsing with 1.5 % hydrogen peroxide solution and then with sodium bicarbonate). If this had not been the case I might have discovered the cause of the symptoms earlier because of the mouth inflammations.

Further symptoms were: intellectual exhaustion and depression, lack of energy and ability for work, especially intellectual work, increased need for sleep, trembling of my stretched fingers, often also my eyelids, pains in various places, stabbing pains in my back and in limbs, pressure around the liver, sudden need for urination and diarrheas without special reasons. Slight vesicles on the inner sides of my arms and on the upper half of my legs.

The manifestation which was most severe for a person with intellectual work was the loss of memory. My originally very good memory got worse and worse so that I, two years ago, was near total amnesia. Only with the help of extensive notes and with considerable effort was it possible to write a paper or to hold a lecture. I would forget the phone number on my way from the telephone directory to the telephone; I would forget almost everything I had learnt by heart, the contents of books and theatre plays I had recently read and seen, the contents of my own papers I had published. It was impossible for me to remember numbers or

names. Often I could not remember the names of close friends. Especially the ability to calculate, to do mathematical thinking, also to play chess, was severely affected. The depressed ability to remember and the difficulties in calculating seem to be a special sign of insidious mercury vapor poisoning. This was also evident with my collaborators and with other persons, for a long time exposed to mercury vapors, cases which have now become known to me. Shortly after we had discovered what was wrong, I and two collaborators were trying to finish writing a paper which needed calculations. None of us had the ability to add 10-20 large numbers without errors!

In contrast to only a small effect on bodily strength, for instance during mountain climbing, the intellectual capacity was also in other ways depressed although not as severely as memory. In addition there was psychic depression, a painful inner unrest, with time also causing disturbed sleep. By nature fond of company and full of enjoyment of life, I withdrew in misery into myself, avoided public relations, people and social contacts, lost love for art and nature. Humor rusted in. Difficulties which I earlier had cleared with ease (and today again can clear with ease) appeared insurmountable. The scientific work required considerable efforts. I forced myself into my laboratory but could not produce anything of value despite all efforts. My thoughts were heavy and pedantic. I had to give up participating in matters which were not of immediate importance. The lectures, previously something I liked, became tormenting. The preparation of a lecture, the writing of a paper, even a simple letter, required immense efforts in handling the contents and language. Not seldom it happened that I wrote words wrongly or forgot letters. To be aware of these shortcomings, not to know their cause, to know no way of getting rid of them, to expect further deterioration - that was not nice.

All efforts to improve my condition failed. Several weeks in the mountains was of no use; I did not feel less miserable there than in Berlin. The nasal treatments and operations often gave short, not lasting improvements. It was remarkable that all psychic symptoms disappeared for hours when the doctor treated certain places of the upper nasal mucosa with cocaine; if the correct spot was treated, headache and vertigo disappeared, often within a few minutes. Memory, ability to work and good spirits reappeared, however, only as passing guests. I often used the method to recall my ability before a lecture, an important meeting etc.

As I have already mentioned, also my collaborators in the laboratory; assistants, Ph.D. students, technicians, had various symptoms: depression without apparent cause, bad memory, headaches and dizziness, now and then gastrointestinal troubles, limb pains, slight mouth inflammations, nasal catarrh etc. With one person some symptoms were worse, with another some other symptoms, apparently for each person at his weakest point. All showed tiredness and depression of intellectual capacity. However, nobody got the idea that there could be a common cause for all of us. Not until a happy-unhappy event finally opened our eyes.

In order to save money we had in 1921 disconnected the ventilation aggregates of the Kaiser-Wilhelm Institute of Chemistry; aggregates which consumed much expensive electric current. Since the middle of 1923 two of my collaborators, an assistant and a spanish guest, were working on density measurements in a small room. The measurements required constant temperature and therefore windows and doors were kept closed. The work had to be finished before early 1924 since my assistant was to take up a post in industry and the spanish colleague had to go back to his home country. Therefore the work was rushed and the careful cleanliness we at other times kept, was neglected in this room and scattered mercury was left unattended in cracks and joints in the floor and under laboratory stands. Instead of an insidious mercury poisoning the conditions were given for a more acute and more easily recognizable mercury poisoning. The assistant fell severely ill, not just with headaches and intellectual depression but also with severe bodily deterioration, ulcers in his mouth etc. His brother, a doctor, thought that the condition reminded him of mercury poisoning. The renowned toxicologist L. Lewin whom we called for, examined the laboratory personell and declared, that according to his experience, we were all with certainty suffering from mercury poisoning.

Mercury was found in the air of the laboratories as well as in the urine of all affected persons. The mercury concentration in the air varied from room to room, from a few thousandths to a few hundredths of a milligram per cubic meter. That is only a small fraction of what air can contain when saturated with mercury vapor (about 12 mg/cubic meter). Since a human being breathes about 1/2 cubic meter each hour and the inhaled mercury, as it appears, is largely absorbed in the lungs, only a short visit in mercury saturated air is sufficient to elicit an acute mercury poisoning.

When air containing small amounts of mercury is inhaled, it will take a long time until the poisoning becomes apparent. For one to several years the symptoms can be restricted to tiredness and slow deterioration of the intellectual ability and memory. For instance with the spanish guest, inflammations in the mouth did not appear until at the end of the year he stayed with us and reached its peak a month after he had left us and was not exposed to mercury any more. The psychic effects he had felt earlier without knowing their cause. "It was as if I became more stupid in Germany." And similar observations I could make on my other collaborators. Almost all Ph.D. students in my laboratory had difficulty qualifying for the doctor degree. If the students and assistants left the laboratory after a few years, they recovered without knowledge of the mercury poisoning. On myself, the effects of the minimal amounts of mercury developed as I have described.

Especially significant for this type of insidious mercury poisoning are sudden changes in the condition. After a few weeks of better health follows, often quite suddenly, a time of worse conditions. This also holds true for the relapses during recovery. When my disease was at its peak, the general rule was: one or two days of endurable conditions, then increased salivation and nasal catarrh including catarrh in larynx and bronchi, inflammation around teeth, severe weakness and dizziness, tormenting headache, often also

joint pains and diarrhea. The headache, dizziness and weakness of memory are connected to the nerves in the upper part of the nose as the effects of the cocaine treatment has shown.

The recovery from insidious mercury poisoning, after elimination of the poison source, is extremely slow and there are often relapses. Professor Lewin told us so and the development of our conditions has proved him right. The necessary time apparently depends on the length of the poisoning, maybe also on the person's age. My collaborators who left the laboratory fortunately recovered within one or two years from all symptoms and have recovered their powers of thinking and memory to the full extent. But also these persons had to endure relapses of psychical and physical character (especially mouth inflammations). Some of the assistants and technicians continue working here and we can unfortunately not avoid using mercury. They have now, nearly two years after the poisoning, clear but ever weaker symptoms. I was exposed to the damaging effects for more than 20 years and the complete recovery apparently takes the longest time; the capacity for work is almost back, only occasional relapses (headaches, dizziness and mouth inflammations) affect me slightly. Judging from the development of recovery so far, I do not doubt that all of my collaborators and myself will completely recover from all symptoms. It is likely that it takes years to excrete the mercury which has been taken up by the body for years.

It appears that from a mercury poisoning follows a special sensitivity towards a new exposure to mercury vapor. Some of us, who because of work or faults in the ventilation system, were again exposed to mercury, felt it immediately as an increasing number of relapses. That seems understandable since the long time for development of the disease shows that a certain threshold must be reached before symptoms appear. The threshold will certainly easily be reached again during recovery and any additional amount of mercury will worsen the condition.

We tried in various ways to enhance the recovery on advice from doctors; using diuretics and substances to promote fecal excretion, taking hot baths, eating small amounts of sodium iodide. I have not the impression that the recovery was substantially enhanced through these measures. Iodine is supposed to bring the metal into solution from insoluble organic mercury compounds, the form in which mercury probably is bound in the body. I could not demonstrate on myself that significantly higher amounts of mercury were excreted in the urine after iodine intake. We did not expect the diuretics to have any effect since we had shown that mercury excretion in the urine soon stopped. The art of medicine unfortunately has no substance which can detoxify the body from mercury.

To be in the fresh air seems to be most useful for making subjective symptoms less felt. Novalgin has some effect on lighter headache and dizziness. In general one has to let time take away the disturbing influences on the body. Some weeks visit in the mountains and a voyage at southern latitudes brought me hardly any faster recovery than at home, although the psychic rest had a positive effect on my nerves.

Why was our disease not recognized as mercury poisoning earlier? I have often asked myself this question, not without reproach. The first symptoms of the slow mercury poisoning, before any oral symptoms appear, are hardly known to the medical world. They are tiredness, depression of thinking and memory, light headache and dizziness, occasional diarrhea. Neither was it known that the nose and the upper airways were affected. Just this started myself and my doctors on the false track and has also fooled others I know of. One of my assistants was for a long time treated for sinusitis until the true cause was found. Also the difficulties in thinking make it difficult for the affected person to make a correct diagnosis of his troubles: *Quem Mercurius perdere vult, demetat prius!*

It is appropriate in this context, to warn of another source of insidious mercury intoxication: dental amalgam fillings. Prof. Lewin advised me immediately he had diagnosed the mercury poisoning, to exchange for other materials the amalgam fillings I had in considerable numbers since early youth. He called attention to a case he knew of, a university colleague who was on the border of psychical and physical collapse when the cause, in the nick of time, was found to be the numerous amalgam fillings he had since youth. After their removal he slowly recovered.

This colleague recently gave me a shaking account of his sufferings for several years until the cause was discovered. (transl. note: *Z. angew. Chem.* 39, 1926, 984).

The dentists formerly preferred copper and cadmium amalgam and today use silver amalgam for filling teeth since these amalgams are easy to manipulate and fill the cavities well. Silver amalgam is better than the other amalgams which corrode considerably with time. However, also silver amalgam gives off mercury vapor at oral temperatures, which the following experiments proved. (compare also G. Tammann & O. Dahl. *Z. anorg. allgem. Chem.* 144, 1925, 16).

We sealed silver amalgam pieces in glass tubes, bent into right angles, evacuated them and heated the horizontal part with the amalgam to 30-35°, cooled the other part in ice or liquid air and determined the amount of mercury which distilled over.

1. Amalgam piece, carefully prepared by a dentist from metal powder and mercury for this experiment. Weight 0.801 g, sealed into the glass tube 24 h after preparation, heated for 23 days, ice cooling. Amount distilled over: 11.2 mg mercury.

2. Similar, weight 0.810 g. Three weeks after preparation to obtain as complete hardening as possible and then sealed in a glass tube. Heated for 12 days, cooling with liquid air. Distilled over: 15.3 mg.

3. A piece of amalgam, carefully prepared with as little mercury as possible. weight 1.000 g, three weeks hardening, 9 days heating, cooling with ice: 8.2 mg mercury.

4. Amalgam filling which had been in a tooth for a year and had fallen out. Weight 0.894 g, 14 days heating, liquid air cooling: 29.4 mg mercury.

Undoubtedly fillings like these will also slowly give off mercury in the mouth and give the inhaled air a low level of mercury which must be harmful in the long run. The old copper and cadmium amalgams should be even more dangerous.

One of my faculty colleagues suffered since a long time from occasional headaches and dizziness without obvious cause. After he had removed an old amalgam filling which caused slight inflammation near the tooth, the problems disappeared after some time. The filling was fragile and full of mercury droplets after removal.

Dentistry should completely avoid the use of amalgam for fillings or at least not use it whenever that is possible. There is no doubt that many symptoms: tiredness, depression, irritability, vertigo, weak memory, mouth inflammations, diarrhea, loss of appetite, chronic catarrh often are caused by mercury which the body is exposed to from amalgam fillings, in small amounts but continuously. Doctors should give this fact their serious consideration. It will then likely be found that the thoughtless introduction of amalgam as a filling material for teeth was a severe sin against humanity.

Insidious mercury poisonings are certainly much more common than is generally thought. This is especially relevant for chemists and physicists who often have much to do with mercury. The danger gets too little attention, the real cause of troubles and diseases are often not recognized. In the literature almost nothing is reported on this (An exception from recent times is the report by A. Blomquist, Ber. d. deutsch. Pharmaz. Ges. 23, 1923, 29, on a general mercury vapor poisoning at the institute of Physiology, Uppsala University). After the resolution of our unhappy fate, I have come to know about a dozen certain cases of insidious mercury poisoning among my acquaintances alone, almost always with the same symptoms, mostly with wrongly diagnosed causes and therefore falsely treated. A typical example is a colleague from another country who has worked a long time with mercury equipment. When he visited me and I asked him if he never had felt any symptoms of mercury poisoning, he definitely denied this. Further questions about his health was answered with: "I am in a bad state of health; I have suffered from neurasthenia for several years, I have had to abandon my laboratory for long periods etc." The doctors had tried various treatments, had treated him for stomach-, intestinal- and chest-diseases, treated him with special food etc. In reality he had a pronounced mercury poisoning, something which has now been established without doubt.

Faraday was certainly a unsuspecting victim of mercury poisoning. In the late three to four decades of his life which ended after 76 years, he suffered more and more from troubles which made the scientific work harder and harder. He has described this in his letters and in his description of his life where it takes large space. By his doctors it was interpreted as neurasthenia and premature atherosclerosis. It consisted of periodically pronounced exhaustion and intellectual depression, in irritable weakness, headaches, vertigo, "rheumatism" and primarily in ever increasing loss of memory (comp. E. Jentsch: Faraday's loss of memory. Naturwissch. 3, 1915, 625 & 637).

Spared serious "bodily" diseases; even at advanced age a hiker and a swimmer, Faraday avoided other people in the third part of his life. His scientific work and his lectures he continued, with long breaks, into his last year. One is deeply affected when reading the great scientist's letters where he describes how he often had to visit his medical friends to complain about vertigo and headache, how he could not remember any names, how he lost contact with his scientific colleagues, how he forgot his own work and papers, his correspondance and did not know how to write words. "The affected organ is my head. The result is loss of memory, confusion and vertigo." All these symptoms makes it likely that Faraday suffered from an insidious poisoning because of the mercury which was used in his laboratory. It is a disturbing thought how apparently easily it could have been to rescue this gifted man from his sufferings and how much he could still have given science if the cause of the problems had been recognized and removed. Perhaps was also the strange disease which the mathematician, physicist and philosopher Blaise Pascal (1623-1661) suffered from in his younger days, a mercury poisoning. Prof. E. Jaensch, Marburg, notified me about this. Pascal worked much with mercury during his well known barometer experiments. His problems (periodical headache, vertigo, pains in the teeth, loss of appetite, severe cholic) constitute a complete picture of an advanced, slow mercury poisoning.

Undoubtedly mercury, which research can not be without, caused science severe damage in the past as well as today since it depressed the ability of so many scientists. I hope this warning will help to more clearly recognize and avoid the hazards of this devious metal.

(transl. comment)

In Faraday's laboratory, preserved until today, his experiments with the electrical motor and generator are on display. The apparatus consists of metal rods, immersed in open beakers with kilograms of liquid mercury.

Louis Lewin, 1850-1929, was the foremost toxicologist in Germany at the turn of the century and the world's first professor of toxicology. When A. Stock suspected mercury poisoning he called for Lewin who also put him into contact with prof. Jaensch, Marburg (see later paper).

Lewin is considered to be one of the great names in the history of Science. There are still conferences held in his name. He published several books on toxicology, the best known is *Gifte und Vergiftungen*, 1928. The fifth, unchanged edition was printed in 1962. Few scientific books have such a long life. His most famous book, however, is *Phantastica*, 1924, "A book of extraordinary scientific depth" according to A. Hoffman, head of research at Sandoz and the discoverer of LSD (by mistake). This book laid the foundations for psychopharmacology and ethnopharmacology. These areas have, good and bad, resulted in a major part of today's drug industry and also use and abuse of drugs.

From Lewin's toxicology book (1928) we cite: "Mercury has a high toxic energy which often, also after medical use, manifests itself in an unpleasant way. In any form, mercury is a strange substance, harmful to tissues and life... From amalgam plombs, especially from copper amalgam, the metal can evaporate in the oral cavity or in any changed form be absorbed into the circulation from the cavity in the tooth and cause a chronic poisoning. This manifests, apart from local effects in the mouth, especially as an impaired function of normal brain- and nerve function. Such disturbances do not always depend on a special sensitivity towards mercury. I have lectured on this subject since the turn of the century and also informed people with such fillings, who have contacted me because of nervous symptoms. I have always arranged to have such fillings removed and in that way produced recovery, even among professors. Prof. Stock was informed about this matter by me and recovered.

ON THE QUESTION OF THE HAZARDS OF MERCURY VAPOR

Dipl. Ing. A. Schmidt, Charlottenburg

Z. Angew. Chem. 39, 1926, 786

In no 15 of this journal prof. Stock published a paper on the hazards of mercury vapor.

It is surprising how easily most chemists and not least prominent scholars and scientists have passed the question of the hazards of mercury. When prof. Stock means that not enough has been published on the dangers of mercury I must refer to two books, appearing in the beginning of the 90ies: 1. Dr. J. Hermann in Vienna: *There is no constitutional syphilis. A comfort for all humanity.* 2. "Mercury treatment is a crime against humanity"; Hermann Risel & Co Publ. Hagen in Vienna. These books did not suit contemporary medicine and were silenced to death by all methods. In these books, however, the dangers of mercury are strongly emphasized and also described are the symptoms which mercury produces among workers who have a lasting exposure to mercury, e.g. in mercury mines, in mercury mirror factories and in the thermometer and barometer factories. If these publications had got a wider attention much bad health could have been avoided, at least during the latest 3 1/2 decades.

I was once suspicious about the amalgam fillings because of these publications, but all dentists I spoke to about this matter, declared that they were completely harmless.

After Stock's irreproachable experiments one can not doubt that they are very harmful. What has the Ministry of Health to say on this matter? Will they, since no further investigation is needed, produce a document which strictly prohibits the further use of amalgam fillings, or will they, as is always the case in Germany, go into further evaluations?

When prof. Stock writes that the unusually strong ventilation of the Kaiser Wilhelms-institut is not sufficient for removing mercury vapor from the air, this is not surprising for someone who has some experience with ventilation equipment. It is known that not only liquids with different densities, but also gases with varying densities often only partly mix (Dog-cave on Capri); gases with high specific weight will stay beneath. If mercury vapor is to be removed effectively, air can not be removed upwards as usual but it has to be removed from the deepest places. Hempel demonstrated this more than 35 years ago and he constructed laboratory ventilation with evacuation at low sites. It is necessary, where mercury is used, to know what Hempel taught and to construct the ventilation accordingly.

It would be a blessing if prof. Stock not only published his results in *Z. f. angew. Chemie*, but also in the daily newspapers, so the public is made aware of the insidious hazard.

(Translators note: Mercury vapor is not heavier than air and does not flow along the floor. It apparently drifts in the air in the same way as tobacco smoke. If the source of the vapor is on the floor or in cracks in the floor, the vapor concentration will naturally be

higher near the source. An excellent photographic demonstration of the evaporation of mercury can be found in National Geographic Magazine, oct. 1972 p. 507, Quicksilver and slow death.)

Dr. Georg Pinkus, Berlin-Fridenau. Z. Angew. Chem. 39, 1926, 787

The warning by prof. Stock, based on his own disease story, will not appear without effect. A large number of chemists have similar symptoms as Stock have described them and since there is not a single chemists who not at some time comes into contact with mercury or at least has amalgam fillings in his mouth, many will find an explanation for their symptoms in a insidious mercury poisoning. One must hope a suggestion that such diseases are of any real importance among chemists will not have too much effect. This is in order to counteract any far reaching worry among lay people and to prevent premature conclusions. The removal of all amalgam fillings which Stock recommends, means an enormous task and concerns a much wider public than a small group of chemists. To prevent this it seems necessary to point out that there are also experiences showing that workers and chemists have worked in nearly mercury-impregnated rooms for decades without the slightest harm.

It is known that the vapor from metallic mercury is poisonous. Every student is made aware of the dangers with mercury distributed into corners and cracks. Skin affections among doctors when they have broken a thermometer in their pocket are not rare and during the anti-luetic ointments, when the mercury has an especially large evaporation surface, salivation, mouth-, tooth- affections are even common. Even if it is known that mercury can pass the intestines without harm when it is swallowed in order to clear intestinal obstructions, it belongs to every chemists basic knowledge that the vapors are toxic.

One can imagine my surprise when I, with this knowledge, in 1923 entered a company where the owner since more than 30 years was occupied with the purification of mercury for dental purposes and with the manufacture of amalgam. I saw that in large, light, carefully cleaned but not ventilated rooms, relatively large amounts of mercury (up to 50 kg daily) were handled. It was not possible to completely avoid scattering of mercury. Not only in the corners of the floor but also on the working tables were constantly mercury drops. Only when the mercury was heated did the work take place under an exhaust; as soon as it had cooled it was placed freely in the room.

The copper amalgam is rolled out in large sheets during manufacture and these square meter sheets were day and night open in the room. I must explain here that silver-amalgam, gold-amalgam and platinum-amalgam are mercury-free alloys and amalgamated with mercury by the dentist. They are not discussed here. Copper amalgam, however, is commercially delivered as a real amalgam, becomes softer by heating and can be filled into a tooth. Copper amalgam always contains an excess of mercury and the large surfaces have excellent opportunity to give off mercury to the air.

Despite these circumstances which, to the best of my knowledge, are similar in other such factories, not one of the chemists or workers have fallen ill with the symptoms described by Stock. All workers have been employed for many years, some more than 20 years and one of the managers, as already told, more than 30 years. Most of them are robust and appear to be in good health.

The same observation on the harmlessness of mercury have been made at the Hoechst Farbwerke where 70.000 kg have been used in 10 years (comp. Schardt, this journal 39, 1926, 668). Also Loesch (Deutsche dentistische Wochenschr., München 1926, p.443) has made thousands of kilograms of sublimate tablets from metallic mercury in open vessels without any harm to himself or his collaborators.

I like to present these realistic and contrasting facts against the observations by Stock which presumably also are correct and I dare, respectfully, suggest an explanation: When a chemist - also Stock - discusses medical matters, he can draw no better conclusions than any layman. He has, in addition to what the layman knows, his occupationally learned fright for real conditions he knows about but can only draw conclusions from his own experiences. The general survey and the possibility to compare are lacking. I will not, because of this, go further into the question, but will restrict myself to my own experience.

More than 20 years ago I fell ill with intestinal catarrh which was so severe that I had to give up my position in industry. Quite analogous to Stock who blames mercury for his disease, I was at that time of the opinion that a certain chemical compound was the cause. I will not mention its name in order to avoid another anxiety. But none of my collaborators, chemists or workers, became sick although the latter came into much closer contact with the material than I did. Only I was, because of coinciding psychic agitation, susceptible for the poison. The psychic problems were hardly alone sufficient to harm a healthy intestine, neither was the organic poison alone sufficient to harm, something the health of the others showed.

The symptoms of the disease was almost completely the same as those described by Stock as mercury poisoning: general neurosthenic problems, although mercury, disregarding a few amalgam fillings, was clearly not involved. This poses some doubts on the etiology of Stock's disease. As in Stock's case it took years until everything was in order again. I can with certainty say that my condition during the latest three years, when I breathe mercury-containing air, has not become worse; my memory is neither better nor worse today. The ability for mental calculation and to add figures has in fact improved.

I conclude from all this that also for mercury poisoning another factor is necessary besides mercury; it could be a psychic or a physical one. In support of this I can mention the "Ärztlicher Merkblatter" which is published by the medical doctors of the German chemical industry (1925, J. Springer Verl p 8), that the disposition for occupational mercury poisoning is "individually very varying" and that its occurrence in Germany is very rare.

All this is, however, only possibilities, maybe at best only likely causes and an explanation can not be expected from publications by chemists, describing single cases. Now the medical doctor and the statistical scientist must intervene. I consider it to be false and premature and the suggestion of damage as a calamity, if because of a single case the daily press and the journals take up the question and cause unrest in wide circles before medical statistics are available. Before such wide reaching demands are made, i.e. removal of the amalgam fillings from the mouths, a statistical connection between these fillings and nasal-, intestinal- and nervous-problems as described by Stock must be established. It does not seem an exaggeration if the number of persons with amalgam fillings is estimated to be 100 million. Then it must be possible, even if it means much work, to obtain statistics on 5000 or 10000 cases, maybe with the help of the insurance bureaus of the major factories, in order to compare the health of the amalgam carriers related to number of fillings, age and occupation.

Only in this way can the value or lack of value of Stock's observations on himself be evaluated.

Summary:

1. It is known since a long time ago that mercury vapors are poisonous. To obtain intense effects (ointments against lues) one has always used finely divided mercury and distributed it over the skin to enhance evaporation by the body heat. (however, all statements by Wassermann are in need of medical examination: before lues was known to produce paralysis, many direct luetic consequences were blamed on mercury).
2. Then most of the mercury enters the body through the lungs. Metallic mercury can pass the stomach and the intestines in large quantities without producing beneficial or harmful effects.
3. Stock has, for the first time, described the subjective conditions of an insidious mercury poisoning and blamed, not salts of mercury but evaporation of metallic mercury, and amalgam fillings.
4. Amalgam fillings, which might be present in 100 million persons, have so far been considered completely harmless (Witzel: Das füllen von Zähnen mit Amalgam, 1899, Berlinische Verl.). Stock's suggestions contradicts this and a careful study on the connection between health problems or lack of them and amalgam fillings is desirable. To cause anxiety before such statistics is available is premature.

Prof. Dr. H. Reihlen, Karlsruhe
Z. Angew. Chem. 39, 1926, 788.

After A. Stock recently with emphasis has pointed out the dangers of mercury vapor, many chemical laboratories have been searched for mercury and this with such a result that it is a small wonder that mercury poisoning is not a normal condition among laboratory chemists. It seems to me as if the finding of mercury in all laboratories which are carefully enough searched, could lead to an underestimate of the poisonous effects of this element.

I will report on some cases of light mercury poisoning and on a case where it did not happen, despite apparent danger. In my laboratory the collaborators of my predecessors worked much with mercury; the laboratory was therefore, when we took over a year ago, carefully cleaned, at least in a manner I then thought sufficient; all tabletops were taken out and cleaned and about 200 g mercury was recovered. I found an even larger amount in the drains. The latter might not have been dangerous since it was always covered with water. In the summer working period nobody working in the room had any problems with health. Today we consider that the open windows helped us since, at the end of the winter period, both of my collaborators, working in the room, fell ill with severe gastrointestinal problems. I developed dry but intense dermatitis with small red vesicles on the inner side of my left arm and later on the inner and upper parts of my legs.

At the same time all three of us had constantly running noses, something I personally already had some predisposition for. We suffered from the manifestations which are generally called semester tiredness to a degree which was less than endurable.

The skin problems were diagnosed by the prof. of occupational medicine, Holzman, as side effects of medicines and were treated with zinc-containing cream without results. Dr. Wirz, dermatologist in Munich, prescribed a tar-sulfur soap, containing bismuth and zinc oxide and promised a cure within a few months.

The semester has passed and I traveled with my ointments to Schwarzwald for a few days. Contrary to my expectations, the soap and a few days of sunbathing helped as if by magic; after a week the skin eruptions were not to be seen and only a light irritation remained.

Apparently two fortunate circumstances were present. Primarily the room is long and narrow and door and window are opposite each other facilitating ventilation. Secondly, the room next to the laboratory is the hydrogen sulfide room and the wall is porous and often hydrogen sulfide penetrates the wall. It is possible that the hydrogen sulfide reacts with the mercury vapor and precipitates the metal as harmless sulfide. This could also explain - the idea was communicated to me by prof Stock - why mercury poisonings so far have not been reported from teaching laboratories.

Finally I must also remark that no disease of the oral soft tissues, something which is generally considered characteristic of mercury poisoning, did appear among any of us three. Two of us are heavy smokers, the third one does not smoke at all. His teeth are in a remarkably good condition, something which also is explained by a particular care and is also necessary for smokers because of the otherwise appearing bad-looking, yellow deposits which are formed. Also the gastrointestinal problems of my collaborators disappeared during the holidays. It is likely that they must have been connected with the work in the laboratory.

Since we now only work with harmless compounds, we again thought about the possibility of a contamination of the laboratory and mercury poisoning. We again removed all tabletops, cleaned all drains etc. Then we discovered a few drops of mercury in a drawer which we had cleaned the day before. The table top above the drawer was used for all major distillations etc. and was covered with a large piece of slate, held in place with putty. We broke it off with force and really found a lake of 300 g mercury beneath it. It is noteworthy that you can hardly imagine a worse place for mercury spillage than beneath the cover of a table for experiments using heat. We did not wonder any more where the source of our mercury exposure was. However, I wonder why another collaborator, working with vacuum equipment in another room since two years and constantly in contact with mercury, has shown none of these disturbances.

Dr. F. Gradenwitz, Berlin
Z. Angew. Chem. 39, 1926, 788.

The results from the four experiments with dental amalgams can, according to my opinion, not be directly applied to oral conditions, something also prof. Stock has confirmed in a private communication. The experiments which will certainly be described in the dental journals, could be falsely interpreted; in the newspapers from Voss there has already been an extensive report and in this the attention was especially focussed on the dangers of dental amalgams. I do not exclude the possibility that scared patients will cause troubles for their dentists when amalgam filings are suggested.

If I have clearly understood the experiments by prof. Stock and his collaborators, they have placed fillings in the form of cylinders or spheres in tubes, sealed by melting and then heated. Then the whole surface can give off mercury. In the mouth whole crowns of amalgam are seldom used (earlier this was common) and usually a small or large cavity is filled with amalgam. The free amalgam surface in the mouth is perhaps a fifth of that used in Stock's experiments. I also can not exclude that the saliva which wets the teeth and the fillings regularly, also will inhibit or reduce the evaporation of mercury. Primarily the small surface area will alter the conditions. Apparently a somewhat mercury-poor layer will form on the surface of the filling after some mercury has really evaporated and after a short time no noticeable amounts of mercury will be released.

If my considerations can not be disputed, then the objections from prof. Stock and prof. Lewin will have less weight than it appears from the reported experiments.

One can not dismiss that amalgam fillings and especially copper amalgam are very easily worked and cheap materials which protect especially childrens teeth from premature deterioration. It can only be excluded from the stock of materials which the dentist uses if the latter can report harmful effects. The dentists will certainly now carefully watch their patients because of Stock's warnings.

One has especially to avoid placing amalgam fillings near metals (gold fillings, gold bridges and bridges and plates of alloyed gold). In such cases there will be electrolytic currents which also destroy the deeper parts of the amalgam fillings and can cause evaporation of larger amounts of mercury in the mouth.

A note added to my previous rebuttal of prof. Stock's paper:

Shortly after sending my rebuttal I found in Zahnärztl. Rundschau no 19, may 9, a paper by the dentist Dr. Jarecki, "The hazards of mercury vapor" in which the paper by prof. Stock was reported in more detail and at the end is a request that control experiments should be made at the dental research institute "to evaluate the results" Jarecki recommends "that discussions which have already appeared in the daily press should be disregarded in the interest of the matter itself and the patients."

In connection with the report by Jarecki, there is also in Z.R. no 9, a publication by the Berliner university professors Dr. Schroeder and Dr. Schoenbeck: "On the question whether amalgam filings are harmful." "From various places we have been asked to give a statement on the publication by prof. Stock in Z. angew. Chem. on the hazards of amalgam fillings. Immediately after its publication we decided to carefully study the dental side of the question with our own experiments. Primarily because Stock's experiments did not simulate real conditions in the mouth and therefore the results could not immediately be considered relevant.

Above all, the evacuation of the tubes which he used in his experiments must be the subject of consideration since this is different from conditions in the oral cavity."

It should be valuable if also the readers of *Z. Angew. Chem.* were made aware of the opinions of these authorities on practical dentistry and dental filling materials.

On the question of the hazards of the amalgam plombs, we have received the following paper: **THE HAZARDS OF AMALGAM FILLINGS**

A dental rebuttal to the paper by Alfred Stock. by dentist Dr. Gustav Haber, Berlin. *Zeitschr. angew. Chem.* 39, 1926, 905

The statements by prof. Stock are of basic importance and the accusations against dentistry concerning the use of amalgam fillings have such wide implications that each dentist must ask himself if the further use of a filling material for which mercury is used can be allowed.

Prof. Stock and his collaborators approached with open eyes their psychical and physical destruction without being able to help themselves or to obtain help. A tragic picture which can only evoke anyone's compassion. We are happy and feel relief when we read that the art of medicine has succeeded to bring prof. Stock and his collaborators back to their full psychical and physical powers. We have the task of evaluating if amalgam fillings could be responsible for a mercury poisoning.

Prof. Stock describes in every detail the insidious sufferings, discusses the causes and asks rightly why the mercury poisoning was not recognized earlier. One must agree with Jarecki when he writes (*Zahnärztl. Rundschau* no 19) that it is completely incomprehensible that none of the doctors got the idea, considering the occupation of the patient, to analyze the urine for mercury and that it took nearly 25 years until finally the toxicologist L. Lewin found the correct diagnosis and then opened the way to recovery.

The observations which prof. Stock made on the causes of the mercury poisoning in connection with the description of his sufferings, must be critically examined from various points of view. In the centre is the warning for the amalgam dental fillings as a little recognized source of insidious mercury poisoning. To support this suggestion is the following: 1. Laboratory experiments with three pieces of amalgam and a filling which had been in a tooth for a year and then fallen out. 2. The clinical observations by Stock of his own body, the ones by prof. Lewin of another university professor and similar observations which a faculty colleague of Stock made on himself. This material only supports the suggestion of mercury poisoning from amalgam fillings. Prof. Stock concludes, based on the four laboratory experiments and the three clinical observations by the patients themselves (it is not known whether medical evaluations support the information from the patients) that: "Dentistry should completely avoid the use of amalgam for fillings or at least not use it whenever that is possible. There is no doubt that many symptoms: tiredness, depression, irritability, vertigo, weak memory, mouth inflammations, diarrhea, loss of appetite, chronic catarrh, often are caused by mercury which the body is exposed to from amalgam fillings in small amounts but continuously. Doctors should give this fact their serious consideration. It will then likely be found that the thoughtless introduction of amalgam as a filling material for teeth was a severe sin against humanity."

Is then this annihilating accusation against amalgam as a dental filling material so securely based that it can be accepted without consideration? I first notice that Stock and his collaborators always used equipment with mercury like pumps, manometers etc and that the amounts of mercury which was scattered in the laboratory experiments could not at all be used for comparison. It should also be valuable to know how large the amounts of mercury were in the amalgam fillings in order to evaluate the amount distilled over and the relation between the used and the released amount of mercury. It appears completely possible to me that the amounts of mercury vapor released from the equipment during experiments could be several hundred times more than the minimal amounts released from excess mercury, even if all 32 teeth were filled with amalgam.

Apparently the evaporation from the mercury equipment will be very varying in relation to time, temperature and use. Tests showing the effects of these conditions on the release should be carried out before information in the literature can be simply dismissed as prof. Stock does. Prof. A. Witzel has, in his book "Das Füllen der Zähne mit Amalgam" p.232, listed the cases reported in the *Berliner Klin Wochenschr.* 1895. He points out the danger for the dentist when he presses out mercury from the plastic amalgam through leather or between the finger tips, does not collect the mercury under water but lets it fall carelessly onto the floor of the clinic, he writes: "That the dangers are not imaginary but is something which surrounds every dentist who handles mercury carelessly, the following examples, reported by Lewin, can show: He describes the ointments where inhalation of vapors released from the body were a major factor; Gerhardt in Wurzburg had a piece of linen, impregnated with grey ointment, hanging in a room. The syphilitic symptoms reduced, one sick person even got a mercurial ulcerative stomatitis. - A girl, who had nothing to do with mercury but who lived together with a woman who worked in a mirror factory, got typical mercurial stomatitis from the vapor of the minimal amounts of mercury which had been trapped in the clothes of the woman. In two quite similar cases, completely healthy persons, living in the same rooms as persons treated for syphilis, fell ill with stomatitis and also had other symptoms of a mercurial intoxication.

Finally I like to mention the events on the English ship *Triumpf*, known also from the literature. Three large vessels with mercury broke and the vapors, despite all efforts to clean and ventilate the ship, poisoned the whole crew on the short trip between Cadiz and England. Several members of the crew even died. The same happened to animals which were onboard. Any dentist who has up to now been careless should learn from this to carefully collect any excess mercury from the preparation of amalgam in order to prevent it from being lost and evaporated in the clinic."

Concerning the laboratory experiments by Prof. Stock where it was shown that mercury releases mercury at mouth temperature, one has to note what Prof. Schroeder and Schoenbeck recently communicated in *Zahnärztl. Rundschau* no 19: "that Stock's experiments did not simulate real conditions in the mouth and therefore the results could not immediately be considered relevant. Above all, the evacuation of the tubes which he used in his experiments must be the subject of consideration since this is different from conditions in the oral cavity". - But even if Stock's experiments were relevant for oral conditions, they could only be used for an evaluation whether amalgam fillings can cause mercury poisoning if shown that the mercury comes free, is absorbed into the body through the lungs or skin and its total excretion is not possible. I have already noted the information on this type of chronic mercury poisoning in the dental literature.

Stock's presumption that "amalgam as a dental filling material was a severe sin against humanity", is only relevant if it, without any possible objection, can be shown that mercury droplets in the amalgam filling are set free and are not excreted from the body and thus remain for ever in the body. In contrast to that we have information from other well known authors. Stock's observations on four amalgam fillings is to be contrasted with the many thousand amalgam fillings and the many hundred different materials which Witzel studied and presented already 30 years ago in his book: "Das Füllen der Zähne mit Amalgam".

The tables by Witzel comprise a material which is more than one hundred times larger and where all aspects have been studied in detail. It is too much to go into details here. I can only mention that Witzel was not content with the simple determination of how much mercury was released in each case but that he noted in tables amalgamation and hardening experiments with pure metals, metal mixtures and metal alloys. Witzel did chemical-mechanical and chemical-electrolytic dissolution studies in acids and by abrasion of amalgam disks, also in acids and with contact with metals; chemical and electrolytic dissolution in lactic acid; he studied the chemical-electrolytic processes in sodium chloride solutions and in mixtures of sodium chloride and lactic acid. He did comparative chemical-electrolytic experiments with different amalgams and solutions at various temperatures and he calculated how much was swallowed as lactic acid salts from an amalgam filling each day and during a year when different amalgam alloys were used.

Witzel has reported in detail on the simple and combined amalgams, also on the form changes of the hardened amalgam and the amalgam surfaces in the mouth. Witzel has carefully studied the electric currents which the teeth with amalgams and metals are exposed to. Besides other important chapters in this classical book there are experimental studies and practical experiences of copper amalgams and all other amalgam alloys and there is an additional chapter which is only devoted to the question: "Can metal- and especially mercury-poisonings be caused by amalgams as filling materials". Witzel arrives at the following result which I quote literally: "I have not, among thousands of patients, observed any symptoms of a chronic poisoning which could be ascribed abraded or dissolved parts of our copper amalgam fillings. I emphasize: although I have filled innumerable children's teeth with copper amalgam, I have not seen any case similar to that published by Roussy. However, I will not state that this filling material never has caused such diseases of the gastrointestinal tract.

We must in any case consider that, when the saliva is very acid, the presence of large copper amalgam fillings might harm the patient. If this is also possible from a number of large, tin-containing copper amalgam fillings, is not yet possible to decide. That also this material can be markedly degraded by dilute acids and electrolytic processes in the mouth is clear from our experiments and the figures in our tables.

We know about the complex amalgams with platinum, gold and nickel which are much more resistant against the oral liquids and will be little degraded, hardly noticeably abraded after several years because of chewing and that we never can find free mercury on the surfaces whether these are dark colored or polished. Our simple but very sensitive test with gold foil has demonstrated this.

The results of all these studies allow us to conclude that we, with the complex platinum- and gold-containing silver amalgams, have an excellent filling material, completely harmless for health."

More recent research has confirmed the statements by Witzel. We find the following information in "Dental Progress" by Misch: "Urine measurements of dentists and dental assistants have shown that these always have mercury in the urine, however, in very small amounts - 0.05 mg daily (Schulte). The highest levels in urine were found in those who worked with large amounts of copper amalgam, irrespective of whether the amalgam was worked with the hands or contact with the body was avoided. It thus seems that the mercury did not enter the body because of direct contact but as vapor, inhaled through the airways."

This information contradicts the statements by prof. Stock, based on the scientific data from four amalgam fillings and simple excretion tests. The removal of the amalgam fillings from prof. Stock's mouth and the other two stories of disease can not be used to give a verdict on amalgam. Stock's public accusation that amalgam was a severe sin against humanity is only valid if he can offer an experimental material which is as large as that from Witzel. This material must then be tested in every way, just as Witzel's, and his results disproved. Since it has been shown that the poisoning is caused by mercury in vapor form and that Witzel's studies show that a poisoning from amalgam fillings is not possible, there is no doubt that the symptoms of poisoning which prof. Stock and his collaborators showed was exclusively caused by the mercury equipment and the use of mercury.

It should also be investigated whether the clinical observations by the professors Stock and Lewin and the information from the other university teacher could be considered proof or supporting evidence for the validity of Stock's laboratory experiments. Prof Stock, was advised by prof Lewin and after recognition of the mercury poisoning to exchange the amalgam fillings he had in considerable numbers since early youth for other materials. We lack information without which a dentist can not properly evaluate the situation: 1. Was there immediately an improvement of the general health after the removal of the amalgam fillings? 2. Were there among Stock's mercury affected collaborators also persons without amalgam fillings and if so, how did this affect the types or severity of the symptoms? 3. Had the treatment of the mercury poisoning already started when the amalgam fillings were removed; had an improvement of the health already started before the fillings were removed? 4. The most important question: were the pulps and the root canals dead beneath the fillings. If this is confirmed, were the canals filled or infected? If only one root canal was infected, then the improvement can not be ascribed to the contemporary removal of the mercury in the amalgam fillings but with the opening of the root canal and the "airing". The airing is connected with a release of the putrefication gases which had caused an increasing pressure on the nervous system of the head in the region surrounding the root canal. When therefore prof Stock, to support his opinion on the hazards of the mercury droplets in the amalgam fillings, reports on the case of his faculty colleague, I am completely convinced, even if I do not know the case myself, that the troubles disappeared only because the root canal, filled with putrefication gases, was opened and treated. It is further reported that the filling, after removal, was brittle and full of mercury droplets. The fragility can have several causes, e.g. the amalgamation, the binding of the mercury to the powder was not sufficient or the quality of the "amalgam" was not good or the filling was exposed to the biting pressure before it was enough hardened, or the articulation and occlusion was not enough considered which could cause wrong loading and fracturing of the amalgam filling. We see that many causes can contribute to the fragility. However, rarely mercury droplets.

The case contributed by prof. Lewin: "a University colleague who was on the border of psychical and physical collapse when the cause, in the nick of time, was found to be the numerous amalgam fillings he had since youth. After their removal he slowly recovered. This colleague recently gave me a shaking account of his suffering for several years until the cause was recognized." Also concerning this case one must state that without an answer to the questions to prof. Stock, only part of the sufferings and their removal can be ascribed to the mercury in the dental fillings.

The verdict is quite different when one has to consider whether amalgam fillings should be placed into a mouth where there are already gold fillings or gold bridges. In this case one must, if possible, avoid any amalgam filling, also when they consist of platinum or gold amalgam. All amalgam fillings must also be removed from teeth which are to be filled with gold or have crowns of gold. The amalgam fillings must also be removed from the neighbouring teeth and antagonists (however, not when platinum crowns are placed, something I will report on elsewhere). The same requirement for amalgam removal is also necessary for teeth which are in contact with the edges of a metal plate and which serve as support for the metal hooks of a protheses (also non-noble ones of e.g. steel). This must be rigorously adhered to, also if it means the removal of every faultless amalgam filling.

This rule is not at all because of fear of health disturbances, although there are possibilities for this because of electrolytic processes when gold and amalgam come into contact. When the mercury is not under pressure from the gold there is rarely a release of mercury into the gold. However, when the gold in contact with amalgam is subjected to pressure or rubbing, its indifferent state ceases and there will be an amalgamization of the gold and a destruction of the latter. Witzel has shown that hardened amalgam is transformed into a ductile form when it is subjected to strong pressure, also biting forces.

The answer on the question what can be used as a substitute for amalgam as a filling material is more than can be answered in this communication; I have discussed it in the chapter "On the contact between amalgam and gold" in my book "The root as a support for protheses" by Dr. G. Haber. In the book I concentrated on showing that a general condemnation of the use of amalgam fillings is not substantiated. The removal of amalgam fillings and their replacement with tin-gold, silver alloys or gold something I have done for years, has other causes than the ones reported by Stock.

Summary: 1. The analyses and clinical observations, reported by Stock, are not sufficient to disprove the hundred and thousand times larger results by prof. Witzel.

2. The amalgam fillings are not harmful for the patients but their preparation constitutes a risk for the treating doctor. The danger increases with the number of fillings prepared and with neglect of precautions.

3. Amalgam fillings are no hazard for the human organism. - Infections in the body and other damage has in no case been proven to be caused by the mercury in the amalgam fillings.

4. The number of cases, reported in the literature, with damage because of mercury in amalgam fillings constitute a considerably smaller percentage than the damage caused by drugs and injections. Then one has also to consider that in the latter cases there is mostly a clear connection, something which is seldom the case in presumed amalgam damage.

5. Just as the medicament or the injection solution can not be blamed for too strong doses which are given, the use of amalgam fillings can not be totally condemned because some compositions with increased mercury content and unsuitable alloys might cause damage if they are improperly made, something which still has to be proven.

When I, as a non-chemist, took up the task of opposing the views of one of our greatest scientists and reject his material as not sufficient proof, then it was because I, as a dentist, have been studying this question. I have rejected amalgam as a dental filling material only under certain conditions, namely in connection with gold and idiosyncrasies which people sometimes acquire if they have occupations which bring them into contact with mercury. These exceptions, however, can not form the basis of a general condemnation like that expressed by Stock.

On the question of the hazards of amalgam fillings.

L. Sterner-Rainer, Engineer, Wien. Z. angew. Chem. 39, 1926, 907

Concerning the discussion which the paper by prof. A. Stock in no 15 of this journal has started, Dr. G. Pinkus writes in no 26, that now the medical doctors and the statistical scientists must have the word. Regarding the hazards of mercury vapor this does not at all seem to be necessary; in this respect we are all grateful to prof Stock that he has made us aware of an almost generally underestimated hazard. However, to find enough material to evaluate the hazards of amalgam fillings for carious teeth and to compile the results, doctors and statistic scientists will need more time. Also metallographic specialists must be allowed to illuminate the problem. Prof. G. Tammann, senior scientist in metallurgy, has together with O. Dahl at the inst. for physical chemistry, Univ. of Göttingen, published an extensive study of the composition and properties of silver-tin-amalgams in Z. anorg. allgem. Chem 144, 1925, no 1. These are the ones which are mainly used in dentistry. Prof Stock also refer to this paper in a footnote. Older studies by Ogg (Z. phys. Chem 285, 1898) and Reinders (Z. phys. Chem 609, 1906) do not contradict the results by Tammann-Dahl. The experiments which have been carried out at the metallographic laboratory of G.A. Scheid's Affinery in Wien during the latest 3 years and which include amalgams with gold, platinum, palladium, copper, lead, zinc, cadmium etc, in addition to the basic silver-tin alloy, agree in all major respects with these results.

I notice, when I carefully read the paper by Stock, that when he warns of amalgam fillings on p.465, he always writes about silver amalgams. Such amalgams are, however, not used by dentistry and it should be silver-tin alloys he used to manufacture the amalgams for his experiments; The "amalgam manufacturers", whom prof Stock addresses in no 26 of this journal, produce no silver amalgam but alloys of pure silver with tin, with or without additions of small amounts of other metals. It is the dentist who, in the presence of the patient and after disinfection of the cavity in the tooth, places the amalgam he has just manufactured by mixing silver-tin chips with mercury and pressing out the mercury which was not absorbed. The amount of absorbed mercury varies according to composition of the silver-tin alloy and the pre-treatment of the filings. Silver-rich alloys absorb more than tin-rich, "aged" ones, e.g filings which have been made a long time earlier and which have been placed in the sun or at 100 °C for an hour. These bind much less mercury, something which already Joyner and Knight (J. Chem. Soc. 1911, 1913 and 1914), G. Black in Chicago (Die Technik des Zahnfüllens 1914 bd II) determined. Tammann and Dahl have recently studied the ability of silver-tin alloys with various compositions to take up mercury and found that the alloy, especially recommended by Black, 73 parts silver + 27 parts tin, takes up 170 parts mercury if freshly prepared and in aged condition 78. The often used 60 parts silver + 40 parts tin alloy takes up 112 and 29 parts of mercury respectively and holds it with a pressure of 35 kg/cm².

What happens then with the ternary alloys silver-tin-mercury in the few hours when it hardens and thus a profound change in properties occurs? Also on this the work by Tammann-Dahl gives a clear account. The alloy transforms into a mixture of the following crystals: Ag₃Sn, Ag₃Hg₄ with a little (about 2.5%) tin and the mixed crystal Sn-Hg. Free mercury is thus not present in a properly made and hardened amalgam dental filling but chemical compounds and a saturated solution of mercury in tin with the approximate composition 85 parts tin + 15 parts mercury. The amounts of this phase is less if the original alloy is silver- rich. The mercury which Stock distilled from amalgam in vacuum can only come from this solid solution since a decomposition of the chemical compound Ag₃Hg₄ at a temperature of 30 ° is not to be expected. However, also the crystalline, solid solution Sn-Hg will not decompose under normal oral conditions since then gamma- tin must precipitate. The author of this communication has worked with the purification and reuse of metals from scrap for 42 years and has never been able to measure a loss of weight from hardened amalgam scrap, delivered from dentists and kept in open vessels.

That the equilibrium conditions of metals in alloys change, not only with temperature but also with pressure is known to every metallurgist (phase rule of J.W.Gibbs). It is no doubt that the large evaporations from amalgam fillings in extracted teeth which

Stock demonstrated recently (no 26 this journal), was only produced by the vacuum. If three large fillings can give off 150 mg mercury in three days at 30 °, then a 3 g plomb, prepared from fresh 60 silver + 40 tin alloy, according to Tammann-Dahl, containing 1.59 g mercury, should in one year become mercury-free and disintegrate. A similar one, prepared from aged alloy and containing 0.675 g mercury, should have given off all its mercury in less than five months. Such consequences are against all experience.

Amalgam fillings, properly prepared from silver-tin filings, with excess, not binding mercury pressed out before it is placed in the tooth cavity or to which no excess mercury has been added, can not be hazardous. With this confirmation, the anxiety which has affected not only dentists and assistants, but also has been spread by the daily press to the carriers of the dental fillings, can again disappear.

Ludwig Wolf, Berlin
Chem. Inst. of the University
Z. angew. Chem. 39, 1926, 789

Recently a paper appeared in this journal in which the harmful effects of mercury vapor were described in detail. The symptoms were so appropriately described that any reader who like me has suffered from mercury poisoning will find his disease described in detail. Then it might appear superfluous to deal with the subject any more - however, I will anyhow do this.

The reason is that one can hardly often and strongly enough warn for the hazards of mercury vapor. Anyone who has himself experienced this poisoning needs no further warning, - but others who work with mercury and not rarely consider it harmless, should once more with emphasis be reminded of the unhealthy effects caused by the drops which use to be scattered in most laboratories.

I had to suffer severely myself from the consequences of my thoughtlessness. Some years ago I was visited by prof. Pregl when he stayed in Berlin and he warned me sincerely when he saw the large amounts of mercury, not only in the equipment but also scattered as small drops everywhere in the room. If I had given my full attention to prof. Pregl's sincere warning, I could have been spared many bad conditions. However, I did not believe in such a danger from mercury vapor since I thought that such small amounts could not be harmful. Then I was already a constant guest at the medical clinics in order to have my completely unexplainable symptoms from throat and nose examined. In addition to this, I had just as prof. Stock, unbearable headaches, pains in my ears and nearly all symptoms which prof. Stock has described. Neither I nor my doctors got the idea that all these symptoms could be connected with mercury poisoning. Only when vesicles appeared in my mouth, something which was known by my doctors as characteristic for mercury poisoning, I got a correct diagnosis.

To me it seems that the signs of an insidious mercury poisoning are not enough known. For instance, a doctor friend of mine had the same symptoms as prof. Stock and did not know their cause. The paper by prof. Stock convinced him that he had mercury poisoning; some time later he got vesicles in his mouth and this confirmed his suspicions. His poisoning is without doubt caused by gas analytical work when he is constantly in contact with mercury.

My collaborators, who worked much with vacuum apparatus and mercury, also suffered from the symptoms prof. Stock has described. When they left this work their symptoms disappeared with time. Mercury vapor appear to affect the kidneys of females especially. Two female collaborators fell ill with kidney inflammation, a third case outside our institute is known to me. All persons are not equally sensitive towards mercury vapor; it seems as if many are quite resistant.

However, also in such cases there is need for extreme caution. In winter one has to arrange an especially good ventilation and open mercury should always be covered. The heated mercury in the seals of mercury vapor pumps appear to be sources of contamination. If the pumps can not be placed under an exhaust, it is possible to cover the mercury seals with solid paraffin and other seals can be covered with liquid paraffin.

Just as prof. Stock, I have tried all sorts of healing methods without success. The most successful ones are time and extreme caution during mercury work, especially in heated laboratories. A good prophylactic and antidote seems to be the well known method of daily drinking one litre of milk.

Observations on mercury poisonings by arabic alchemists and doctors.

J. Ruska, Heidelberg
Z. angew. Chem. 39, 1926, 790.

The observations on the symptoms of insidious mercury poisoning which prof. Stock has reported in this journal reminded me of arabic descriptions of mercury poisonings which I have published many years ago and also of an, up to now, unknown description by Gabir ibn Hajjan in his "Book of Poisons".

The description has been collected by al Qazwini (dead 1283) in the mineralogical part of his cosmography. According to Avicenna (dead 1037), mercury vapor causes paralysis and tremor and the smoke destroys the ability to see and often causes watering eyes among chemists. It also takes away the ability to hear and causes foul smell from the mouth.

An unknown author has described the symptoms in even more detail: Heated mercury causes - if the vapors are inhaled - paralysis, numbness, unconsciousness, yellow color, tremor of arms and legs, foul smell from the mouth and dehydration of the brain. Mercury dust, mixed into dough and placed as a bait, kills mice. Ointments with mercury kills all parasites which are on the body. Snakes, scorpions and other animals leave the house or are killed when mercury vapors are inside.

I will relate the description by Gabir (dead about 820) completely. It can be found in a large work on poisons, up to now only known from a citation in a dissertation on famous alchemists by Berthelot and it had been considered lost. It has, however, been rediscovered by M. Meyerhof in Cairo and is in my possession as a handwritten text. The text is as follows:
Quicksilver: This element belongs to the major (strong) poisons and this is both when it is killed (ashed, oxidized) and when it is sublimed (evaporates) or is treated in any way which is known to men who know the art (chemistry, alchemy). The killed quicksilver causes strong stomach pains and pains like knife- stabs in the abdomen, anxiety, then arrests the movement of the blood and finally kills; however, the killed quicksilver is less dangerous than the sublimed, this is because the sublimed quicksilver is deadly in several different ways.

If it is sublimed once, twice, up to seven times, it will attack the internal organs and heart however, in a way which can easily be cured and treated by medical methods. It will, in the beginning of the poisoning, cause much arrest of blood; one who swallows it will feel an unendurable pain in the abdomen and is rapidly killed.

Regarding the living (metallic) quicksilver, it is harmless; humans will only be frightened (by its coldness?). If it is harmful, it is only slightly and this is connected with the fright; only if some of it is poured into the ear or the nose will it kill or cause long-lasting disease.

The quicksilver which has been sublimed 30 times or more is a poison of great potency. A person who smells it (inhales) loses his memory and his wit, it causes the blood to stagnate, brings it to the pores of the body and will kill him rapidly. I do not doubt that it is more potent than aconit and the other strong, simple or combined poisons. It cuts the intestines and the stomach and throws them out in pieces. Recovery is possible, death more likely; if you do not hurry, no help is possible.

According to Lippmann (Origin and Extent of the Alccemy p 603), the story about poisoning through the ear is extremely old, also the use of mercury in the form of ointments against parasites. It should be very valuable if persons who know middle age medicine could follow up the matters discussed above.

The Hazards of Mercury Vapor. Comments on the communications by Gradenwitz, Pinkus, Reihlen, Ruska and Schmidt.

Alfred Stock, Berlin-Dahlem
Z. angew. Chem. 39, 1926, 790

I have, as Dr. Schmidt has written, not at all considered that "not enough has been published on the dangers of mercury" (the comments in my first paper only related to the hazards of mercury for chemists and physicists), but only that, as the communication by Ruska shows, also the oldest) is rich in papers on the damaging effects of mercury. I will only point out the very detailed work by A. Kussmaul: "Studies on constitutional mercurialism and its relations to constitutional syphilis", Wurzburg 1861. In this book several hundred cases are carefully described with all symptoms, nervous, catarrhic, those affecting the teeth and the gastrointestinal tract and several others. One obtains a thorough impression of the hell people had in the old amalgam mirror factories. The frank occupational mercury poisonings have become rarer after the mirror factories abandoned the use of amalgam; in wide circles one has forgotten what a dangerous and devious poison mercury vapor is. The former careful precautions have been neglected. Apparently not only in the scientific laboratories but also in the technical workshops! Reading the communication by Pinkus, one is amazed to find that amalgam for dental purposes can be manufactured without any special precautions. Pinkus is himself the owner of such a factory and must know the conditions. It is incomprehensible to me and certainly to anyone who knows the literature, that "there are also experiences which show that workers and chemists have worked in nearly mercury-impregnated rooms for decades without the slightest harm." A more careful study should lead to a less optimistic opinion. It must be noted that noticable damage from mercury vapor often might not appear for years (therefore the case described by Reihlen that someone had worked for two years with mercury equipment, is not remarkable. Also in my laboratory some of the persons did not notice any consequences of a mercury exposure until years had passed.)

The symptoms can be restricted to nervous ones which the manual worker does not notice so much as far as they are endurable. To appear to be in good health means less; that can remain, as my own case showed, when mercury vapor already had caused pronounced nervous disturbances.

Mr. Pincus presumes that the problems in my laboratory were not caused by mercury but, at least partially, had a nervous origin. He mentions his own case which he blamed on a certain chemical compound whereas his collaborators, working with the same compound, remained healthy. Our case is, however, different since all persons working in the laboratory, without exception, fell ill. In any case, neurasthenia does not produce salivation, mouth inflammations or loose teeth!

Mr Pincus refers to the "Arztlichen Merkblätter", which states that "mercury poisonings in Germany are rare." According to my experience, this is not true. I have received numerous letters and communications after the publication of my paper. They tell about many poisonings where the cause had been unknown.

And now to the objections on amalgam fillings by Gradenwitz:

It is certainly correct that the conditions for mercury evaporation from amalgam fillings are quite different from those in the laboratory experiments I described and where the amalgam was heated to 30-35 °C in vacuum. The smaller surface area, saliva, the lack of vacuum will reduce the mercury evaporation. Fortunately! If the fillings released mercury vapor that fast in the mouth they could be deadly! On the other hand, there are also conditions in the mouth which act to enhance the degradation of the amalgam fillings e.g. mechanical load on the fillings during chewing, chemical influence of the saliva etc.

However, even if the evaporation of mercury is far slower in the mouth, this can not cause the undisputable fact disappear from the world, that mercury in amalgam, even in the best silver amalgam, is volatile and has a noticeable vapor pressure. Amalgam fillings must therefore evaporate mercury also in the mouth. How much and how fast is related to conditions in the individual case, to size and position of the filling, mechanical influence during chewing etc. Even if mercury evaporation in the mouth is only a hundredth or even a thousandth of that in the laboratory experiments, it must cause health disturbances during years and decades if the conditions are less favorable.

It is not at all, as Gradenwitz presumes, that the surface of an amalgam filling, after it has lost mercury, is poor in the metal and then does not give off any more mercury. On the contrary, the surfaces become rough, porous and fragile, mechanically more vulnerable (one can often clearly see scratches because of chewing), more easily abraded and new, mercury-rich layers are exposed. This can easily be seen on old fillings with the help of a microscope.

To add further data to our previous studies, we have measured how much mercury is released from silver amalgam fillings, still present in extracted teeth. They were placed in vacuum for 3 days at 30 °C, thus considerably below oral temperatures.

1. Three large fillings (surface area together 300 mm²) in two teeth (mainly chewing surfaces). Evaporation: 150 mg mercury. A frightening amount!

2. A filling of relatively good appearance (70 mm²): 1.3 mg mercury.

Even a small, especially blank and smooth filling of only 25 mm² surface area (not a chewing surface), released over 0.1 mg mercury in three days.

The damage caused by amalgam fillings should be of all degrees, related to individual conditions. From the most severe cases where there are a number of large copper amalgam fillings with a large surface area and which will lead to deterioration of body and mind, to slight, hardly noticeable symptoms and to lack of noticeable symptoms. I have not considered, as Pincus writes "to recommend removal of all amalgam fillings". However, anyone who has symptoms which, without any other recognized cause, suggest a mercury poisoning, whether it is from his amalgam fillings, from occupational contact or from other causes (e.g. living in a room where a mercury thermometer has been broken), should as fast as possible have all amalgam fillings removed since he will be especially sensitive towards even traces of mercury.

Amalgam fillings will always constitute a source of danger. Anyone who interprets my statements on amalgam fillings as a warning should interpret it as it was meant and not falsely. And when "scared patients cause troubles for their dentists when amalgam fillings are suggested", it is for their own best and they have the right to have their very well founded suspicions taken into consideration.

It will certainly not be easy to find a good substitute for the easily manipulated, cheap and relatively long-lasting amalgam fillings. Maybe they can still be used, if they are small, in the milk teeth of children since they disappear again when the teeth are lost. The amalgam manufacturers should, however, be more concerned with the task of finding a harmless substitute for the amalgam than to fight against the well founded warning for mercury vapor.

In addition, one must point out that the removal of amalgam fillings must take place with extreme caution. When the amalgam fillings are drilled out, the inhalation of the fine amalgam dust which is produced, should be carefully avoided in order to prevent an even more pronounced damage by mercury.

I agree with Pinkus that it should be highly desirable to obtain the largest possible material, comparing the health status of amalgam carriers with the number, size, age and conditions of the fillings (which also recognizes the special hazards of neighbouring amalgam and gold fillings which Gradenwitz pointed out). Such an investigation should as soon as possible be conducted by concerned authorities.

Amalgamfüllungen u. Quecksilbervergiftung

Umschau der Wissenschaft 30, 1926, 476-479

Dr. med. Fritz Kleinsorgen.

The publications by Professor Stock at the Kaiser-Wilhelm- Institut in Dahlem on mercury poisonings (Zeitschrift für angewandte Chemie Nr. 15, 1926), have caused considerable attention; especially the statements on the dangers of mercury poisoning by the use of amalgam fillings have caused considerable anxiety in a large parts of the population. Indeed, professor Stock states "that the thoughtless introduction of amalgam as a filling material for teeth was a severe sin against humanity."

If we consider that most persons in the population have amalgam fillings, often a dozen or more, we can understand the excitement which has been caused among all who have learnt about Stock's paper. Short reports in the daily press have made the widest dissemination certain. Just the renowned scientific place from which the warning for amalgam fillings has emanated makes it especially necessary for serious consideration.

Considering the ubiquitous distribution of amalgam fillings since decades, it is strange that the symptoms of chronic mercury poisoning has so completely escaped attention that they have remained undiscovered until now. One must therefore ask: Are the symptoms of poisoning so uncharacteristic that they could be overlooked by medical doctors or has professor Stock exaggerated with his warning?

If one reads the publications by Stock and studies his descriptions of his experiences of mercury on his own health, we certainly can understand that the slow, chronic poisoning by mercury vapor has a fluctuating course and can remain undiscovered. The symptoms of mercury poisoning, as they are described, is for a long time within the limits of general nervous symptoms as they appear in neurasthenia or the nervous exhaustion which is characteristic of the stressed and overworked person in our civilization. It is therefore very difficult to distinguish between these diseases.

Memory disturbances, headache, dizziness, nervous unrest, vertigo, irritated mucosa, lack of initiative etc. were, according to Stock, present for 2 1/2 decades and worsened with time. However, these are also the typical symptoms of general nervousness in the population and offer nothing characteristic.

The characteristic symptoms of mercury poisoning like salivation, loosened teeth etc. appeared first after 25 years of exposure to mercury vapor in the laboratories of the Kaiser-Wilhelm- Institute. This quickly led to the recognition of the true cause of the symptoms.

The development of the chronic mercury poisoning overlaps to a large degree with the development of nervousness caused by other conditions.

When now professor Stock, based on a series of experiments with amalgam fillings, states his conviction that they are harmful and constitute a sin against humanity, it is understandable that carriers of amalgam fillings with nervous tendencies (which should include the majority of persons with amalgam fillings), discover that they are mercury poisoned.

In relation to the anxiety which has been caused and already has resulted in the refusal to have amalgam fillings placed in dental clinics and the demand to have the already present ones removed, it is urgent for the involved circles to take a scientific stand to Stock's publications.

In this place one can add: amalgam are compounds of mercury and various metals like copper, tin, gold, silver. These compounds with metals are chemically labile and already strong heat will remove part of the mercury.

The experiments which professor Stock has made with both new fillings and old ones, were carried out in evacuated glass tubes where the amalgam-end was heated to mouth temperature and the other end cooled to 0°C and partly even colder. After 8 to 14 days mercury was found in the cooled ends.

Such experiments do not prove the release of mercury in the mouth. Such pressure- and temperature-differences are not applicable to the mouth. Therefore it must be said that there is today no need to fear mercury poisoning from amalgam fillings under normal circumstances. However, this does not mean that they are completely nonexistent.

Under special circumstances mercury poisonings might occur. This depends both on the quality of the amalgam fillings and on special conditions in the mouth.

Amalgam fillings which have no defects do not have a risk of poisoning. However, earlier there were amalgam fillings which dissolved in the mouth. I do not know if they are still used. This relates to copper amalgam fillings. These were, and are if they are still used with the same composition, a constant risk for the carrier.

In addition, there might be circumstances which also make normal amalgam fillings risky.

When different metals in the mouth come into constant or intermittent contact, electrolytic processes can occur. Such processes are not rare when gold- and non-noble alloys are used for crowns and hooks for cautchuk dentures and these are in direct or intermittent contact with amalgam fillings.

Dentists should therefore be careful not to place crowns of gold or other metals on teeth which contain amalgam. One must then place a thick enough cement layer between the metals. One must also take care to prevent contact with fillings in neighbouring teeth. Dentures and hooks of metal must not come into contact with amalgam. It is also dangerous to the repair of old amalgam fillings. New amalgam must not be placed close to old amalgam without a cement barrier; also one should avoid placing amalgams of different manufacture or composition close to each other.

Many dentists are ignorant and sin against these rules and they must especially have their eyes on these circumstances.

To reassure the public with amalgam and other materials one must state that there is no reason to fear any form of metal poisoning if the teeth are regularly carefully examined by a dentist.

Amalgam fillings and mercury poisoning (Amalgamfüllungen u. Quecksilbervergiftung)

Umschau 30, 1926, 479

Dr. med. P. Windmüller

In dental circles, especially in America, there has been considerable argument whether amalgam dental fillings are acceptable or not. I have shown for over 20 years that it is possible to work without amalgam fillings and I have shown it in my own practice!

We are in the lucky position in dentistry to have materials available which can be incorporated in the body and teeth and which are not only neutral and biological, but which can have a health promoting effect on the cells in the tissues.

Scientific research and experience from clinical practice have confirmed this fact since several years. Every alert doctor and especially dentist has without doubt noticed that the gingiva does not adhere closely to the teeth if it is in contact with amalgam. More or less dirt collects at these places and they will be inflamed. This is a proof that amalgam are foreign to the body and must be harmful, in contrast to fillings like cement, metal-cement, porcelain and especially gold-fillings.

When two metals touch each other, for example amalgam and gold in neighbouring teeth or opposing teeth which come into contact when biting, and the saliva has an acid reaction or acid food is eaten, then an electrogalvanic element is created. The more or less happy owner of such a battery experience an unpleasant taste, sometimes even electrical discharges with pain. The same happens with amalgam-filled teeth in contact with a denture hook of gold.

Gold has a yellowish color of its own. In the vicinity of a biting contact between an amalgam filling and gold or gold hook there will in most cases be a whitish discoloration of the gold together with a destruction of the noble metal. Every alert dentist can recognize it as a mercury deposit on the gold. When a large number of amalgam fillings are present there will be a more or less strong evaporation of mercury which manifests physically as time goes by in the form of a contraction of every amalgam filling. This reduction in volume constitutes a certain hazard for the teeth and causes eventually "secondary caries", i.e. an empty space will form under the amalgam which will fill up with rests from food. The recurrence of caries is certain.

Certain diseases have to be treated with mercury. The patient will take on a pale color and the metallic poison leads through the saliva to severe gingivitis. Even if the amount of mercury from amalgam is much less than that used in the ointment treatments, it is completely certain that a reduction in the use of amalgam or the total abstaining of this questionable metal mixture for filling teeth will protect the patients from mercury damage.

Even if the majority of persons who have amalgam fillings do not have any health disturbances, such a negative finding is not proof of the neutrality of the amalgam filling material. If the dentist removes the amalgam fillings from a patient with many general health problems before these have become too severe, the problems will disappear within a relatively short time.

THE HAZARDS OF MERCURY VAPOR AND AMALGAM

(Die Gefährlichkeit des Quecksilberdampfes und der Amalgame)

Alfred Stock, Berlin-Dahlem

Zeitschrift für angewandte Chemie, 39, 1926, 984-989

My warnings for mercury vapor and amalgam fillings have made a more than expected echo; in personal communications and letters, in papers in especially the dental journals and unfortunately often in erroneous desk products, published in the daily press.

I recently briefly reported at the Dental Society and at the Berlin Medical Association on the material I have received. The contents of these lectures will be published in "Medizinischen Klinik". In addition and leaving out material which is already known by the readers of this journal, I will also publish it here since many colleagues should be interested in the developments of this question.

Our experiences let us suspect that there should be many other victims of mercury poisoning besides us. Mercury is very much used in science and industry and is almost never treated with the absolutely necessary caution. Actually, conditions are much worse than we had expected. After the publication of my paper on the hazards of mercury vapor, I received a flood of written and oral communications, reporting of mercury poisonings of various severity, almost always with the same symptoms, all too well known by us and their cause not recognized. Often it was reported that the symptoms had slowly disappeared when mercury contact had ceased. The largest number of such reports were naturally from the circle of our own colleagues, from chemical scientists and industrial chemists, people I was personally acquainted with or met at conferences. Today I know nearly 50 chemical scientists who suffer, or have suffered from chronic mercury poisonings; among these persons there are several well known scientific names. Also in the chemical industry the mercury poisoning turned out to be relatively common. Certainly I have only obtained reports on a small fraction of all poisonings. There must be many more cases also among physicists; these use in general even more mercury than the chemists and often handle it very carelessly. Also from other groups: technical, medical, dental, teachers, many letters told about mercury poisonings. The contents were nearly always the same: "When I read your paper, the scales fell from my eyes and I now finally know the cause of my problems; my doctors have not recognized the cause etc."

Sources of the mercury vapor poisonings were, in addition to scattered and in cracks of the floor discovered mercury, work with mercury switches, mercury retifiers, mercury seals of tube connections, ozone equipment, mercury air pumps and other mercury apparatus, use of alkali amalgam for chemical reactions, prolonged stay in rooms where earlier a thermometer or a barometer had been broken etc. In most cases one could estimate that the mercury levels has been equally low as in our laboratory.

From many of the communications one could learn about the despair the affected persons felt in their condition which affected their work and the ability to carry out the tasks their position required.

As examples I will cite some passages from letters. They come from known scientists:

Dr. H wrote: "In november 1924 our institute bought an apparatus for exact gas analysis according to Ott; Mercury was used as a sealing liquid", and he reports of several mercury poisonings, both his own and his collaborators, because of this apparatus. For instance: "Dr. G, then scientist at our institute, suffered during the time we used mercury and also afterwards, from constant tiredness. He complained about loss of memory, had problems from his teeth (bleeding gingiva). I met Dr. G. at the Kiel meeting. His problems have now nearly disappeared. He left us a year ago."

Dr. S. now director of a research institute and earlier working in a chemical factory, reports on a mercury poisoning he acquired when mercury was used to seal tubing: In the beginning I had light headaches, then more severe and with shorter intervals. I had also a profound unrest which affected me more and more. As especially characteristic I find the sensitivity to colds, affecting the respiratory organs and causing inflammations of the nose and nasal mucosa. A doctor I asked for advice suggested that the symptoms were caused by a latent spanish flu. The formation of vesicles and inflammations of the tongue, especially at the lower end.. appeared about three years ago. These symptoms were especially painful. The doctor explained also these symptoms as caused by flu... Bleeding of the teeth during the slightest brushing.. In addition to the above symptoms I had also an ever increasing tiredness, pains in various places and a profound need for sleep." Dr. S tells about another colleague in the factory who also suffered from mercury poisoning. "Concerning myself, I felt a clear improvement, apart from the bleeding gingiva and some dizziness, after I had left my work at... "

Dr. Kolle, director of the Inst of Experimental Therapy in Frankfurt, also reports on his own and others mercury poisonings. "I have suffered for years from the same symptoms you have described. In addition to rather severe disturbances of the gastrointestinal tract, primarily the nervous disturbances were quite similar to those you have described. I was, for a long time, not aware of what

the cause of my health disturbances was.. later completely healthy although I, at the time, had the impression that I suffered from a rather severe disease.. Many of my collaborators had quite similar experiences."

From a letter by the laryngologist prof. G. in Berlin: "My patient, chemist at a large company here, suffered from general tiredness, severe inflammation of the mucosa near the teeth and severe catarrh of the upper airways. He complained less of headache but one could notice profound change in his appearance. In the beginning of the treatment he liked a glass of Moselwine but after some months he lost interest in life and became depressed. On my advice he visited a dental expert.. The patient was then sent to various resorts by us, however, when he came back to Berlin he became sick again. Finally he himself got the idea to search his laboratory and found in the floor considerable amounts of mercury. After this adverse condition had been corrected, he recovered remarkably fast from both the symptoms in the upper airways and primarily in general health."

Compare the communication by L. Wolff (Z. angew. Chem 39, 1926, 789). This might be sufficient. I could add considerably more material.

However, it has been demonstrated that prolonged inhalation of also very small amounts of mercury (daily hundredths or thousandths of a milligram) cause health disturbances. These are in the beginning very non-specific and affect mainly the nervous system and the upper airways (primarily the nasal mucosa; this is repeatedly pointed out in the communications), usually without the mouth inflammations, otherwise considered characteristic for mercury poisoning. The symptoms generally agree for all affected persons. If there is immunity against the effects of mercury, it is rare.

Metallic mercury is one of the most insidious of poisons because of its volatility, lack of smell and insidious effects with aftereffects for years. These can so far only be helplessly endured. In addition to the cases of certain mercury poisonings there is certainly an even larger number where the symptoms restrict themselves to the first stages, a depression of intellectual capacity without any other signs and the real cause is never known. If they are noticed, they are explained by overwork, nervous exhaustion, age etc.

However, the hazards of mercury are not only a matter for scientists. Also other groups are threatened by it. Consider e.g. mercury thermometers. Many mysterious disease cases might be caused by the breaking of a mercury thermometer in a living room and the scattering of its contents as dust in cracks and joints. The amount of mercury in a thermometer is quite sufficient to give the air a harmful level of mercury for years. What is sooner or later the fate of almost every fever thermometer? One day, when it is hurled to press down the mercury, it slips from the hand and is broken; this mostly even happens in a bedroom. The possible consequences can readily be imagined: tiredness, unrest, dizziness, headaches, catarrh, gastrointestinal troubles. The cause will hardly be recognized by anyone; the breaking of a thermometer can even have been done by someone who lived in the room earlier. If the problems in such cases are caused by mercury can only be clarified with an, unfortunately not so easy, air analysis or the finding of mercury droplets (magnifier) in the joints of the floor boards.

Much more important is the general use of mercury in the form of amalgams for dental fillings. Originally the dentists only used copper amalgam. This is bought ready-made, is heated by the dentist and then softens; in the tooth it rapidly hardens. The later introduced, so-called silver amalgams, are prepared otherwise. The commercial metal alloy (a third to two thirds silver, a few hundredths of other components and the rest tin; if it contains platinum or gold it is called "platinum amalgam" or "gold amalgam") contains no mercury. It is mixed with mercury by the dentist; a plastic amalgam is formed, which also hardens after a short time. The amount of mercury used for the preparation varies within large margins according to the methods practiced by the dentist. He subsequently presses out excess mercury from the plastic mass. The mercury content of the final filling can therefore be very variable.

The filling with amalgam is also a hazard to the dentist himself since with common practice mercury evaporates and mixes with the air. The copper amalgam gives, when it is heated and especially when it is heated more than necessary, off considerable amounts of mercury as vapor, mercury which can precipitate as a fine dust in the surroundings. When silver amalgam is mixed and even if instructions are carefully followed, the pressed out excess mercury will often be left in the room for a considerable time or falls even on the floor. The dentists handle mercury very differently but are apparently often too careless. The beginning of chronic mercury poisonings are not rare among them, among older ones even rather common. This is shown to me by communications I have received. It can also be found in the literature. Before my own paper on the hazards of mercury appeared, Dr Lowy (Medizinische Klinik 1926 p 608), for instance, wrote in a paper on occupational diseases of doctors : "Also dentists are threatened by mercury.. even if they have not symptoms of an acute poisoning.. , general tiredness, loss of interest in work, easy exhaustion, irritability, anxiety, loss of sleep and general decrease in psychic ability is apparently caused by a latent, chronic mercury poisoning." And Dr. M. Jarecki, himself dentist, writes (Zahnärztliche Rundschau 35, 1926, 327): According to the urine analysis by Schulte (who found considerable amounts of mercury in the urine from almost every examined dentist) it seems very likely that the considerable nervousness which many dentists show, has its cause in an insidious mercury vapor poisoning." Considering our own experience one must agree with this conclusion. If the dentists should use amalgam, they must be far more careful than now in order not to be endangered. A simple exhaust which leads to the outside must belong to the equipment of the operatory (it is easy to obtain one equipped with a small electric fan). All handling of mercury and amalgam should take place under this exhaust. Naturally, rests of mercury and amalgam scrap must be stored tightly sealed.

Concerning the hazards for the carriers of the amalgam fillings, there is certainly a large difference between copper and silver amalgam (and the varieties of these).

Copper amalgam is strongly degraded in the mouth. It will be generally degraded and fragile, gives off copper and copper compounds and simultaneously mercury is released, often in the form of visible drops. The copper amalgam is degraded and disappears with time. As it appears today, copper amalgam has no defendant any more among the professionals, although it was highly praised when it was introduced, also because of its disinfecting properties! In a statement at the Brandenburger Dental Society meeting, June 5 this year, a meeting which dealt with the amalgam question, I heard, to my astonishment, distinguished spokesmen of the dental profession say that "copper amalgams should not even be discussed". The well known Würzburger pharmacologist F. Flury recently wrote (Münchener Medizin Wschr. 73, 1926, 1022) about the "old binary copper amalgams with their unsuitable composition and which can produce mercury droplets" and about the recognized defective copper amalgams". These "recognized defective" copper amalgams are, however, extensively used in Germany, in the insurance-paid practice they are even dominating dental filling materials only because they are cheap and very easy to manipulate. One can ask: How is something like this possible? and must sincerely wish that concerned authorities, e.g. the Ministry of Health, brings this question up to discussion as fast as possible.

The silver amalgams are more durable, more mechanically and chemically resistant. However, also these change slowly in the mouth and their surfaces become rough, scratched and fragile, something which can easily be seen by a microscopical examination of older fillings. New layers of amalgam will continuously be exposed. Freshly prepared amalgam will even give off much mercury vapor. But also after long storage and after long use in the mouth they give off considerable amounts of mercury as vapor, at least such amalgams as are used in practice. We have published such laboratory experiments (Z. angew. Chem 39, 1926, 791). The results are confirmed by the following experiment which we made with one of our collaborators at our institute, Dr. D.:

D. has about a dozen fillings of good appearance in his teeth which always were kept in good order. Most of them are silver amalgams; maybe one or two are copper amalgams. He held a glass tube between his closed lips and we let about 400 l air pass from his nose and out through the tube by suction. The air was led through liquid air and the condensed liquid was analyzed for mercury as previously described. Result: weak but clear mercury reaction. In a control experiment we of course determined that the air in the room was mercury-free. It should be emphasized that nothing had been done to Dr. D.'s fillings for three years. After this experiment Dr. D. had a new silver amalgam filling placed. When we repeated the experiment four days later, the mercury reaction was considerably stronger. Quantitatively such experiments tell little since of course only a small fraction of the air stream comes into contact with the dental fillings and since also the saliva flows especially much when you have an unusual thing like a glass tube in your mouth. Qualitatively, however, the results are quite convincing.

In addition it is not at all stated that amalgam fillings are harmful because of evaporated and in the lungs inhaled mercury exclusively or even mainly. Also the mercury which enters the gastrointestinal tract because of the general destruction of the fillings and that in very finely divided and almost atomic condition should be absorbed in a similar way as the inhaled. The generally known fact that large amounts of mercury in compact form can be swallowed and passes without harmful effects through the body, will not, because of the enormous difference of the mercury surface, contradict this presumption.

When I pointed out, in my first publication, the possibilities of harmful effects because of amalgam fillings, there was a storm of distrust and protests from wide dental circles (e.g. P. Ritter, Zahnärztl. Rundschau 35, 1926, 415). Nobody had observed any mercury poisoning among millions of persons who had amalgam fillings! Others meant that the very few cases of harmful effects because of mercury from amalgam were "idiosyncrasy". What is this idiosyncrasy? Nothing else than a high sensitivity towards mercury. Our observations now clearly demonstrate that many, apparently most, humans are sensitive towards mercury. Thus, mercury-"idiosyncrasy" can not be dismissed that simply.

The dentists are seldom in a position to recognize general effects of amalgam fillings or even to learn about them. When the patient suffers from nervousness, intellectual exhaustion, catarrhs etc. they do not go to the dentist whom they also usually do not tell about their problems since they are prevented from talking during the treatment. The family physician, nerve specialists, laryngologists, internists are the ones they discuss these problems with.

The dentists who try to give the impression that the amalgams are harmless also quite forget the strong opposition amalgam met from the beginning among physicians and dentists and still meets. Just two recent voices:

Dr. P. Windmüller (Die Umschau 30, 1926, 479): "Every alert physician and especially dentist has undoubtedly in his practice had the opportunity to observe that the gingiva does not adhere firmly to places where it comes into contact with amalgam.. Even if most of the patients who have amalgam have no noticeable disturbances in health, such a non-demonstration is not at all a proof of the neutrality of the amalgam filling material. If the dentists remove the amalgam fillings from patients with many general problems and fill the teeth with neutral material, the problems disappear within a relatively short time."

Dr. Lichtwarck (Zahnärztl. Rundschau 35, 1926, 363): "I have, since a long time, observed the harmful effects of mercury from copper amalgam fillings. I do not place copper amalgam plombs since many years. I have in my practice recorded a considerable number of cases where I suspected them to cause headache, discomfort, indisposition, strong salivation, neurasthenic symptoms and stomach problems and where a spontaneous disappearance of the problems occurred when they were removed."

A German-American writes me from New York that dentists there do not use amalgam since years ago. He adds an objection to the German dentists' views on the warnings for amalgam "this should reduce their reputation in the opinion of famous dentists here". Whether this information is correct I certainly do not know.

When one knows that already extremely small amounts of mercury are harmful to humans and that amalgam filling continuously give off mercury to the body, one will be convinced that amalgam fillings are objectionable. This view has been supported by numerous communications which I obtained because of my paper.

I will describe one case in detail since it is important for judging in this question. It concerns the well known, today again healthy and working, professor of psychology at the University of Marburg, Dr. E. Jaensch. From the report Prof. Jaensch wrote about his experiences with amalgam fillings and which he generously allowed me to make public, I will cite some parts:

"You do humanity a favor when you take up the question about amalgam. At about the age of 15 my teeth were, as the saying is, put into order. I had fillings in a large number. Gradually persistent troubles appeared which first restricted themselves to the nervous system. The condition was diagnosed as "hypochondriac neurasthenia" since the symptoms were only of a nervous character and since I in general appeared to be in good health.

At the end of my student time I had again distinct nervous and also bodily symptoms. The troubles increased year by year. The beginning of the deterioration was clearly associated with an unusually large and especially unskillful dental treatment. I had mostly so-called contour fillings and a distinguished dentist now told me that "to prevent anything more from happening" he had to connect the adjacent fillings in the molars and he made these solid connections.

From 1909 my condition deteriorated... chronic, worse and worse diarrheas. 1912-16 I had to go to the toilet ten or more times each day and it is understandable that I lost much weight. In addition I had intense pains in all parts of my body.. I could sleep less and less, ..inflammations in my mouth with increased salivation.. worse inflammations in the upper airways, especially in my throat.. painful asthmatic condition, intense anxiety and deterioration of my physique so I could only leave my bed for short times.. complete impairment of my intellectual abilities.

I was on sick-leave since a year and my life was a futile wandering around to medical specialists in Baden-Baden, in hopeless resignation, when I there in summer 1916 met my former acquaintance Prof. Sommer from Giessen. I told him about my condition and also of a recent thought. Suffering from toothache I had, in front of the mirror, contemplated my set of teeth with its in part very large amalgam fillings (18 silver amalgam fillings). Then I had recalled a remark which I had often heard from my doctors. I had suggested also unusual causes, also that I had contracted lead poisoning because of work with accumulators. From the physicians I then got answers like: You have certainly not a lead poisoning, the symptoms are more similar to a mercury poisoning. But that's an impossibility - where should that have come from?

When I now contemplated the large amount of amalgam in my mouth I got the idea that might it not after all be a mercury poisoning? Sommer then told me that he had a significant number of similar cases where the puzzling disease state upon closer examination had turned out to be toxic polyneuritis.

My urine and saliva were tested for mercury. The clinical and chemical examination gave the results which are written in the records of Prof. Sommer. (In these records from 1916 one can read: In the urine was mercury in considerable amounts. In the saliva mercury could not be detected with certainty. The source of the mercury seemed to be the many amalgam fillings the patient had in his mouth for many years. The previous history fits completely the assumption that it is a toxic disease caused by mercury).

Now, however, we faced the almost impossible task of finding a dentist who could be persuaded to take out and replace the fillings. Again and again I was dismissed. Everywhere the dentists pointed out that the harmlessness of the amalgam plombs was proved, therefore the records from Sommer could not be believed and that no dentist from a dental standpoint could take the responsibility for such a large and "unnecessary" operation. Prof. X at the Emperor's court, told me: "You can send me reports from all the medical specialists in the world - I do not believe it."

And all that only because Witzel was said to have proven the harmlessness of amalgam fillings, partly against a considerable resistance against the older dentists. When I had obtained Witzel's book (Witzel: Das Füllen der Zähne mit Amalgam, 1899; Witzel played the same role as Black in the USA, transl. note) I was shocked by the shallowness of these proofs..

It might not have been possible to find a dentist who could exchange the fillings if prof. Binswanger had not explicitly asked a relative of his who was a professor of dentistry. When the large plombs were drilled out I had increased troubles... when we sucked away the amalgam dust during the rest of the work the problems did not appear.

Immediately after the removal of the amalgam fillings a considerable improvement of especially the diarrheas started, at least compared to the previous condition. Even if the rest of the recovery was slow.. the time of the amalgam removal was a turning point after which all symptoms from the digestive and respiratory organs as well the nervous system, steadily decreased so that now, for the first time, I really know what it is to live.

Only time has really helped me, after the exchange of the amalgam fillings for gold, everything else only to a small extent. How many people might suffer in the same way, even if it is to a lesser degree and how many such cases might forever remain undiscovered?

Prof. Jaensch deeply affecting story needs no comments. It generally agrees with the experiences we unfortunately had ourselves.

This severe case is not at all the only one. Dr W., chemist, wrote me: "When I read your paper in Z. angew. Chem...I found the symptoms of my wife described in every detail... strong catarrhs of the upper throat... headaches and vertigo up to being unbearable.. tight nose, pains over the eyes (diagnosed as sinusitis by the physician)... the condition needed medical care during the latest two years because of psychic depression which added to the continuously increasing bodily problems (neuralgias in face and head, painful cramps in the liver area)... eleven amalgam fillings (the oldest and biggest ones of copper amalgam).. the fillings were immediately removed. Then they turned out to be in a very bad condition, especially the copper amalgam filling in the molar was fragile and with a completely changed color. ... Undoubtedly the most severe symptoms from the throat, the changes of the oral soft tissues, the neuralgias and the pains of the liver have disappeared. The psychic depression has also continuously improved; there is no doubt about it although the improvements take longer time than with the above described symptoms."

A quite similar case with an elderly woman is described by Dr. Lichtwarck (Zahnärztl. Rundschau 35, 1926, 363): tiredness, loss of sleep, easily irritated, tinnitus, sick feeling etc. up to a suicide attempt. Treatments without results by stomach- and nerve-specialists until the removal of a large amalgam filling with a gold crown finally brought complete health. Amalgam and gold next to each other is, because of the electrolytic processes which then appear in the mouth, dangerous and should be avoided; compare also e.g. Dr. G. Haber, Zahnärztl. Rundschau 35, 1926, 395.

In the literature one can find descriptions of many similar cases. I also know several similar cases among my own acquaintances. We analyzed the urine of two of these and it did contain mercury.

The problems must certainly not always be so severe. The effects of amalgam will pass through all stages according to number, condition and position of the fillings; from the most severe cases of psychological and physical deterioration up weak, hardly noticeable symptoms or from the affected himself not noticed effects (depression of intellectual functions). On each severe case there will be a hundred, maybe a thousand or ten thousand slight ones. Alert medical observations, directed at the connections between the amalgam fillings and the symptoms of chronic mercury poisonings, should soon produce important information. That such information really exists, apparently to an amazing extent, seems certain from the reports which voluntarily are sent to me. Again and again is reported, that after placement of amalgam fillings, symptoms which had not been present before, appeared: dizziness, vertigo, bleeding gingiva, chronically running noses and catarrhs (the location was almost always the connection between throat and nose) etc. In cases where the amalgam fillings, because of tooth extraction or falling out, had been removed, the problems had slowly again disappeared.

The recognition of the beginning of a chronic mercury poisoning is not simple since the first only psychic and nervous symptoms are so little specific (They appear, with the exception of mouth inflammations, also in other chronic poisonings, e.g. by arsenic or hydrogen sulfide). They are more reliable when also chronically irritated nose and catarrhs, oral symptoms (vesicles, bleeding gingiva, loose teeth), diarrhea etc appear. The most convincing fact is certainly the demonstration of mercury in saliva or urine; this requires a certain training and skill when the amounts are small (the chemical laboratory of Dr. A. Buss, Berlin SW 47, Grossbeerstr. 31, has already declared that they can determine mercury according to our methods). As we have already demonstrated the excretions are often periodically mercury-free although mercury poisoning has been present and mercury is still in the body.

In most of the severe cases known to me, there have been copper amalgam fillings present. How extensive the damage because of silver amalgam is, must be determined on a larger study group. The possibility for such damage exists since also the silver amalgams give off mercury in amounts which are harmful because of the high sensitivity of many persons towards mercury.

These important questions demand the attention of all physicians. Perhaps it should be useful if the Ministry of Health published a mercury bulletin, similar to the lead bulletin, where questions could be resolved. The fight against the copper amalgams as dental filling materials should immediately be taken up.

The dental profession, as told above, at first completely dismissed the matter but now quite other views can be heard from these circles. For instance, at the end of a recent paper by Dr. A. Werkenthin (Zahnärztl. Rundschau 35, 1926, 451) one can read: "If this "amalgam-alarm" results in a prohibition of copper amalgam fillings (as lead fillings, plombs, once were prohibited), then we should be grateful for this sound scare (alias shaking-up)."

Fortunately the medical profession gives the question of chronic mercury poisoning their attention. Dr. His reports in the Medizinischen Klinik: "The discussion of Stock's report in the the medical and dental profession has resulted in the desicion that it is necessary to clarify to what extent damage because of chronic mercury poisoning, especially from amalgam fillings, exists. Therefore a place must be organized where people, who think that they have mercury poisoning, can be carefully examined, both regarding their symptoms, the condition of their plombs and the presence of mercury in the urine. Such an institute will be arranged at the 1st Medical Clinic where a physician and a dentist and it will also be arranged that the urine of the patients can be analyzed for mercury according to the methods which Stock has developed. The organization of this examination and counselling place will take a few weeks; according to our plans it will open in the middle of september and the medical profession will be notified about it in due time."

Then this question will be in the right hands and one can calmly wait for the results of this professional study without further involvement of the press.

Mercury poisoning, caused by amalgam fillings **Quecksilbervergiftungen, von Zahnfüllungen ausgehend**

Prof. Dr. E. Meyer, Berlin

Die Medizinische Welt, 4, 1930, 703

In No. 9 of Med. Welt Arnoldi makes his colleagues aware of mercury poisonings, caused by Hg-containing air in laboratories. I would like to point out another source of poisonings - the amalgam fillings which, despite the publications by Stock and others, have not received enough attention in medical practice. Two recent similar observations makes me emphasize this type of etiology for Hg-poisonings.

Case 1. The 7th. of januar 1930 Mrs. R.F., 40 years old, came to my practice. She complained of burning tongue, especially in the mornings and evenings, not related to type of food, of mouth and throat dryness and of gingival inflammation. General health, sleep, appetite and gastrointestinal tract were disurbed, menstruations irregular. The patient is depressed, can not concentrate enough to read books. Earlier she was an intellectual and had several such interests. She complained ove pins and needles and numbness of her hands and feet. She had lost 10.5 kg in one year. The patient considers her illness caused by a gastrointestinal catarrh one year ago. Because of her oral problems she had been under dental treatment for a long time.

At examination I found a glossitis superficialis with rather unaffected margins of the tongue, some rest signs of a gingivitis and a chronic tonsillitis. Inner organs nothing notable, slightly exaggerated reflexes. The discrepancy between the few objective changes and the strength of her problems was remarcable. The blood examination by prof. Schilling showed an atypical picture with elevated leucocytes and low color index which indicated a toxic anaemia, originating in the gastrointestinal tract. Since no other changes other than hyperacidity were present in the gastrointestinal tract, I looked for other explanations to the blood changes and the clinical state. I found a number of old amalgam fillings in her teeth, something which made me suspect a Hg-poisoning. I therefore asked the treating dentist to remove the fillings which partly consisted of old, degraded copper amalgam fillings. At the same time I sent an urine sample for mercury analysis to the Hauptgesundheitsamt. The result was 4/1000 mg Hg, calculated on a daily urinary volume of 1,5 liter urine.

The result of the removal of the fillings was rather remarcable. Within a few weeks the patient had recovered completely, she is again healty to body and soul. The depressive state has disappeared, the gingiva has healed; the only remaining symptoms is a lightly burning tongue, however much less than earlier.

From the clinical story the diagnosis is evident. The finding of Hg in urine explains the clinical picture and the blood changes completely. That the copper amalgam fillings were the sole cause of the mercury intoxication is evident from the lack of any other contact with mercury and from the improvement in health in direct connection with the removal of the fillings.

Case 2. Mrs. G.M., 32 years old, complains since a long time over burning mouth and throat, over tiredness, lack of appetite, gastrointestinal disturbances, poor sleep. She connected her problems with her pregnancy. However, since no improvement had occurred six weeks after delivery, Prof. Paul Strassmann sent the patient to me. In addition to a light rhino-pharyngitis I found a

swelling of the right margin of her tongue with clear impressions of her teeth, a thin mucosa. No changes in the gingiva or inner organs.

In the molars there were fillings of both copper- and silver amalgam. Since also in this case there was a remarkable discrepancy between the complaints and the objectively demonstrable changes and there was no other obvious cause, I thought about a Hg-poisoning from her amalgam fillings. I therefore had the copper amalgams removed. The urinary analysis at the Hauptgesundheitsamt showed 6.25/1000 mg Hg, calculated on a daily urine volume of 1500 ml. The effects of amalgam removal were not that remarkable as in case 1. According to a letter from the patient, who departed soon after the amalgam removal, the symptoms had diminished after 14 days, but not disappeared. This is, however, not remarkable since it usually takes a long time to improve after a mercury poisoning.

Based on these observations I would like to stress that Hg- poisonings are more common than generally thought. In cases where a mercury poisoning might be suspected must, if no other cause is found, the amalgam fillings be considered. If such fillings are present, their immediate removal is absolutely necessary. A urine- and feces-analysis must support the diagnosis. Therapeutically, after the removal of the fillings, one must enhance elimination of mercury from the body by a healthy lifestyle and by medical treatment and to assist a general improvement in strength.

Discussions about the hazards of amalgam were also published in other journals than the chemical ones.

Some abstracts, mainly collected from: Huber CD, **Darstellung der durch Stock ausgelösten Diskussion um das Problem der Schädlichkeit von Amalgam-füllungen an Hand der Litteratur. Dissertation from the Klin. f. Zahn-, Mund- und Kieferkrankheiten, Munchen 1957 (Report on the discussion, caused by Stock, on the problem of the hazards of amalgam fillings, according to literature, 54 pages)**. This seems to be a fairly accurate report on the discussion from 1926 to about 1931. Huber does not judge who was right or wrong but his recommendations are that copper amalgam (with or without additional metals) should never be used and silver amalgam very conservatively e.g. never on occlusal surfaces if it comes into contact with an antagonist tooth, never when the cavity borders on the gingiva etc. The removal of old amalgam should also be done very cautiously to prevent poisoning of patient and dentist.

Abstr: Mayer, E. (Prof. Breslau) Untersuchungen von Amalgam auf die Abgabe von metallischem Quecksilber. Dtsch. Monatschr f. Zahnheilk. 1927 p226. Mayer used Stock's method with amalgam in closed glass tubes; the amalgam part heated to 37 degrees and the other cooled in ice. The experiments were conducted at atmospheric pressure in contrast to Stock's. Detection of mercury was by weighting any distilled mercury after three weeks. Results:
Copper amalgam 0.640 - 0.960 mg
Silver amalgam 0.130 - 0.265 mg

Conclusion by Mayer: Since every human, whether he has anything to do with mercury or not, daily excretes up to 0.5 mg mercury as something completely normal, then silver amalgam can be considered harmless, but copper amalgam, with its high release of mercury, must be considered harmful. Copper amalgam should therefore not be used but only silver amalgam. (transl. note: Whether the figure in the original paper really is 0.5 mg has not been controlled. The experiments confirm the results by Stock and that without vacuum).

Rohrer, L. Gibt es eine chronische Quecksilbervergiftung durch Amalgamzahnfüllungen? Munch. Med. Wochenschr 1927, p 1346: Can amalgam fillings cause a chronic poisoning? Rohrer finds that dental metallurgy has advanced so much because of its systematic studies of amalgam, that today there are amalgams on the market which are without objection. These can certainly not give off any free mercury if they are correctly prepared. This does not apply to all kinds of copper amalgams, with or without additions. These should not be used because of their mercury release which can not be denied, also after they have reached their final hard condition. Stock's studies could, however, not be confirmed by most experiments afterwards. Especially the in vitro experiments can not be compared to oral conditions. It must be the task of internal medicine, neurologists, rhinologists and dermatologists to collect observations since the very first symptoms of chronic mercury poisonings can be expected in these areas. The pharmacologists have in general dismissed the possibilities of chronic mercury poisonings because of amalgam fillings.

Werkenthin, A. Kupferamalgam über Bord, Zahnärztl. Rundschau 1929, p451. Copper amalgam overboard is the absolute requirement from Werkenthin. Rests from copper amalgam fillings must be completely removed before a new silver amalgam filling, which is completely harmless, is placed. Also the neighbouring tooth and antagonists must not have copper amalgam fillings. Silver amalgam does not at all prevent the placement of 22-carat gold rings for crowns or caps. It is, however, necessary to wait 5 days after the placement of amalgam before the ring is placed. Silver amalgam beneath a gold cap can even be considered

recommendable. If the amalgam-alarm from Stock could bring the authorities to prohibit copper amalgam, then we should be grateful.

Witzel, A. Zur Frage der Quecksilbervergiftung durch Zahnfüllungen, Munch. Med. Wochenschr. 1926, 1021 (Author of the previously mentioned book) wrote: Based on own extensive studies the presence of large copper amalgam fillings when the saliva is very acid, might be harmful to health. The gold- or platinum- containing silveramalgam fillings are without objections and constituted completely harmless filling materials. When properly prepared, amalgam fillings of silver-tin-mercury alloy, contain no free mercury. Thus they can not give off free mercury in the mouth. The levels of mercury vapor should be minimal in the oral cavity. The possibilities for mercury poisonings from dental fillings seem today, with the improved amalgams, much less than previously and even then the recognized faulty copper amalgam fillings only rarely led to noticable damage. Anyhow, one should for ever leave copper amalgam and specialize on noble amalgams.

Schoenbeck, F. (Prof. Biesenthal) Die Amalgamgefahr, Zahnarztl Rundschau 1926, 415; Gefahren der Amalgamfüllungen, Zahnarztl. Rundschau 1926, 449; Amalgamfüllungen und Quecksilbervergiftung Deutsch. Monatschr. Zahnheilk. 1926, 435; Die Amalgamfrage, Munchn. Med. Wochenschr. 1927, 1694; Untersuchungen über Quecksilberausscheidungen bei Trägern und Bearbeitern von Amalgamfüllungen Dtsch. Monatschr. Zahnheilk. 1927, 208; Schädlichkeit der Amalgamzahnfüllungen Zahnarztl Mitteil 1928, 390; Zur Amalgamfrage Dtsch Zahnarztl Wschr 1928, 151. The question of poisons can not be simplified since all metals have a certain toxicity. In addition, the preparation and the conditions in the oral cavity will have influence. Experiments have shown that copper amalgam, before and after preparation, at 37 degrees continuously releases mercury vapor. Microscopical examination of copper amalgam in fillings shows clearly free mercury, containing some copper, besides pieces of copper. This is understandable since the solubility of copper in mercury is small.

From these facts one must conclude that pure copper amalgam must disappear since these might be dangerous. However, these hazards can be reduced by addition of 2-3% tin. Then such combined copper-tin amalgams can be used without hesitation. Concerning the noble amalgams, conditions are quite different. The reaction products are Ag_3Sn , Ag_3Hg_4 and mixed crystals of tin and mercury if the proportions during mixing are correctly chosen. One can thus state that such a correctly prepared noble amalgam, after complete hardening, should constitute no risk for the patient. However, this only applies to conditions when the alloy has been manufactured on a scientific basis and the proportions between alloy and mercury is correct; most amalgam fillings, prepared according to practice up to now, have an excess of mercury. Especially the electrical processes which can occur when amalgam fillings come into contact with gold fillings have been observed by Schoenbeck. The amalgam filling will be the less noble electrode with the potential of tin and dissolve and its corrosion potential will partly be carried over to the gold. Mainly tin will dissolve. Even if an immediate danger for mercury poisoning because of corrosion does not exist, one must consider that the amalgam surface is changed because of the dissolution of tin, e.g. it will be enriched in silver and mercury. The resistance against mechanical influences will then be reduced and there is the possibility that mercury-containing pieces are released and taken up by the body. In any case, contact between amalgam and gold alloys should be avoided if the saliva as electrolyte has access to both.

Feiler, R. Ein Beitrag zur Amalgamfrage, Zahnarztl. Rundschau 1927, 797-98. Feiler points out the dangers for the dental personell in addition to that for the patient and that amalgam can not at all be considered an ideal filling material. The use of copper amalgam can not further be trusted because of the reasons Stock has given and which he completely supports. But not only the copper amalgam fillings but also noble (silver) amalgam fillings undergo changes in volume and marginal adaption, despite careful preparation. This should mean a reduced use of amalgam fillings and duty to search for a substitute. Feiler finds that the cast silver filling and a new type of porcelain are good substitutes.

Seifert, K. Zur Streitfrage über Quecksilberabgabe aus Amalgamfüllungen. Zahnarztl. Rundschau 1926, 516. supports Stock's conclusions to some extent because of his own experience. He has concluded, based on observations, that persons with amalgam fillings have extremely little syphilis, that mercury in the fillings must act prophylactically against luetic infections. Thus, a continous uptake of mercury in the body must take place, an uptake which immunises the body against lues without harming the body. The uptake is not of the extent that one has to fear a mercurial poisoning.

Joachimoglu, G, Die Gefährlichkeit des Quecksilberdampfes. Med. Klin 1926, 1275. J. has the opinion that the statements on the hazards of amalgam fillings can not be correct. The removal of amalgam fillings, which Stock and Lewin recommends, is an exaggeration. The mass experience has shown that poisonings do not occur with these compounds. Single cases, where the symptoms disappear after removal of the amalgam fillings, prove nothing since these are contradicted by millions of cases where amalgam fillings, even after 25 years have not led to any symptoms at all. The syndrome, which Stock describes as light mercury poisoning, is difficult to differentiate from neurasthenic symptoms which are so common today. When the symptoms disappear after the removal of a small amalgam filling in such cases, then the causal connection is not at all proven. The post hoc ergo propter hoc is a dangerous line for medicine. Any experienced physician knows that suggestion plays an enormous role in such cases.

Ritter, P. Die Gefährlichkeit des Quecksilberdampfes, Med. klin. 1926, 1279; Gefahren der Amalgamfüllung, Zahnarztl. Rundschau 1926, 415; Die Gefährlichkeit der Amalgamplomben Zahnarztl. Rundschau 1926, 449; Entgegnung auf Stock zur

Amalgamfrage, Zahnärztl. Rundschau 1926, 553; Zur Amalgamfrage, Zahnärztl. Rundschau 1929, 1471; Die Giftigkeit des Kupferamalgams, Med Welt 1930 no.51. writes, that it is known that copper amalgam fillings, when they are lege artis prepared and have sufficient marginal adaption, are completely durable and without any harmful effect for the carrier. It is different when improperly made copper amalgam is used. But after the reports in the literature and practical experience, these side effects, if they appear in rare cases, are without any serious importance. The premise for the durability and harmlessness of any filling is certainly a sufficient mouth care which any dentist must inform his patients about. Stock's fight has ended and it ended with the amalgam filling again back in its old, good place which it has had for one hundred years. Stock has been defeated but not without a hard fight. He should now have the courage to withdraw his opinion in the newspapers; he should add: errare humanum est.

Maschke, A. Experimentalphysiologische Untersuchungen über die Beeinflussung geistiger Leistungen durch Amalgamzahnfüllungen Zahnärztl. Rundschau 1930, 990. Maschke systematically observed patients after placing silver amalgam or gold and porcellain as controls. The fillings were placed by skilled dentists who were very good in technical methods. Improper methods were therefore excluded. Nevertheless, within a rather short time the patients had erethismus and tremor mercurialis but no lymphocytosis could be observed. The symptoms appeared especially during stressful situations. "These symptoms clearly show that also the use of noble amalgams as filling material and when the fillings are properly placed, poisonings are not excluded. In the cases studied by me, the removal and exchange of amalgam for gold was therapeutically positive with increase of the psychical functions which were studied. On myself I could also observe that a violent migraine which I had every tenth day was reduced to a few times each year. It should be evident that people harmed by amalgam really need help."

Borgzinner, U. Die Giftigkeit von Amalgamfüllungen, Munch. Med. Wochenschr. 1927, 1346. The author points out the importance of a mercurial etiology in unclear cases of ulcerative colitis. He noticed this because of a case of ulceration of the colon, positive for mercury in the urine. The patient had some time earlier got four copper amalgam fillings. No other source of mercury was found, despite careful search. "Should not this case alert us to stop using amalgam. If it apparently can cause ulcerative colitis, it should be able to cause many other lighter diseases.

Muller, O. Vorstellung eines Kranken mit abgelaufener Quecksilberintoxikation durch Amalgamplomben Munch. Med. Wochenschr. 1929, 651. reports a case with gastrointestinal symptoms, exhaustion, sweating, pronounced loss of weight and increasing paleness. He had also anemia with a pronounced number of punctured red blood cells which indicated a disease similar to lead poisoning. In his mouth were two large and two small copper amalgam fillings. Two of these were in contact with a gold hook. The fillings were 2.5 and one year old. In feces there was large amounts of mercury. Eight weeks after removal of the fillings most of the symptoms had disappeared. There can be no doubt that large amounts of mercury passed into the body in this case. There was no other contact with mercury. The presence of the copper amalgam and the contact with gold makes it very likely that the source of the mercury was to find in the amalgam fillings.

Wannenmacher, E. (Prof. Zahnärztl. inst. Univ. Tübingen) Die Amalgamfrage, Munch. Med. Wochenschr. 1927, 1694; Ein Beitrag zur Amalgamfrage Dtsch Zahnärztl. Wochenschr. 1928, 152; Schädlichkeit der Amalgamzahnfüllungen Zahnärztl. Mitteil. 1928, 390. W. arrives, after a 3 years study, at the conclusion: The verdict on copper amalgam, with or without tin, cadmium or similar additions is negative. All experimental studies show that mercury is released from these amalgams in quite remarkable amounts. There is also the well founded danger that copper dissolves. In addition the preparation (heating) is especially dangerous to the dentist.

With the silver-tin-amalgams there is also a possibility for mercury release if not special proportions between alloy and mercury are followed. With carefully chosen proportions it is almost impossible that mercury is released from silver-tin- amalgams after hardening. The dentist should have access to an alloy with constant composition and which binds a constant amount of mercury, otherwise it is not possible to avoid a mercury excess. Any amalgam, copper or so called noble amalgam, which shows free mercury after complete hardening, should be rejected since then it is very likely that mercury can be released and there is a possibility that the patient can come to harm. In addition, one must be careful that no amalgam filings are placed close to gold crowns. Then the gold will be tarnished or even destroyed and also in such cases there is a possibility that considerable amounts of mercury can be absorbed by the patient.

At the meeting of the Society for Natur- und Heilkunde, may 1927, H. Fuhner reported on: Chronische Quecksilbervergiftung und Amalgamgefahr. He stated that so far no chronic poisoning has been reported with urine mercury of hundredths of milligrams daily but poisonings have been noted with levels of tenths of milligrams. From silver amalgam there are only rarely levels of that magnitude in the urine and this should more originate from dissolved mercury than from evaporated. It is the task of the dentist to prevent the resorbtion of the amalgam fillings in his patients by persuading them to practice good mouth hygiene and to eat suitable food. Copper amalgam should not be used. Under certain conditions; no contact with gold and other metals and not too large amalgam surfaces, the use of silver amalgam fillings seems to be completely without danger.

Rebel, H. Bericht über das Amalgamreferat des Zentralvereins deutscher Zahnärzte zu Dusseldorf, Deutsch Zahnärztl Wochenschr. 1926, 485. Rebel states: According to the reports from dental institutes, inner medicine, pharmacology and chemistry,

on the current experience and laboratory experiments, also animal experiments, the objections against amalgam as a dental filling material are without foundation. Only in rare cases of hypersensitivity to mercury, something which also occurs against other medicines and certain foods, copper amalgam fillings might be harmful to the organism.

Kruger, R. Gibt es eine chronische Quecksilbervergiftung durch Amalgamzahnfüllungen? Munch. Med. Wochenschr. 1927, 1346; Eine zweckmässige Amalgamfüllung. Dtsch. Monatschr. Zahnheilk. 1927, 266. Kruger considers the copper containing amalgam to be an especially appropriate filling. He emphasizes the good properties of copper amalgams, mainly the good marginal adaptation. The less good properties: easily abraded, the mercury release and the coloring of the tooth can be prevented by the addition of tin and silver. The final amalgam of choice thus consists of mercury and nearly equal parts silver and tin and more or less copper. The main advantage is that these amalgams have a stability which no other amalgams can reach and it has also a noble composition. Also teeth with such fillings have an extremely small incidence of secondary caries at the margins. Gold, in contrast to other metals in the mouth, is not at all a contraindication for the use of amalgam. Also the placement of new gold fillings close to amalgam is possible and completely harmless. A necessity is that no excess mercury is present in the fillings. There are thus no health objections. The fact that macroscopically, also after several years, not the slightest change, not the slightest loss can be seen, indicates that nothing from the fillings has passed into the body. No mercury could be found in any urine sample.

According to Lewinski, E. Ein Todesurteil über das Kupferamalgam? Zahnärztl. Rundschau 1926, 517; Die Amalgamfrage Deutsche Monatschr. Zahnh. 1926, 208., copper amalgam has the following advantages: 1. It is more resistant than noble amalgams. 2. It is very slowly abraded when the biting force is strong. 3. It is strongly antiseptic. To prevent dissolution an addition of 2-3 % tin should be used. 4. It is three to four times cheaper. One must, according to Lewinski, try to escape the mercury psychosis which started after Stock's alarming paper and not let oneself be forced into a corner by more or less amateurish statements.

Finally, jan. 1, 1932, "The Ministry of Health has, in connection with the statements by prof. Stock, taken the initiative for extensive studies on dental fillings. We herewith state: Gold-, silver- and copper-amalgams are completely harmless. The state governments have been informed about these results."

Amalgam Fillings as a Possible Source of Mercurial Poisoning.

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Dental Items Interest 48, 1926, 637

The close relationship which the teeth bear to the general health has been proven in numerous cases and, in consequence, the medical profession is liable to blame infected teeth for many ailments. Some patients have been cured by the removal of offending teeth but doubtless the matter has been carried to the extreme in numerous cases.

And now, news comes from Germany which will send a wave of despair through the dental profession and may also disquiet the public at large.

Professor Alfred Stock Director of the Kaiser Wilhelm Institute of Chemistry in Dahlem, Berlin, believes that amalgam fillings cause a stealthy, chronic form of mercurial poisoning, which manifests itself in enervation, neurasthenia and a weakening of the memory (Stock, A. Zeitschr. angew. Chemie No.15, 1926).

Before going into the details of Stock's report, I wish to say that we must not be hasty in forming our conclusions. The stakes are too large to be lightly cast aside, nor should we blindly accept the verdict of one man in a matter of such vital importance. If amalgam as a filling material would have to be discarded, we can safely say that the mass of the people would not be able to have any permanent dental work done because gold inlays are still a luxury. On the other hand, if Stock's contention should prove to be true, then amalgam as a filling material must go, or the technique must be so modified as to make it safe.

Prof. Stock's Experiments: Professor Stock, a noted chemist has for many years, in the course of his experiments, been in constant contact with mercury. During this time, he suffered from various symptoms, which increased as time went on, until he despaired of continuing his work. His memory, which was previously excellent, seemed to become weak; lack of energy set in as well as an inability to solve mathematical problems. In 1923, the electrically driven ventilation plant was stopped on account of the expense of running the motor. From this time on, the symptoms appeared in aggravated form and finally mercurial poisoning was diagnosed, not only in Stock but in all who worked in this laboratory.

The air in these rooms was analyzed and found to contain only a thousandth to a hundredth of a milligram of mercury per cubic meter. Air having 12 milligrams of mercury vapor is considered saturated; we therefore see that the quantity found in the analysis of the air in Stock's laboratory was infinitesimal. As man consumes approximately one-half a cubic meter of air per hour, we note that the amount of mercury vapor inhaled by Stock and his assistants was minute. And yet this minute quantity did cause a slow poisoning, even though it was so difficult to diagnose.

And here the possibility appealed to Stock that dental amalgams may likewise be a source of mercurial poisoning. He, therefore, experimented with both copper and silver amalgam fillings and found that, if extracted teeth containing such fillings are heated to about 30° C. (body temperature is 37° C.) considerable fumes of mercury are given off. It is to be noted that this ensued not only from new and freshly mixed amalgam, but also from old fillings.

These are the experiments which have alarmed the German public, and it is imperative that an able chemist should corroborate these findings.

After the exact amount of mercury vapor, given off at body temperature has been defined for a specified mass of amalgam, a toxicologist must decide whether such a quantity can affect the health of an individual. It is also of vital importance to discover whether the formation of mercury vapor continues for years after the placing of the filling, for if this is the case, we must take all the amalgams in the mouth of the patient into account.

One specific case is cited by Stock: A colleague, suffering from continued headaches, had a large amalgam filling, around which the gingiva was considerably inflamed. Some time after this filling was removed, the local and general symptoms disappeared.

In answer to this case, I say decidedly and emphatically that we must not jump to conclusions, particularly not with such scant proof! I will wager that every dental practitioner, who has a pair of eyes and uses them, has noted marked gingivitis around many a large amalgam filling. But the cause of this inflammation of the gingiva is not the amalgam nor the mercury; it is the result of a lump of metal overhanging the margin of the cavity, because when this is carefully trimmed away and smoothed, the irritation subsides.

The dental profession of Germany, headed by Professors Schoenbeck, Schroeder and Ritter do not accept Stock's contention. They have not, in consequence, modified their use of amalgam.

Even though this matter may pass off with a simple scare, it will serve to show the importance of care in the use of mercury by the chemists and physicists. It will also sound a note of warning to dental practitioners to thoroughly condense amalgam fillings, and to remove every trace of excess mercury. This can best be done by the use of annealed gold pellets for they then take up the mercury more readily.

Whatever the future may bring, we must await the results of the above described chemical tests. In the meantime let us keep both feet on the ground and not allow the pendulum of fadism to swing from one extreme to the other.

Pelham, N. Y., July 15, 1926.

THE EFFECTS OF MERCURY VAPOR ON THE UPPER AIRWAYS

(Die Wirkung von Quecksilberdampf auf die oberen Luftwege)

Alfred Stock Chemischen Institut der Technischen Hochschule, Karlsruhe Naturwissenschaften 23, 1935, 453-456

The chronic mercury poisoning which had almost been forgotten, is again considered after I, nearly ten years ago, told about the bad experiences I and my collaborators had and which I emphatically described (Comp. Die Gefährlichkeit des Quecksilbers und der Amalgam-Zahnfüllungen, Z. angew. Chem. 41, 1928, 633; Med. Klin. no. 29/30, 1928; Zahnärztl. Mitt. 19, 1928, 370, 377, 390). In many places the hazards of the devious, volatile, metallic poison are still underestimated. The poison does not only threaten all persons who occupationally come into contact with it (physicists, chemists, physicians, dentists, workers in mercury-using factories, in hat factories etc), but also many other persons (amalgam dental fillings, broken thermometers, old mirrors etc). Because of my publications, hundreds of cases of chronic mercury poisoning have become known to me, most of them because of occupation; a considerable number, however, also because of amalgam dental fillings.

Together with a number of collaborators (F. Cucuel, F. Gerstner, R. Heller, H. Kohle, A. Kreyer, H. Lux, E. Pohland, W. Zimmermann), I have tried to clarify a number of questions connected with mercury poisoning: improvement of the analytical determination of very small amounts of mercury, analysis of mercury in organic material, the distribution of traces of mercury in nature, the oxidation of mercury by air, mercury levels in human excretions normally and during poisoning, the distribution of absorbed mercury in the body etc.

Mercury which enters the body through the respiratory tract is extremely more unpleasant than a several times larger amount swallowed into the gastrointestinal tract. Primarily this is because mercury more easily and rapidly enters the blood and lymph circulation; to a large extent, however, because of the circumstances which will be described in this communication. In real life, chronic mercury poisonings are nearly always caused by inhaled mercury vapor.

As is generally known (comp. E.W. Baader & E. Holstein, Das Quecksilber usw. Berlin: R. Schoetz 1933) the symptoms of chronic mercury poisoning, apart from the nervous-psychic disturbances, appear at the places of excretion of the metal; in the gastrointestinal tract (necrosis of mucosa, diarrhea, bleedings) and in the kidneys (inflammations up to deadly damage). The central nervous system will also be more or less involved. An accumulation of mercury occurs mainly in the kidneys. Apparently, small, continuous doses of mercury (The presence in the body of mercury in milligram amounts, absorbed as vapor for a long time, disturbs already noticeably the human organism. Mercury in this form belongs to the most potent of poisons.) act in similar ways as today is known about the actions of lead (According to F. Blumenthal & K. Jaffe: Eczema and Idiosyncrasy, Berlin: S. Karger 1933): "The action of lead is a continuous migration of lead through the body and the total amount excreted is equal to that taken in. The organism itself remains almost free of lead. The chronic lead poisoning is thus not the result of a chemical accumulation, but a dynamic accumulation. Continuously repeated insults finally, after a symptom-free period, produce the picture of a chronic poisoning: stomach pains, arthralgia, paralysis and encephalopathies. These symptoms follow an irregular, remitting course, appearing also during long periods without contact with lead."

The effects of mercury on the sites of entrance into the body, the nose and related areas, have been too little discussed. Already Fleischmann (Dtsch. Med. Wschr. 1928, no 5) emphasized in his report from the "mercury study" of the Berlin Charité, started by Kraus, that the patients almost always complained about symptoms from the upper airways, about catarrhs of the olfactory mucosa etc. and I have described this effect of mercury in my first publication of 1926. However, the work by Baader & Holstein reports only little on this subject (p 122): "In addition to a tendency for bleeding noses (enlargement of the nasal veins), wet or dry chronic catarrhs of the nose (Bruggemann), which exposed persons often complain about, no specific nasal disease has been noticed." The mentioned work by Bruggemann (Z. Laryngol. 15, 1926, 107) has the title: "A rare cause of chronic nasal irritation (insidious mercury poisoning)." She describes a case of occupational mercury poisoning and arrives at the conclusion: "for us rhinologists, it is especially important that, during an insidious mercury poisoning, besides general nervous symptoms, the nose and the upper airways will be affected by catarrhs and chronic irritation, long before the typical mouth affections appear... In all cases where there is a possibility for inhalation of mercury vapor, one should think of an insidious mercury poisoning when one finds nasal irritation with an unclear etiology."

This is quite correct. However, such cases are not at all rare. It is the intention with this short report to notify the readers of Naturwissenschaften, including many persons who come into contact with mercury and also many physicians, about this affection. A more extensive report will later be published elsewhere.

An effect on the nasal mucosa can be expected. It is certainly the first place the inhaled metal has opportunity to be oxidized and transformed into soluble form under the influence of water vapor, air and heat. This primarily happens where the inhaled air stream contacts the mucosa; the ethmoid cells and the nasopharynx. In these places bacterial infections often start and dust and smoke deposits form, very likely enhanced by the vortex formation. The mercury which is not trapped here, will then be almost completely absorbed in the lungs with their enormous surface area, something we have previously determined.

The binding of relatively large amounts of mercury in the upper airways could be demonstrated in animal experiments (we acknowledge the generous help from prof. E.v.Gierke. The analyses were made by A. Kreyer). Two rabbits were placed in weakly mercury-containing air (vessel with mercury in the cage). In the nose and upper nasal mucosa we found 6.5 ug and 6.1 ug mercury in the two rabbits, whereas the mercury levels in the mercury-accumulating kidneys were not more than 19.3 and 32.6 ug, a proof that the total amount of absorbed mercury was rather small.

That mercury affects the mucosa of the nose seems also quite understandable considering the sensitivity of other mucosal tissues (e.g. the mouth and the intestines) towards the metal.

In the first report on my own poisoning (Z. angew. Chem. 39, 1926, 461) I wrote: "Soon also the upper airways were affected; in the beginning light and occasional nasal catarrh, then permanently tight nose, later almost continuous catarrhs of the olfactory mucosa with often bloody mucus production and crust formation, violent throat inflammations and pains in my ears connected with impaired hearing and smell." These observations have then been confirmed by many other cases of poisoning. In addition, not rarely chronic problems appeared in connection with the immediate mercury effects, especially sinusitis (and in the mouth the teeth and jaw bones were affected). These problems remain after the poisoning has disappeared and require special treatments.

The nasal problems are nearly always accompanied by "nervous- psychic" disturbances: Pressure and headache between the eyes, tiredness, depression, lack of interest in intellectual work, impaired memory etc. Connections between affections of the nose and such impairments of general well-being are generally known from e.g. when one has a stuffed nose. That the characteristic "nervous-psychic" disturbances which are called erethismus mercurialis, at least during the first stages of mercury vapor poisoning, are connected with this and not with a more general disturbance of the nervous system (which undoubtedly appear later during the poisoning), is demonstrated by several different observations. If the irritated nasal mucosa is anaesthetized with cocain, rinsed with physiological saline or even exposed to fresh, cool air, then the symptoms diminish or disappear. The effect of cocain is not a general cocain effect since improvements only result if certain places in the upper nose are treated. Most clearly the role of the nose is shown by the facts described below.

The chronic mercury vapor poisoning leads often to an allergic hypersensitivity towards traces of mercury vapor. Baader and Holstein state correctly: "The hypersensitivity is often the only consequence of a mercury poisoning." Concerning myself, this is exactly what happened, which several years of observations have shown. Numerous reports, obtained from colleagues, physicians, dentists etc, show that this also applies to many others. I will describe my own case more in detail since I know that best and since it apparently is typical of many other cases.

I presume that I was not especially mercury sensitive by Nature. First after a long -and I must today say - very thoughtless contact with mercury, the chronic poisoning developed. In the ten years which have elapsed since the poisoning was recognized and after which I have been very careful with the poisonous metal, all of it must have disappeared from the body. The excretions contain since several years not more mercury than normal levels (comp. A. Stock & F. Cucuel, Z. angew. Chem. 47, 1934, 641). The allergic mercury sensitivity has, however, remained to such a high degree that the staying in laboratories in which the air contains just a few micrograms per cubic meter (as unfortunately is the case with many laboratories at the Karlsruhe Chemische Inst.), already after half an hour causes symptoms which increase with prolonged exposure. The levels will not affect other persons in such short times. The symptoms will follow the course described here: light dizziness, "irritation", impaired thinking, light pressure between my eyes, tiredness, headache in the forehead, a feeling of tight nose (mucosal swelling without mucus production), impaired hearing and light ringing in my ears because of blocked eustachian tubes, a "furry" feeling of dryness in the upper nose and throat, the formation of thick, white secretion. With longer or repeated staying in such rooms there will be slightly bloody secretions, some blood clots and crusts (In the area of the ethmoid cells, not the nasal septum. Very characteristic for mercury effects! Also when I have severe, ordinary catarrhs, these manifestations do not appear.), intense headache with vertigo, finally intense catarrhs which might give opportunity for subsequent infections which also will affect the throat. In the first stages, the symptoms disappear quickly when mercury exposure ceases, especially if I stay in fresh air. At later stages the complete disappearance will take several days up to a few weeks.

That the symptoms really are caused by mercury follows from the experiment with sublimate solution which will be described below. Other irritating vapors have not been present in the rooms at all. No words of explanation are needed to understand how disturbing such an idiosyncrasy is for anyone who can not avoid visiting such mercury-containing rooms. One can not enough call upon care in the handling of mercury. The danger of acquiring a lasting idiosyncrasy is a new reason for a warning. Once acquired it will not go away again. Also after a long holiday it remains unchanged.

In addition, in my case the sensibilisation of the nasal mucosa because of mercury is not restricted to only mercury but also extends to other chemicals (e.g. sulfur dioxide and chlorine) and tobacco smoke (Such extensions of allergic manifestations are not unusual. Comp. the mentioned work by Blumenthal & Jaffe'). In the latter mercury might also have a role. Cigarettes and cigars contain various amounts of mercury (A. Kreyer found up to 0.4 ug mercury in each cigarette), which during smoking is transferred to the air (not to the smokers mouth as we determined in special experiments).

It seems evident that this can not be a general poisoning and a profound disturbance of the nervous system when we have such rapid effects but must be a local reaction of the metal at the site of absorption. Then the previous conclusion is further supported: that the first "nervous-psychic" symptoms which accompany chronic mercury poisoning have their origin in the upper airways. The following "experimentum crucis" appears to give a definite proof: I tested the effects of an extremely dilute mercury II-chloride solution on my nasal mucosa (Also the normal nose is generally sensitive to sublimate. A.J Kunkel, Handbuch der Toxikologie (Jena 1901), p. 145: "The mucosa is extremely sensitive towards mercury solutions: still 1:50 000 is corrosive when the nasal mucosa is rinsed with it and 1:100 000 (i.e. 10 ug/ml) will still be unpleasant.")

One day, when I felt healthy, both objectively and subjectively and when I was in no other way in contact with mercury, I sprayed, with a fine vaporizer, 3 ml of a 0.6% saline solution containing 0.05 ug mercury as sublimate, into the upper nose. Most of this solution certainly again came out. The amount of mercury which the mucosa really absorbed might be estimated to 1/100 ug (1/100 000 000 g). However, the effect was not to be mistaken about. After about two hours I had weak pressure between my eyes, after another two hours the tight, furry-dry nose and after another few hours light headache. Blowing the nose demonstrated a thick, opaque-white slime which apparently caused the furry feeling. The white, thick secretion lasted, accompanied by an uncomfortable naso-pharyngeal catarrh and dizziness, about 24 hours and then disappeared rather quickly and completely with all other symptoms. The whole series of events was in all details similar to the symptoms which a short stay in weakly mercury- containing air precipitated.

Then there should be no doubts about the connections between the irritation of the nasal mucosa and the first "nervous-psychic" symptoms which mercury causes. The extent of such manifestations should, in the individual case, be determined by the anatomy of the nose and the properties of the nasal mucosa. In addition, the nasal affections are similar when the mercury poisoning is caused by amalgam dental fillings. This supports my previously stated presumption that, when amalgam fillings cause health disturbances, it is the mercury vapor which enters the airways which has a major role, apparently a more important one than the much larger amounts of mercury which passes from the amalgam into the gastrointestinal tract.

Various observations indicate that the primary nervous-psychic symptoms of a chronic mercury poisoning is caused by traces of mercury which passes from the nose into nearby parts of the brain. We will report elsewhere on such studies.

THE MERCURY CONTENT OF HUMAN EXCRETIONS AND HUMAN BLOOD

(Der Quecksilbergehalt der menschlichen Ausscheidungen und des menschlichen Blutes) A. Stock & F. Cucuel Zeitschr. angew. Chem. 47, 1934, 641-647

Mercury levels of human excretions, in feces and urine, are of importance for the diagnosis of chronic mercury poisonings (In exhaled air there is hardly any mercury even after considerable exposure; whether mercury evaporates through the skin has not yet been studied; it is not likely).

Today we know that chronic mercury poisoning is more common than was presumed ten years ago (A. Stock, this Journal 41, 1928, 633; Med Klin no 29/30 1928; Compare also A. Zangger: Arch Gewerbepathol. Gewerbehyg 1, 1930 539)

Its first symptoms, almost only nervous-psychic, e.g. transient depressions, headaches, impaired memory, are so little specific that the clinical diagnosis often is difficult. It will be more clear when certain later symptoms appear: easily bleeding gingiva, oral inflammations, chronic catarrhs, sometimes diarrhea, kidney inflammation etc. The patients will often be treated by neurologists, laryngologists, internists etc, and mercury will not be considered the cause.

Opportunity to absorb mercury and for chronic mercury poisonings are frequent. Because of its specific properties (permanence, liquid form, high density, electrical conductivity, formation of plastic amalgams) the toxic metal finds increasing applications in industry, science and also as a dental filling material (Compare E.W. Baader & E. Holstein: Mercury, its production, technical use and toxic properties with extensive documentation of occupational mercury poisoning, including therapy and prophylaxis. Berlin. R. Schoetz Publ 1933. This excellent work deals with several of the questions which are discussed here. Unfortunately it was not possible to include the new research which improved methods of mercury determination have made possible).

The liquid properties and most importantly the considerable volatility already at ordinary temperatures, enhances its dissipation and its unnoticed entry into the human body. Mercury uptake and thus the possibility for chronic mercury poisonings is present e.g. for all persons who work in mercury-using industries; thermometer-, mercury rectifier-, mercury lamp-, amalgam-, felt hat-manufacture etc. and in several other occupations: physicists, chemists, medical doctors (blood pressure measurement) etc, but also many persons who occupationally have nothing to do with mercury (for instance because of amalgam fillings, treatments with mercury-drugs, broken thermometers and similar causes). As not previously recognized sources of mercury, felt hats must be noted. During manufacture, a tanning solution of mercury and nitric acid is used. We could measure that felt hats, also after long-term use, released noticeable amounts of mercury to the air. A hat which had been in use for a year was placed in a glass jar of 15 l for two hours at room temperature. In 20 l of air which was led through the jar (10 l/h) 0.5 ug was found. With four new hats from various manufacturers: 0.5 ug, 0.6 ug, 1.3 ug and 2.3 ug mercury. The latter hat delivered at 35 °C not less than 60 ug mercury when we repeated the experiment. Since the hats will reach similar and even higher temperatures in summer and since it is known that our body also absorbs mercury through the skin (mercury ointments!), many persons must absorb mercury in this way. It can not be excluded that also the mercury which is absorbed through the skin can have harmful effects. If this is correct, it should be a positive change, not only for the workers in the felt hat industry (information about the chronic mercury poisonings in this industry can be found in the book by Baader & Holstein) but also for the carriers of the hats if the mercury-tanning disappeared from the manufacture.

If mercury poisoning is suspected, the doctor will often ask: is there mercury in the excretions and do the levels suggest a mercury poisoning? Unfortunately it is not that simple that mercury poisoned persons excrete mercury whereas urine and feces of healthy persons are free of mercury. All humans take up some mercury with food and excrete it regularly again. As we have reported earlier (Naturw.sch. 22, 1934, 390), there are traces of mercury at an average level of 10^{-8} , i.e. 1/100 mg per kilogram, in every inorganic and organic natural substance, also in the ground, in water and in all food. According to our measurements, a human with ordinary eating habits will on the average ingest - with large variations - 5 ug mercury with food daily (thus the observations by P. Borinski a few years ago have been experimentally verified; Klin. Wochenschr. 10, 1931, 149; comments on this A. Stock Ibid 10, 1931, 454).

Reliable studies on such questions, which require the analytical measurements of very small amounts of mercury down to 1 ug and less, have only been possible after the development of new analytical methods (Determination of these small amounts of mercury in organic material: A. Stock, F. Cucuel & H. Kohle, this journal 46, 1933, 187. All analyses in the present study have been performed according to the methods described there). The older analyses can only be considered reliable to a limited extent (this is the case for our own measurements as well as those of other researchers, e.g. Borinski's, who often found no mercury in the excretions although we now know it is always present).

The analyses can frequently have contained too much mercury because of the previously overlooked mercury content of most reagents; more often the mercury levels must have been far too low since the treatments of organic material is more difficult than presumed.

We have therefore used the new analytical methods to examine the often disputed question of the mercury content of the human excretions again. Three groups of persons have therefore been examined:

- A. "Mercury-free" no exposure to mercury except with food is apparent. Especially they have no amalgam fillings.
- B. "Amalgam carriers" with amalgam dental fillings but without other apparent contact with mercury
- C. "Mercury workers" who also come into contact with mercury in other ways.

Since mercury excretion often varies from day to day, we have analysed feces (F) and urine (U) from the test persons for several consecutive days if possible. The recorded amounts of mercury refer to the amount of daily excretion and the weight or volume is recorded. Within brackets we have also noted the amounts of mercury for 100 g feces or 1000 ml urine to obtain an evaluation of the concentrations.

A. MERCURY-FREE

It is difficult to find such persons. One can hardly believe how seldom the absence of amalgam fillings (also persons who previously have had amalgam fillings and who might retain mercury in the body are not suitable) coincides with an occupation which completely excludes any contact with mercury. For instance, most students at our university (Techn. Hochschule, Karlsruhe) were not suitable because of the mercury levels in the air of the laboratories and the workshops; especially the urine from amalgam-free students contained clearly a little (a few micrograms/1000 ml) more mercury than from really mercury-free persons. It is actually only possible to talk about really "mercury-free" with reservations. It is e.g. always possible that the persons live or work in rooms where once a mercury thermometer has been broken. This can have the consequence that the air in the room contains mercury for years which can elevate the mercury levels of the excretions.

We report of three cases which, according to information we could obtain, could be considered really mercury-free.

I. D. Six year old boy.

Day	Feces g	ug Hg (ug Hg/100g)	Urine ml	ug Hg (ug Hg/l)
1	85	0.45 (0.5)	1000	0.3 (0.3)
2	133	0.4 (0.3)	500	0.6 (1.2)
3	115	1.75 (1.5)	1000	1.7 (1.7)
4	80	8 (10)	1000	0.7 (0.7)

II. O. 55 year old worker in a soap factory

1	245	2.3 (0.9)	1000	0.3 (0.3)
2	80	0.4 (0.3)	765	0.2 (0.3)
3	183	3.5 (1.9)	1050	1.1 (1.0)
4	260	6.5 (2.5)	1060	0.4 (0.4)

III. S. 22 year old woman, no occupation

1	300	4 (1.3)	860	0.6 (0.7)
2	102	1.4 (1.4)	700	0.7 (1)
3	180	1 (0.6)	680	0.5 (0.7)
4	195	12.5 (6.4)	830	0.7 (0.8)
5	102	1.4 (1.4)	945	0.7 (0.8)
6	200	6 (3)	850	0.4 (0.5)

To obtain more material we collected urine from several persons at various places and measured the average mercury level. The donors had no amalgam fillings and, according to what we could find out by asking, not anything else to do with mercury. The urine mercury level from 19 patients, collected at a doctor's office was 1.1 ug/1000 ml, a little more than the mean of the measurements above. Also here there is a possibility that one or more of these patients had absorbed mercury from other sources and that the mean thereby was elevated. The drawbacks of these average measurements, lacking a careful evaluation of each case, we learned from the following experience. A collection of 40, not amalgam, urine samples from a hospital yielded 390 ug/1000 ml! Investigations showed that the collection vessels had been disinfected with sublimate solution and that 1/3 mg of mercury had come into the sample.

Since we, in this study, will examine lowest levels of mercury present in human excretions, the carefully controlled single cases are the most valuable.

The three analyses above are in many ways informative: The mercury content of the feces varies from day to day within a rather wide range, related to food. Our analyses of seven dinners at the Karlsruhe student restaurant showed mercury levels between 0.25

and 3.3 ug, mean 1.6 ug (Naturw.sch. 22, 1934, 392). Especially some food, primarily fish, was quite mercury rich. Also the method of food preparation will affect the amount of mercury which will be in the final meal.

According to experiments described in section D, most of the mercury which has been introduced into the gastrointestinal tract leaves the body through the intestines without being absorbed into the blood circulation. The mean of 14 measurements of feces contained each day 3.5 ug (2.3 ug/100g).

The mercury content of the urine is on the average considerably smaller and less variable than that of the feces. The mean of 14 analyses was 0.65 ug/day or 0.7 ug/1000 ml. Also many other single measurements yielded values between 0.5 and 1 ug in the daily volume of urine from amalgam-free persons.

The mean daily excretion of mercury in mercury-free persons is thus 4 to 5 ug, i.e. the same amount as that taken in with food. An accumulation of mercury in the body does not take place; this is also apparent from the fact that there is no noteworthy difference between younger (I) and older (II) persons and is also shown by analyses of autopsy material. This will be reported elsewhere. A direct relationship between mercury levels in feces and in urine was not demonstrated.

B. AMALGAM CARRIERS

In this group the amount of mercury which will be released in a single case will be closely dependent on the number, surface area, condition and age of the amalgam fillings. Perhaps also individual variation in the properties of the saliva will have influence. Average values have therefore little value in this context. We report here three characteristic cases:

IV. V. 22 year old student of construction technology, no occupational exposure to mercury. Several carefully prepared silver amalgam fillings of faultless, polished and silver-white appearance placed by his first dentist (the most recent filling one year earlier. No signs of mercury poisoning.

Day	Feces g	ug Hg	(ug Hg/100g)	Urine ml	ug Hg	(ug Hg/1000 ml)
1	162	8	(5)	750	1.8	(2.4)
2	190	35	(18)	835	0.5	(0.6)
3	82	8.2	(10)	825	2.7	(3.3)
4	165	16	(10)	550	2.4	(4.4)
5	177	25	(14)	700	4.2	(6)

V. H. 33 year old upholsterer. Not exposed to mercury. Several older amalgam fillings. No symptoms.

1	229	21	(9)	720	2.8	(3.9)
2	160	9.5	(6)	940	0.4	(0.5)
3	115	14	(12)	1050	0.5	(0.5)
4	150	10	(7)	950	1.0	(1.1)

VI. S. 22 year old student of chemistry. Many amalgam fillings, several of less good appearance. According to clinical examination a chronic mercury poisoning was likely. No normal kidney function; notably small amounts of urine.

1	205	29	(14)	410	1	(2.4)
2	52	16.5	(32)	260	1.5	(5.8)
3	105	36.5	(35)	450	2.5	(5.6)
4	115	50	(43)	250	1.5	(6)

If this group is compared to the mercury-free group the following differences appear: The mercury levels in the feces are much higher, here on the average 21 ug daily or 17 ug/100g compared to 3.5 ug or 2.3 ug/100g. Also in urine some more mercury was excreted with large variations. In extreme cases also the mercury levels of the urine will be much higher:

VII. Older man who, in addition to many amalgam fillings, had a gold crown in his mouth (something dentistry considers not allowed because of the possible galvanic processes but which the dentists often ignore in practice).

11.2 ug Hg in 780 ml urine (14.4 ug/1000ml). He had suffered from stomatitis for years and had also other symptoms which indicated a mercury poisoning.

VIII. Sm. Chemistry student. 42(!) carefully placed, mostly small amalgam fillings. We will describe this case more in detail since it was investigated carefully, both analytically by us and clinically - the father of the student is himself an MD. The student had for several years suffered from troubles which were, lacking a better explanation, explained by a latent tuberculosis and which finally increased so much that he had to abandon his studies. We found in his urine 1/ in 500 ml 19.5 ug Hg; 2/ in 400 ml 13 ug Hg (mean 30 ug/1000ml). This finding suggested a chronic mercury poisoning. The symptoms were actually nearly all present. The student had all the amalgam fillings exchanged for gold fillings. Also a granuloma at the root of a filled tooth was treated. After a few

weeks he had completely recovered, was full of energy and eager to go back to work. Three months after amalgam removal the mercury level in urine was still 20 ug/1000 ml. 1.5 months later we analyzed the urine on five consecutive days.

Day 1.	urine 490 ml:	5 ug Hg	(10.2 ug/l)
2.	895	10.8	(11.1)
3.	690	9	(13)
4.	615	6	(9.8)
5.	785	8.7	(11.2)

The mercury level had thus further diminished. We took the opportunity to study if the mercury excretion could be enhanced by diuretics (three times daily 1.5 g Diuretin). Such an effect could not be demonstrated.

Day 1.	610 ml:	7.9 ug Hg	(13 ug/l)
2.	640	7.6	(11.9)
3.	560	6.8	(12.2)
4.	1005	5	(5)
5.	715	5.7	(8)

It is remarkable that the mercury level of his blood hardly changed (comp. sect E no XX). It was before removal of the fillings 5.4 ug/1000g and 3 months after removal 4.2 ug/1000g, corresponding to about the normal level. The sustained, only slowly reduced mercury excretion in urine, can apparently be explained by the release of mercury which has accumulated in the kidneys.

There is no doubt that the excess of mercury excreted, by the amalgam carriers, originated from the fillings. In some places it is still disputed that amalgam releases mercury (Here we primarily consider silver (noble) amalgam. Copper amalgam has hardly any defendant. In aged copper amalgam fillings one can often see mercury drops with the naked eye). Therefore no special proof is really needed. It is generally known that also the best fillings in time are abraded, i.e. that material is lost, also mercury (which constitutes 50 % or more of their contents). The corrosion of the silver-tin-mercury alloys to which the so called noble-amalgams for dental fillings belong, have recently been the subject of a careful scientific study by N. Brecht-Bergen under conditions similar to those in the mouth (Z. Elektrochem. angew. physik. Chemie 39, 1933, 927. Dissertation Techn. Hochschule, Karlsruhe 1933).

During this study it was found that first tin dissolves, with the result that the surface will be corroded. Further it was shown that the mercury in these amalgams have a certain vapor pressure which is 10-15 % of that over pure mercury.

Our above results are a new clear proof that also the best amalgam fillings release mercury. According to our results, the main part of the mercury released from amalgam will be excreted through the intestines, certainly partly in the form of finely divided, unchanged amalgam fragments. It is possible, that when amalgam fillings cause a poisoning, it is the mercury which is released as vapor and which enters the lungs, which causes the damage. That the mercury which enters the body through the respiratory organs is much more poisonous than that which comes into the stomach, is proved by animal experiments on which we will report later. When these presumed conditions are present, it could explain why amalgam fillings in some cases cause damage and in others not. The amount of mercury which comes into the lungs must be quite dependent on conditions in the specific case, above all the position of the fillings in relation to the flow of inhaled air. The differences can hardly be explained by different sensitivity to mercury since it is not mercury sensitivity but mercury insensitivity which is the exception, something many publications report and which is also shown by the observations one of us made on himself and his collaborators (comp. e.g. the work by Baader & Holstein or the studies by the Badener prof. of occupational medicine E. Holzmann, this journal 42, 1929, 999 (transl. note: abstract of a paper by Holtzmann, Zentralbl. Gewerbehyg. Unfallverhüt 16, 1929, heft 1))

OCCUPATIONALLY EXPOSED

In the excretions of persons who are exposed to mercury in an occupational setting, the mercury levels are often much higher than in the groups we have described so far. There are many studies in the literature and we again refer to the book by Baader & Holstein and to the analyses which S.D. Rieselman made on workers at the mercury extraction plant at Nikitowka in the Donez area (Arch. Gewerbehyg. 1, 1930, 508). He found between 60 and 2900 ug Hg/1000 ml in 22 urine measurements, an average of 786 ug/1000 ml and in 14 measurements of feces 30 to 4800 ug in each portion. Also he concluded: "Only some individuals show a biological resistance to mercury poisoning."

We have studied two glass blowers who often make mercury manometers. The air in the workshops contained mercury.

IX. L. 27 years old. Glass blower for 6 years. An analysis of the air in the room gave 37 ug/m³

Day	Feces g	ug Hg	(ug Hg/100g)	Urine ml	ug Hg	(ug Hg/1000 ml)
1	126	43	(34)	1350	21.5	(16)
2	185	18.5	(10)	1155	28	(24)
3	287	35	(12)	1100	27.5	(25)
4	120	34	(28)	1020	76	(75)

5	228	2.5	(1.1)	1120	25	(22)
6	70	9	(13)	910	28	(30)

X. J. 48 years old. Glass blower for 34 years. Several symptoms indicating mercury poisoning: headaches, restlessness, insomnia. In the workshop there was 50-120 ug Hg/m³. Not even these relatively high levels are even a hundredth of what mercury- saturated air can contain.

Day	Feces g	ug Hg	(ug Hg/100g)	Urine ml	ug Hg	(ug Hg/1000 ml)
1	163	154	(94)	645	34	(52)
2	23	13	(57)	850	42	(49)
3	115	118	(103)	1245	50	(40)
4	76	235	(310)	1085	50	(46)
5	81	44	(54)	465	40	(86)

We also measured the mercury level of his blood and found 65 ug/1000g, a level far above normal (comp. sect E). Because of the continuous exposure to the mercury containing air, his whole body was impregnated with mercury. Even so, the absolute amount of mercury in the body is even in this case extremely small: only about $6 \cdot 10^{-8}$ of the body weight, i.e. about 5 mg in the whole body. Then we have assumed that the mercury concentration in the whole body was the same as that of blood (which is hardly correct; e.g. in the kidneys it should be far higher.)

Mercury affected this manual worker less in his work than much smaller amounts of mercury affect people who have intellectual work. Maybe also Bacchus protects the glassblowers, with their understandable thirst, against the insidious Mercurius.

After the workshop was cleaned from mercury and rebuilt for mercury work (floor without joints, strong ventilation) the mercury level only reached a few ug/m³ (which could originate from the gas heating), the man's problems slowly diminished. After a few weeks we, however, still found 200 ug/1000 ml in urine but only 6.3 ug/1000 g in blood, about the normal level and a new proof that the kidneys accumulate mercury.

As we have described above, the intellectual performance is affected at far lower levels of mercury. The first symptoms: pressure around the head, lack of interest in work, difficulties to think, impaired memory, will naturally affect the intellectual worker more than the manual one. We could study two new cases where chemists, because of work in mercury-contaminated rooms, had acquired light but evident mercury poisonings.

XI. Dr.B. In the laboratory air 40 ug/m³. In urine 13 ug/1000 ml.

XII. Dr.Br. In the laboratory air 35 ug/m³. In urine 11 ug/1000 ml.

An additional similar case:

XIII. Mrs P. slept in a room in which some years earlier mercury had been spilled. Clear signs of chronic mercury poisoning. In urine 17 ug/1000 ml.

Such mercury levels thus indicate poisonings.

D. Experiments with excretion of orally administered small amounts of mercury.

The observation that mercury excretion often occurs irregularly and intermittently led to these experiments. We gave each one of the mercury-free persons we used in section A 200 ug Hg in the form of a HgCl₂ solution and measured how the excretion took place. The results of the single experiments differed somewhat; the human body is certainly no chemical retort.

a/ XIV. S. (comp. III)

Day	Feces g	ug Hg	(ug Hg/100g)	Urine ml	ug Hg	(ug Hg/1000 ml)
1	244	4.6	(1.9)	1150	1.3	(1.1)
2	34	4.2	(12)	730	21	(28)
3	204	45	(22)	915	0.8	(0.9)
4	45	33	(73)	880	53	(60)

This value corresponded to what we found in III. In the morning of day 2 we gave 200 ug Hg as HgCl₂ solution (1 ml).

5	134	32	(24)	1440	2.2	(1.5)
6	no feces			820	4.6	(5.6)
7	56	9	(16)	1000	18	(18)
8	78	5	(6.4)	880	2	(2.2)
9	200	2.5	(1.2)	835	1.5	(1.8)

The mercury level in urine and feces had again reduced to normal levels. The 200 ug of mercury, administered as sublimate, had been excreted from the body almost completely. We recovered, after subtraction of the normal amount of mercury (5 ug daily), 190 to 195 ug. Of this a little more than half, 105-110 ug, was excreted with the feces in a steadily diminishing amount. The rest was excreted in urine in a remarkably irregular fashion: On the first day a rather large portion, on the second the level reduced to the normal level, on the third almost a quarter of the total amount of administered mercury appeared, on the fourth again almost normal, on the following days again increasing and then finally back to the original level.

Two other experiments followed a similar course only the mercury levels in urine were smaller. They varied, however, again considerably from day to day, even fell below the original value which for unknown reasons were somewhat higher than in the experiments III and IV one year earlier. This variation can only be explained by an inhibition of kidney function which affected the mercury excretion. We describe the values from a fourth experiment where we, instead of measuring 24 h urine, collected 12 h samples:

a/

Day	Feces g	ug Hg	(ug Hg/100g)	Urine ml	ug Hg	(ug Hg/1000 ml)
1	145	2.3	(1.6)	920	3.7	(4.0)
On the morning of day 2 we gave 200 ug Hg						
2	197	5.9	(3)	185	0.6	(3.2)
				330	0.52	(1.6)
3	25	16.5	(66)	470	1.55	(3.3)
				350	1.35	(3.9)
4	160	90	(56)	700	1.25	(1.8)
				415	1.35	(3.3)
5	73	14	(19)	315	2.05	(6.5)
				515	1.45	(2.8)
6	no feces			440	1	(2.3)
				275	1	(3.6)
7	228	15	(6.6)	395	0.4	(1)
				105	0.5	(0.5)
8	198	7.5	(3.8)	470	1.2	(2.6)
				260	0.6	(2.3)
9	97	3.5	(3.6)	470	1	(2.1)
				475	1.2	(2.5)

Also this time the excretion of mercury in the feces was regular (about 130 ug). However, in urine we could not, with one exception, find more than normal values. It is notable that the mercury levels of "morning" and "evening" urine were similar.

A corresponding test with another person (IV) gave the same result. More than half of the added mercury was excreted via the intestines; in urine the mercury level was nearly normal. Why transiently higher levels were also found in urine in experiment XIVa can not yet be answered and must await further experiments which also might give clues to the mechanisms of the reduced mercury excretion in the kidneys. Perhaps variations in the intake of food has a role.

E. MERCURY LEVELS IN BLOOD.

In connection with the described tests, we also determined in a number of cases, the mercury levels of human blood, to see if blood tests could be used for diagnosis of mercury poisoning. Mercury analysis of blood corresponds to that of other biological material, however, the following should be noted: Since blood during treatment with potassium chlorate and hydrochloric acid foams very much, the oxidation must take place in a large (at least 1.5 l) vessel and the hydrochloric acid must be added in small portions. Aggregations which are difficult to divide and which readily form, are broken up with a glass rod. After filtering off undissolved material, a solution is obtained, which after copper sulfate addition and hydrogen sulfide treatment, is viscid, slimy, organic-containing, partly charred and hard to filter. Before precipitating, it is useful to add filter mass (Schleicher & Schull Co) and to heat the precipitate for lengthy time. Because of the presence of organic substances in the solution, often the CuS-HgS precipitation is not complete (with some experience one can recognize the light blue solution which is suitable for the electrolysis). The precipitate, after the sulfide treatment, must therefore be solubilized and once again treated with copper sulfate, hydrogen sulfide etc. For the less experienced in the analytical method this is always to recommend.

The blood, mostly 100 to 200 g, was obtained from the venous vessel of the arm. Our studies are so far rather limited but allow, however, already certain consistent conclusions.

XV. Middle aged woman without amalgam fillings or other apparent contact with mercury.
140 g blood: 0.87 ug Hg (6 ug/1000 g)

XVI. 86 year old woman, also without apparent exposure to mercury and dead because of atherosclerosis.
94 g blood: 0.6 ug Hg (6 ug/1000 g)

In another mercury-free case where also the urine was measured and found to be relatively low in mercury, 100 g blood contained only 0.1 ug Hg (1 ug/1000 g), a value which was so low that it fell outside the range of the other ones.

XVII. Assessor. Some older amalgam fillings
210 g blood: 0.7 ug Hg (3 ug/1000 g)

XVIII. Man with seven amalgam fillings placed within the last year.
122 g blood: 0.5 ug Hg (4 ug/1000 g)

XIX. Chemist, several amalgam fillings
142 g blood: 0.5 ug Hg (4 ug/1000 g)

XX. Chemistry student (see no VII). 42 amalgam fillings; clear chronic mercury poisoning.
115 g blood: 0.62 ug Hg (5.5 ug/1000 g)
In urine: 36 ug Hg/1000 ml (!). A few months after removal of the fillings: In 90 g blood: 0.38 ug Hg (4 ug/1000 g), in urine 20 ug/1000 ml.

XXI. Tailor (see no VII). Many amalgam fillings and a gold crown. Clinical results suggested mercury poisoning.
57 g blood: 1.55 ug Hg (27 ug/1000 g). In urine 14.5 ug/1000ml.
In this case substantial amounts of mercury appeared to have reached the blood from the amalgam fillings. However, also in this case an unknown source of mercury might have been present (broken thermometer etc.). Since the man lived outside the city we could not determine this.

The following cases are persons who presently or previously had been exposed to mercury in their occupation.

XXII. Man who suffered from mercury poisoning two years ago. Since then not more in contact with mercury.
148 g blood: 0.5 ug Hg (3.5 ug/1000 g)

XXIII. Chemist. According to clinical examination light mercury poisoning.
50 g blood: 0.25 ug Hg (5 ug/1000 g)

XXIV. Merchant who for some years had slept in a room with mercury spill. Symptoms of mercury poisoning had been present but had at the time of analysis nearly disappeared.
100 g blood: 0.31 ug Hg (3 ug/1000 g). In urine 3.2 ug/1000 ml

XXV. Wife of the former (see no XIII). The symptoms had not disappeared as much as for her husband.
109 g blood: 0.42 ug Hg (4 ug/1000 g). In urine 17 ug/1000 ml !

XXVI. Man who cleans mercury pumps. General neurasthenic symptoms.
206 g blood: 0.5 ug Hg (2.5 ug/1000 g)

XXVII. Similar occupation. Symptoms suggesting mercury poisoning
187g blood: 1 ug Hg (5.5 ug/1000 g)

XXVIII. Similar occupation.
143 g blood: 1.45 ug Hg (10 ug/1000 g)

XXIX. Chemist (see no XII). Works much in a room with 35 ug Hg/m³. Clear signs of a beginning mercury poisoning.
124 g blood: 0.9 ug Hg (7.5 ug/1000 g). In urine 11 ug/1000 ml.

XXX. Assistant in a chemistry lab. Apparent light mercury poisoning
146 g blood: 1.2 ug Hg (8 ug/1000 g)

XXXI. 55 year old man. Works since 6 years in a mercury rectifier factory. Comes much in contact with mercury. Signs of poisoning
172 g blood: 1.75 ug Hg (10 ug/1000 g)

XXXII. Glass blower (see no X). In the room up to 120 ug/m³. Various symptoms of mercury poisoning.
100 g blood: 6.5 ug Hg (65 ug/1000 g!).

When the mercury level in the air after cleaning up the workshop had been reduced to 2.5 ug/m³, it also dropped fast in his blood to the normal value. In 127 g blood: 0.8 ug Hg (6.5 ug/1000 g). In urine it remained high for a long time (see no X).

According to these results the human blood normally contains a few ug mercury in 1000 g; 6 to 7 ug is still not unusual. The levels do not rise to any noticeable extent when a considerable mercury exposure occurs from mercury-containing air or amalgam fillings. Is this exposure stronger, the mercury level of the blood can be notably elevated (no XXI, XXXI, XXXII). After cessation of exposure, it will soon drop to the normal level, whereas the urine level can be elevated for a much longer time (compare especially no XX, XXV and XXXII). Urine analysis is therefore much better than blood analyses when abnormal mercury levels in the body are to be tested for. The results prove that the kidneys catch the mercury which has come into the circulation and slowly releases it into the urine.

In order to recognize mercury poisoning and maybe also for the treatment, we will give an evaluation of this study together with further experiments which will be reported elsewhere. Below is a summary of what is presently known and what must be considered when mercury analyses are used for the diagnosis of mercury poisoning.

1. Because of the mercury content of food, also persons with no other opportunity to take up mercury, regularly excrete mercury. This "normal" mercury level is up to a few ug daily in urine with small variations, in feces several (up to 10 ug/day) with wider fluctuations. On average, "mercury-free" persons daily excrete a total of 5 ug mercury, i.e. corresponding to roughly the daily intake. An accumulation in the body with increasing age does not take place.
2. Among carriers of amalgam dental fillings, the mercury level in the urine is often only slightly elevated (a few ug/day), in feces, however, mostly considerably higher than among mercury-free persons. The conditions vary according to number, size, sort and condition of the fillings. Under unfavorable conditions, also the mercury level of the urine is elevated to several times the normal. Our experiments also prove that also the best amalgam fillings give off mercury.
3. Many persons are in such a position that they might absorb mercury vapor in their occupation (physicists, chemists, doctors, dentists, workers in mercury-using factories etc) or in other ways (broken thermometers, felt hats etc). Already after exposure to weakly mercury containing air (1/100 of saturated or less), the levels in urine are markedly elevated above normal. Among people who are occupationally exposed, the amounts can reach several mg/day also in the feces.
4. Small oral doses (as sublimate) of mercury are excreted within a few days, mainly in the feces, in some cases also in the urine (notably irregularly). Mercury absorbed in the lungs differs and has more harmful effects (which will be reported later). Possibly the varying poisoning effects by the amalgam fillings are related to how much mercury enters the body through the respiratory route and how much through the intestines.
5. The mercury level of the blood is normally a few ug, up to 7 ug/1000 g. It is higher as long as mercury is inhaled as vapor. After cessation of exposure or when it is only exposure to small amounts of mercury as from amalgam, it is hardly different from normal, whereas the urine can contain much more. Mercury which enters the circulation is taken up by the kidneys and slowly excreted.
6. For the diagnosis of mercury poisoning the mercury levels of feces and blood are generally of little value. More important is the analysis of urine (methods: A. Stock, F.Cucuel & H. Kohle, this journal 46, 1933, 187. Unfortunately the limit for a simple spectrographic determination of mercury in urine is about 15 ug/1000 ml according to R. Probst, Arch. Exp. Pathol. Pharmacol. 169, 1933, 119, and this is too high for most practical purposes). The equipment and methods for urine are also simpler.

If there are only a few ug in 1000 ml this contradicts a continuing or recent, notable mercury exposure and against immediate health disturbances because of still present mercury (about the not rare secondary, also after the disappearance of the mercury, consequences of a chronic mercury poisoning, we will report in a later publication). If the urine contains a little more mercury than normal (up to 10 ug/1000 ml), a mercury poisoning is not excluded; if it is about 10 ug/1000 ml it is likely. The decisive factor is the clinical finding (nervous- psychic symptoms, depression, pressure in the head, bleeding gingiva, stomatitis, chronic catarrhs, occasional diarrheas etc without other apparent causes). It must be noted that mercury disturbs the function of the kidneys and consequently can reduce its own excretion. Because of the irregular appearance of mercury in the urine, it is recommended that

analyses should be performed on a few consecutive days, or a mean value obtained from several days. The blood analyses can be of value when one has to determine whether a stronger exposure still exists.

On Evaporation, Solubility and Oxidation of Metallic Mercury (Ueber Verdampfung, Löslichkeit und Oxydation des metallischen Quecksilbers)

A. Stock Zeitschr. anorg. u. allgem. Chemie 217, 1934, 241-253 (According to studies by F.Cucuel, F.Gerstner, H.Köhle and H.Lux) (Details in the dissertations by F.Cucuel, Freiburg 1931; F.Gerstner, Karlsruhe 1931; H.Köhle, Karlsruhe 1933)

The observation that mercury evaporates through a layer of water initiated a number of experiments on the solubility of mercury, its evaporation and its oxidation by air (short, preliminary report Naturw.sch. 20,1932, 954). Many of the questions which were touched upon deserve careful quantitative studies. We have not been able to follow up these questions since they were outside our goals.

To determine the small amounts of mercury down to 0.01 µg, we used the methods we have developed in recent years (Z. Angew. Chem. 44, 1931, 200; 46, 1933, 62 & 187; Chem Ber. 67, 1934, 122).

In the absence of oxygen or air, mercury dissolves very little in water, however, in amounts which are measurable (H.Reichardt & K.F.Bonhoeffer, Z. Elektrochem. 36, 1930, 753 showed that mercury at higher temperature, 140° C, dissolved in larger amounts which could be measured spectroscopically). Our most careful experiments used the described apparatus in high vacuum.

In A we placed 100 ml quartz-distilled, vacuum deaerated water and in the thin-walled, evacuated vessel B, we placed a few ml of highly purified, vacuum-deaerated mercury. After complete evacuation, we separated the connection to the pump by melting at the constriction (A cooled in liquid air), broke B by careful shaking and placed the apparatus for a few days in a thermostat at 30°C. The circulation of the thermostat caused a certain movement of the liquid. Stronger movement was avoided in order to prevent colloidal dispersion of mercury in the water. Then we tipped part of the water into D, still in vacuum, disconnected at E and determined the mercury content in D. Consistent results from several determinations: 0.02 - 0.03 µg Hg/ml. If the separation of mercury and water was done in air instead of vacuum, the measured amounts of mercury rose markedly already after a short exposure to air to 0.06 µg/ml and higher.

Fig. 1. Determination of the solubility of mercury in water in the absence of air.

At elevated temperatures the solubility is higher. We found 0.3 µg Hg/cm³ of water at 85°C; 0.6 µg at 100°C.

In dilute potassium hydroxide and -chloride the solubilities at room temperature did not differ from those of pure water.

In the presence of air considerably more mercury is dissolved because of oxidation.

After the publication of our previous paper we also found that similar observations had been made earlier by the medical profession (comp. K.Korr, On the uptake of mercury and its compounds in the body Lieb Ann 104, 1857, 341; W. Braunwart, On the solubility of metallic mercury in various liquids of the body. Dissert. Wurzburg 1898). In Handbook of Toxicology by Kunkel (Jena 1901), it is stated (p.123) with reference to this dissertation: "Metallic mercury is, in the presence of air, dissolved in traces already in distilled water.. much faster and to a greater extent.. in sodium chloride containing water."

The following experiments were conducted at 30°C:

1. 200 ml water in a 250 ml retort with flat bottom was underlayered with purest possible mercury, left undisturbed. After various times 2 ml was removed by pipette and analyzed. The same study was repeated with quartz vessels.

Time	6	24	30	48	70	94	hours
Glass	0.23	1.4	1.9	2.6	3.7	4.3	µg Hg/ml
Quartz	0.26	1.1	1.7	2.8	3.8	4.5	µg Hg/ml

Thus there was no saturation after 4 days. No difference between glass and quartz; the alkali of the glass does not affect the solubility.

2. Experiment of longer duration to determine the saturated concentration. Experimental setup as in 1. a/ left undisturbed b/ bubbled with oxygen in the water layer (end of oxygen tube closely over the mercury)

Time	2	4	8	16	30	50	60	70	days
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a/undist.	2.65	4.7	6.0	7.9	13.7	19.3	--	--	µg Hg/ml
b/oxygen	3.3	7.1	12.0	17.0	27.0	38.0	39.6	39.3	"

In b/ saturation is reached after about 2 months; in a/ not yet. The dissolved mercury at saturation (39.5 µg/ml, corresponding to 42.6 µg HgO/ml is exactly the solubility of HgO at 30°C. We determined this again since published values varied.

3. Purest possible red HgO was vigorously shaken with water at 30°C. The samples, which were used for determinations, were centrifuged to separate suspended oxide. Results:

Time	4	6	8	Days
	42.6	42.1	42.4	µg HgO/ml, mean 42.4 µg HgO/ml

i.e. the same amount as was found in experiment 2b. That mercury, in the presence of air, dissolves as HgO (or a hydrated compound of HgO) was determined by potential measurements. The series Hg/saturated HgO solution/saturated solution from the experiment in 2b/Hg showed no potential difference. Both solutions exhibited identical behavior during reduction with phosphorous acid and gave colloidal mercury solutions which showed the Tyndall phenomenon.

Energetically the oxidation is understandable: $\text{Hg} + \text{O} = \text{HgO} + 21.5 \text{ cal}$. The slowness with which it takes place, also in the presence of oxygen, is noteworthy.

In aqueous solutions of alkali hydroxide, more mercury dissolves in the presence of air, again as II-oxide. Saturation is somewhat more rapidly reached. Experiments with 5 and 10 % potassium hydroxide (30°C, undisturbed):

Time		1	4	8	12	20	Days
4/ 5% KOH	18.5	35.7	55.0	55.5	54.0	µg HgO/ml	
5/10% KOH	35.0	103	135	135	135	"	

The saturated solution contained in 4/ 58.2 µg HgO/ml, in 5/ 146 µg HgO/ml. When we determined the solubility of HgO in 5 and 10 % KOH we found 56.3 µg HgO/ml and 148 µg HgO/ml. In stronger KOH not much more HgO dissolved; in a saturated solution 160 µg HgO/ml. The increased solubility compared to water can probably be explained by the formation of salt ($2 \text{ KOH} + \text{HgO} = \text{K}_2\text{HgO}_2 + \text{H}_2\text{O}$ or similar).

Mercury dissolves with a similar rate in chloride solutions in the presence of air, then as HgCl and the solution shows an alkaline reaction (Probably in the form of complex salt with the alkali chloride. The opinion in the older literature that HgCl₂ is formed is false, something which already Gewecke showed). Experiments with 5 and 10 % KCl solution (30°C, undisturbed):

Time		2	4	10	16	20	Days
6/ 5% KCl	15.9	22.0	21.0	20.0	21.0	µg Hg/ml	
7/10% KCl	33.0	37.5	42.5	47.5	48.0	"	

The final values correspond to 26 µg Hg/ml and 57 µg Hg/ml. A determination of the solubility of HgCl showed in 5 % KCl solution 26 µg Hg/ml and for 10 % KCl 56 µg Hg/ml. If mercury is left covered with chloride solution, crusts of calomel will form after a very long time.

With regard to the properties of mercury towards the living organism we made a similar study with the physiologically often used Ringer solution which contains the salts dissolved in blood (in 1000 ml: 8.0 g NaCl, 0.1 g CaCl₂, 0.1 g NaHCO₃, 0.07 g KCl). (30°C, undisturbed):

Time	0.5	1	2	3	6	8	Days
8/ Ringer	1.55	2.15	2.5	2.75	2.75	2.7	µg Hg/ml

The final value corresponds also here to the solubility of HgCl in Ringer solution (we found 2.8 µg HgCl/ml, i.e. 2.4 µg Hg/ml). It is lower than in stronger KCl solutions but is reached faster (as the graphic presentation in the dissertation by Kohle p. 31 & 33 especially clearly shows).

That also water and aqueous solutions take up mercury from mercury vapor is shown by some other experiments, conducted at room temperature:

9. When 800 ml water had been in a 7000 ml vessel in the presence of Hg-containing air for 48 h the water contained 1.6 µg Hg, the air 26 µg Hg (3.9 µg Hg/1000 ml).

10. 200 ml water in a 7000 ml vessel with Hg-containing air. Shaken for 5 days. In the water 2.0 µg Hg; in the air 22 µg Hg (3.2 µg/1000 ml).

Also at equilibrium (which was nearly reached in exp. 9) the water will only take up a small fraction of the mercury in the air. This appears to be connected to a dissociation of HgO which is likely to be enhanced by the low vapor pressure of mercury in these experiments (about $3 \cdot 10^{-4}$ mm). That HgO already at ordinary temperatures gives off mercury vapor to the air is shown by the following experiment:

11. Purest HgO covered the bottom of a 4000 ml vessel. In the air above we found:

	2	4	6	Days
a/ at 20°C	2.8	3.0	3.0	µg Hg/1000 ml
b/ at 30°C	7.0	7.2	6.8	"

This corresponds to a mercury vapor pressure of $2.8 \cdot 10^{-4}$ mm at 20°C, of $6.3 \cdot 10^{-4}$ mm at 30 °C. (It can hardly be a simple dissociation $2 \text{ HgO} \rightleftharpoons 2 \text{ Hg} + \text{O}_2$. For this is given that $p_{\text{Hg}} \cdot p_{\text{O}_2} = K$. If, in our experiment, p_{O_2} equal to the partial pressure of O in the air (160 mm), the the dissociation constant will be $(2.8 \cdot 10^{-4})^2 \cdot 160 = 12 \cdot 10^{-6}$. The total pressure which HgO must produce in vacuum follows from $p_{\text{Hg}} = 2p_{\text{O}_2}$ and will be $45 \cdot 10^{-3}$ mm, the partial pressure of Hg $30 \cdot 10^{-3}$ mm, i.e. more than the saturated pressure of Hg at 20°C which is only $1.8 \cdot 10^{-3}$ mm. HgO should thus be unstable in vacuum and dissociate to a O-pressure of about 4 mm. However, we could certify that it does not at all give off such amounts of O in vacuum. Also the calculation of p_{O_2} from other data gives far smaller values than the one above. According to Rothmund, Z. phys. Chem. 31, 1899, 74: 10^{-8} and according to Allmand, Z. Elektrochem 16, 1910, 261: $5 \cdot 10^{-19}$ mm. The question needs further examination.) It is thus considered that the air contained mercury as mercury vapor and not as HgO vapor. This was also the case; we could in such an experiment where the air should contain 14 µg Hg obtain not less than 12 µg in a metal drop after condensation in liquid air. It is remarkable that the dissociation pressure at 20°C was equal to the mercury pressure in experiment 10.

Mercury vapor pressures of these magnitudes but with a greater range were found when we led air through a four-bulb tube with HgO and condensed the mercury which was taken up by the air with liquid air.

Also an aqueous HgO-solution gave off mercury to the air:

12. We led at 20°C air slowly (1 l/h) through a ten-bulb tube with saturated HgO solution (new solution for each experiment). The air took up 1.4-2.0 µg Hg/1000 ml, close to the values found in 10 and 11a. Also here could we with certainty demonstrate the metal by condensing in a capillary.

13. If we, instead of using an aqueous HgO solution, used the more HgO-containing, saturated solution in 5 % KOH, we found in the air at 20°C (1 l/h) in three tests 3.0, 3.1 and 3.4 µg Hg/1000 ml, again in agreement with the in experiments 10 and 11a found mercury concentrations.

The described experiments explain why mercury evaporates through water and aqueous solutions. This can happen in two ways:

1. Mercury dissolves as metal and diffuses into the gas phase;
2. Mercury is oxidized to HgO, dissolves as such, and the HgO- solution gives off mercury to the gas phase. In the absence of air only the first is possible. The following two experiments (room temperature) compare evaporation of mercury through a water layer into air and into hydrogen gas (carefully purified from oxygen); each time mercury was determined in water and in gas:

14: In a gas stream. Hg (40 cm² surface area) with 2 cm water layer over; 2 l gas (1 l/h) was led over the water.

a/ Hydrogen gas. Found in gas 2.0 µg Hg/1000 ml; in water 0.06 µg Hg/ml.

b/ Air. In gas 1.5 µg Hg/1000 ml; in water 1.9 µg Hg/ml.

15. Undisturbed air. Hg in a 2000 ml vessel with 2 cm water overlayer; Gas at atmospheric pressure; 24 h at 11°C. The values are the means of three experiments:

a/Hydrogen gas. In gas 5.3 µg Hg/1000 ml; in water 0.3 µg Hg/ml

b/Air. In the gas 4.3 µg Hg/1000 ml; in water 1.4 µg Hg/ml.

(The vessel I was connected to another of similar size II. The latter was evacuated and we let half of the gas from I into the latter for analysis. The gas in II was then flushed out with 40 l mercury-free air into an U-tube in liquid air in which the mercury condensed.)

In 15a and 15b the gas was nearly saturated with mercury vapor. As expected the mercury levels, both for undisturbed hydrogen gas and for a hydrogen stream, was a little higher compared to air since in the latter some of the mercury in the water will be oxidized.

Thus also the mercury level in the water is higher in the air-experiments than in the hydrogen gas experiments. That the mercury level of the water, in the absence of air, in 14a and 15a is higher than in the previously described experiment in vacuum is explained by the fact that here mercury and water came into contact with air before the samples for analysis were removed.

In 15b the Hg level of the water is about 4 % and in 14b 5 % higher than the level in a saturated HgO-solution. However, the mercury content of the air is nearly as large as in hydrogen gas and the conclusion must be that also in the presence of air, mercury immediately will pass into the gas phase as metal and not in a roundabout over HgO.

Mercury vapor behaves differently towards chloride-containing water. This takes up mercury completely:

16. 300 ml 10 % KCl solution in 7000 ml vessel shaken with mercury-saturated air at room temperature for 24 h. In the air we found 2.8 μg Hg, in the solution 49 μg Hg. Most of the mercury had disappeared from the air. In other similar experiments the Hg level in air was higher. Conditions will be more complicated in these experiments since HgCl, especially when exposed to light, can disproportionate into Hg and HgCl₂.

17. Solutions of HgCl in 10 % KCl solution released considerable amounts of mercury into the air: We led 6 l air at room temperature over 20 ml of such a HgCl-saturated solution (surface area 25 cm²) at a rate of 1 l/h. The air contained 7 μg Hg. Compare also exp. 28b.

Blood completely absorbs mercury from air:

18. 300 ml bovine blood was shaken with Hg-containing air with a high concentration in a 8000 ml vessel for 24 h. No mercury could be found in the air (blind value of 0.1 μg). In the solution we found 38.0 μg Hg. Apparently the HgCl which will form will bind to proteins and other substances and not be released again. This latter experiment makes it understandable that our lungs almost completely absorb inhaled mercury vapor.

In organic solutions mercury dissolves more than in water (in pentane at 65°C 6.5 $\mu\text{g}/\text{ml}$ according to Reichardt & Bonhoeffer). We have studied the conditions in benzene according to the same methods as we used with water (to determine mercury in benzene we burned this after addition of four times alcohol or extracted the mercury with chlorine water. *Comp. Z. Angew. Chem.* 46, 1933, 190). Benzene dissolved, in the presence or absence of air, at room temperature 1.5-2 μg Hg/ml. When we led air or hydrogen gas for 2 h (5 l/h) through the saturated solution, the mercury level sank in both cases to about 1 μg Hg/ml. There is no oxidation by air. Corresponding to the higher solubility, also diffusion of mercury through benzene is faster than through water.

19. Methods as in 15; undisturbed gas; 11°, 24 h. Mean of three experiments:

a/ Hydrogen gas. In gas 6.9 μg Hg/1000 ml

b/ Air. In gas 4.8 μg Hg/1000 ml In a the hydrogen gas was nearly saturated with mercury.

20. Gas flow. Hg surface of 35 cm², over that 1 cm layer of benzene. 20°. Air at 1 l/h. In the air we found 4.5-5.5 μg Hg/1000 ml. Also here the air was nearly saturated with mercury. It is surprising how fast mercury diffuses through benzene.

We report some less systematic experiments which originated from practical, physiological or occupational hygienic considerations.

21. Some solutions were left in contact with mercury-containing air (6 $\mu\text{g}/1000$ ml) for 10 hours under identical conditions: Petri dishes of 10 cm diameter, 1 cm liquid height, room temperature. The solutions contained: a/ distilled water 2.2 μg Hg, b/ egg albumin solution 1.0 μg Hg, c/ bovine blood (undiluted) 21 μg Hg. The egg albumin solution showed no particular property to absorb mercury. That it contained less mercury than water might depend on its higher viscosity. In contrast the blood took up ten times more mercury than water. Apparently, in addition to the chloride content, also the property of hemoglobin to transfer oxygen is important (comp. exp. 18).

22. Mercury uptake by some solid materials. Pieces of similar size (10*10 cm) were hung freely in a vessel through which mercury-containing air passed (again 6 μg Hg/1000 ml). The mercury uptake was on average: Filter paper 3-4 μg Hg, (We have already earlier showed that filter paper, after storage in a laboratory, contains mercury and must be washed with chlorine water before it can be used for determinations of small amounts of mercury.) Cotton absorbed 2.7 μg Hg, linen 4.9 μg Hg, silk 3.5 μg Hg, rayon 2.0 μg Hg, wool 0.3 μg Hg, turnips 200 μg Hg (We measured these since we used them as mercury-containing food for animals in studies on the distribution of mercury in the body. Dry material thus absorbed relatively little mercury. However, the studies showed that clothing absorbs mercury from mercury-containing air. The damp turnips absorbed much more mercury. The mercury penetrated into the inner of the slices:

23. The outer 1-2 mm of a turnip slice contained 20 μg Hg, the inner 5 mm 12 μg Hg. The mercury-treated slices did not release mercury into the air:

24. 170 l air was led during two hours over a slice which had absorbed 225 µg Hg; The total amount in air was only 0.1 µg Hg.

25. Evaporation of mercury through various liquids. Hg surfaces of 30 cm²; over that the various liquids in 1 cm high layer; A slow air flow (6 l air, 1 l/h, Hg-free air) was passed over the liquids (Apparatus: Dissert. Gerstner p. 26); temperature 20°. Mercury in air in µg/1000 ml.

Free mercury surface, uncovered: 12 (which corresponds to the saturated value at this temperature); water 0.2; benzene 6; paraffin oil 0.2; glycerol 0.5; carbon disulfide 3; sulfur chloride 6; phenyl mustard oil 9; through sulfur milk no mercury penetrated (prep. boiling sulfur with calcium carbonate and precip. with HCl). Remarkable is that benzene (exp 19 & 20) and organic liquids, especially the oil, easily lets mercury vapor pass through.

26. Similar experiments with solid substances (again 1 cm layer, apparatus as in 25); µg Hg/1000 ml air: Powdered sulfur 10; tetraphosphorous trisulfide 12; silica gel 1; activated charcoal almost nothing, after 3 months storage 1; iodine-treated activated charcoal nothing, after five months storage nothing. Sulfur and also the phosphorous sulfide hardly inhibits evaporation of mercury. Iodine-charcoal is an excellent absorbent for mercury vapor (It is manufactured by Auergesellschaft, Berlin. comp. A. Stock, Z. Angew. Chem 47, 1934, 64).

27. In some other experiments we mixed air which was passed over uncovered mercury with small amounts of other gases; other methods as in 25. Mercury in µg Hg/1000 ml gas: With hydrogen sulfide (damp, 5 vol%): 9, with chlorine (5 vol%) 0.3; with iodine (1 mg/1000 ml) almost nothing. Here it is noteworthy that the presence of hydrogen sulfide hardly affected the evaporation of mercury. With iodine a layer of HgI and HgI₂ formed within a short time.

28. In the following experiments (methods as in 25) we measured, in addition to the level in air, also the dissolved amount of mercury in the aqueous solutions:

Liquid	In air. µg Hg/1000 ml	In liquid. µg Hg/ml
a/ water	0.2	1.3
b/ 5% KCl	0.2	5.2
c/ 5% H ₂ SO ₄	0.9	6.0
d/ 50% "	0.2	3.0
e/ conc "	0.1	23.5
f/ 1% KOH	0.3	6.0
g/ 10% "	0.6	7.5
h/ 50% "	0.05	0.4

The large mercury absorption by the concentrated sulfuric acid is probably caused by an immediate reaction between this and the mercury. The especially low absorption by the concentrated KOH can be explained by its viscosity. In one of the experiments with dilute sulfuric acid we could demonstrate that mercury again evaporated from the acid and could be precipitated as a metal drop.

Finally some observations on the evaporation of small mercury droplets: The droplets which are obtained e.g. with the micrometric mercury determination, evaporate extremely slowly. With droplets of 8 µg and 80 µg weight (diameter 105 and 225 µm) we could find no reduction in size after several months in air when left undisturbed. When we had distributed 100 µg Hg by careful distillation in a 2 mm tube as a fine surface precipitation and led 250 l air in three hours over it, the air only contained 1.9 µg Hg. This result is surprising when one remembers how fast a large surface of mercury gives off metal to the air (comp. exp 25). An explanation might be that also mercury, as other nobler metals, e.g. silver, is oxidized on the surface and that the thin oxide layer in the small droplets is less easily broken than in larger ones which vibrate in an air flow (The surface oxidation has been suggested several times, recently by K.Schafer, Z. Physik 77, 1932, 212. Maybe also observations like those of K.Freudenberg & H.Eyer, Z. physiol Chem 213, 1932, 232, that mercury of common purity inhibits the activity of insulin whereas highly purified metal does not, can be explained by an oxide content of the less pure metal.)

29. We led an air flow over three mercury drops of various sizes at room temperature (1-2 l/h). The table shows the reduction of the diameter (µm) and the weight (µg):

	I.	II.	III.
Start of exp.	291 µm, 173 µg	143.5 µm, 21.2 µg	80.8 µm, 3.85 µg
After 5 days	286 163	143.0 21.0	not measurable
After 16 "	272 145	138.5 19.0	78.4 3.50
Weight loss	28 µg	2.2 µg	0.35 µg
Loss µg/µm ²	2.4*10 ⁻³	1.6*10 ⁻³	1.3*10 ⁻³

In a similar experiment in hydrogen gas instead of air we found:

Start of exp.	27.4 μg	14.10 μg	7.97 μg
weight loss			
$\mu\text{g}/\text{um}^2$	$6.7 \cdot 10^{-3}$	$8.7 \cdot 10^{-3}$	$9.3 \cdot 10^{-3}$

In hydrogen gas the evaporation is higher than in air, something which is in agreement with a surface oxidation. However, this could also be explained by a more rapid diffusion rate in hydrogen gas. The results from the experiments do not differ much when related to surface area. Before any firm conclusions can be drawn, the experiments must be repeated under more exact experimental methods; careful regulation of temperature and air flow.

Our reports show how the improved methods for mercury analysis have made possible or easier the experimental study of many new questions. The observations on oxidation and evaporation of mercury explain several facts which have been so far hard to understand.

For instance it is now clear that the evaporation of mercury is not inhibited by a layer of water. The relation between mercury, water and air is also one of the causes why we and others had difficulties when we tried to produce an air flow with a certain low mercury concentration by cooling saturated air to a temperature with the appropriate mercury vapor pressure (Comp. A. Stock & W. Zimmermann, Monatschr 53/54, 1929, 786 & 55, 1930, 1; K. Müller & P. Pringsheim Z. Physik 65, 1930, 739). One of the premises is, which has now been shown, the careful drying of the air

Another fact is often disputed. When mercury containing air is inhaled, the mercury is nearly completely retained. Now we know that in lungs are the best conditions for oxidation of mercury, blood with a large surface area, oxygen, elevated temperature. (The mercury is oxidized primarily to HgCl ; According to K. Voit, HgCl reacts with proteins, blood etc under formation of soluble mercury compounds).

Also we have an explanation for the occurrence of mercury in all samples of rain water because of oxidation and solubilisation of mercury in the atmosphere. Mercury, in high dilution, appears to exhibit a circulation; evaporates from the ground and returns with rain water. The general occurrence of mercury in all substances (which we will report next) should be connected with this behavior. Since it is known how effective mercury can be as a catalyst and as a catalyst poison (comp. G. Bredig & K. Ikeda Z. phys. Chem 37, 1901, 63), one can suspect that this distribution of mercury also is of biological importance.

The Mercury Content of the Human Body (Der Quecksilbergehalt des menschlichen Organismus)

Biochemische Zeitschrift 304, 1940, 73-80

XXX Report on the effects and distribution of mercury

A. Stock, Berlin-Dahlem

In a recently published paper in this journal J. Bodnar, Ö. Szep and B. Wespzpremy discuss the natural mercury level in the human body (Biochem. Zeitschr. 302, 1939, 384), i.e. the mercury content of the organs, originating from (mercury-containing) food but not from other sources. The authors determine mercury in various organs of three persons who have died of severe diseases. They were considered "mercury free" and had not, as carefully as this could be determined, been in contact with mercury when they lived and had no amalgam fillings. Bodnar et al obtained the following values (nanograms/g; ng/g = µg/kg wet weight):

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All values in the original paper are in µg/100 g. They have been changed to ng/g (nanograms/g) which is the usual unit today.

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	20 y woman Pneumonia	62 y woman Heart failure	19 y woman TBC	
Kidney	174	223	580	ng/g
Liver	170	103	446	
Lung	53	94	506	
Blood	78	342	346	
Gall bl. +contents	--	--	325	
Spleen	362	700	422	
Heart	255	--	340	
Stomach + intest.	-----» 26	--	310 325	
Brain	6.3	46	445	
Muscle	--	--	6	

The three series of measurements do not agree very well and also give higher values than earlier, singular measurements which have been published. Especially the blood values are too high. In our extensive study on live persons (Stock & Cucuel, Z. angew. Chem 47, 1934, 641) we found in "mercury-free" persons only up to about 7 ng/g whereas these values are 50 times higher (not 500 times as the authors write), i.e. even more than the peak levels which are reached during a mercury ointment (250 ng/g) treatment. We have also, in connection with mercury poisoning, for a long time been interested in the question of normal levels in human organs. And in which organs does it accumulate? We have been able to collect a substantially larger and more conclusive material. We intended to publish it together with still not finished studies but because of the paper by Bodnar and collaborators I will report on the current observations.

In order to possibly avoid pathological complications we took our autopsy material from persons who had died by accident or suicide and not because of diseases (which also the Hungarian researchers plan to do). The University clinic for Forensic and Social Medicine (director: Prof. Dr. Müller-Hess) supported us generously.

We differentiate between the two groups A: Mercury-free and B: Carriers of amalgam dental fillings. Previous work had shown that the excretions from persons in the B group is generally much higher than from group A. A carrier of a few small, insignificant amalgam fillings (case I) has been included in group A where it also doubtless belongs according to the measurements. A good criterium for uptake or not uptake of "unnatural" mercury is found in the Hg-level of the kidneys; the limit is about 100 ng/g. We include an amalgam-free case (case VIII) in group B since in this case there could be no doubt about mercury uptake from some other source.

The analyses were made according to previously reported methods and experience. Again it was evident that there are many sources of errors (e.g. Hg in the reagents, glass vessels, water and laboratory air) which can affect the determination of the smallest amounts of mercury. Mercury determination in organs of 1 g weight or less requires extreme demands on training and self- critique of the analytical scientist.

The table contains our analytical results in ng/g wet weight. After the name of the organ is the usual weight of the organs we obtained for analysis. From this one can obtain the approximate amount of mercury found in any measurement; they were often as

low as a few hundredths of a microgram. 0 means that no Hg was found, and -- no measurement (mostly because we did not obtain the organ).

Cases: A. Hg-free I-VI

- I. 28 y male painter. CO-poisoning
- II. 15 y male plater apprentice. Occupational accident
- III. 18 y female shop assistant. Fall from window
- IV. 26 y male manual worker. Occupational accident
- V. 25 y male carpenter. Occupational accident
- VI. 29 y male shop assistant. Veronal poisoning

B. Amalgam carrirs etc.

- VII. 24 y female servant. Hydrochloric acid poisoning
- VIII. 37 y widow. Drowning
- IX. 31 y male painter. Occupational accident
- X. 60 y male factory superwiser. Sleeping pill poisoning
- XI. 21 y female. Housewife. CO-poisoning

In some of the cases we made some single measurements (ng/g):

In VIII we found: Tongue (61 g)	8 ng/g
Pancreas (39 g)	3
Aorta (18 g)	2
Skin (13 g)	6
Cartilage (16 g)	6
Bone (10 g)	13
Bone marrow (16 g)	19

These measurements did not show anything special; they were in the same range as the other values from heart, spleen muscle.

	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	
	A. Mercury-free						B. Amalgam carriers etc					
1. Cerebral cortex(40g)	8	2	1	3	7	9	15	563	108	23	9	
2. Brain ventral(40g)	9	4	2	--	--	4	13	--	80	17	--	
3. Cerebellum(40g)	6	4	2	3	7	30	14	1180	158	19	10	
4. Basal ganglia(40g)	6	4	2	3	7	4	11	348	60	23	6	
5. Brain stem (10g)	11	4	0	--	--	8	20	515	263	5	--	
6. Olfactory bulb (0.6g)	--	31	87	19	6	--	480	224	191	--	132	
7. Pituitary gland(1g)	133	61	--	--	40	81	232	--	130	158	40	
8. Spinal cord (7g)	5	1	1	6	6	17	14	137	43	9	22	
9. Lymph nodes (2g)	18	4	21	1	0	0	69	160	120	18	6	
10. Thyroid (20g)	18	5	5	9	7	94	30	65	58	354	29	
11. Soft palate(10g)	7	4	12	--	--	12	53	9	12	36	--	
12. Epiphysis (0.9g)	--	--	--	4	0	--	--	--	--	--	--	
13. Salivary gland(10g)	--	--	--	4	0	--	--	--	--	--	34	
14. Tonsils (10g)	--	--	--	10	9	--	--	--	--	--	44	
15. Kidney (40g)	40	46	30	82	76	102	5130	369	141	728	167	
16. Adrenal (10g)	--	--	9	2	46	13	161	2	9	53	43	
17. Liver (40g)	12	47	6	25	42	118	460	61	87	81	115	
18. Spleen (40g)	4	5	3	--	--	5	54	12	9	21	--	
19. Lungs(40g)	9	7	5	--	--	9	49	12	20	16	--	
20. Heart (40g)	7	4	1	3	5	12	55	16	9	22	47	
21. Stomach (40g)	19	5	1	--	--	--	46	--	10	35	--	
22. Large intest.(20g)	--	--	--	--	--	--	--	--	--	--	78	
23. Appendix (5g)	4	11	--	--	--	1	234	22	6	13	--	
24. Gall bl.+ bile(10g)	--	--	--	10	21	--	--	13	--	--	37	
25. Testes or ovary (10g)	--	--	--	1	5	--	--	0	--	--	1	
26. Muscle (40g)	5	3	3	1	5	6	--	8	--	--	15	
27. Fat(10g)	18	--	--	--	--	5	478	4	14	--	--	
28. Blood (25g)	4	4	2	--	--	31	31	6	7	10	--	
29. Hair(5g)	--	--	49	--	--	--	--	216	--	--	--	

In XI we could analyse a gallstone (1.4 g): 11 ng/g

In IV we obtained the kidneys in pieces:

cortex right (22 g) 92 ng/g

cortex left (25 g) 96

marrow right (17 g) 61

marrow left (14 g) 53

The cortex thus contained substantially more Hg than the marrow. We did not otherwise find any great differences between the both kidneys.

We analysed an additional three samples of hair from women (washed and degreased): 1. (46 g) 2740 ng/g; 2. (5 g) 746 ng/g; 3. (25 g) 300 ng/g. These are considerably higher than the also high ones in the table. We do not know how much use of Hg-containing preparations, oils etc and maybe also the high Hg-level in the street dust (see below) or felt hats has to do with this or whether an accumulation of mercury from the body actually takes place in the hair.

For group A, mercury-free, one can draw definite conclusions from the table. Hg is present in most natural animal and vegetable matter and also in the human body to a level of 10^{-9} to 10^{-8} , i.e. 1-10 ng/g. That single measurements differed can not change this conclusion. In some organs it will accumulate. Primarily this is the case with the kidneys as our animal experiments also show. The level will be about 10 times higher than in the mercury-poor organs. In addition, it will accumulate in the liver even if it is to a lesser extent than in the kidneys (the exception VI will be discussed below).

No accumulation takes place in the the heart, lungs, stomach, brain, the relatively mercury-poor muscles and also not in the spleen which Bodnar et al consider the most mercury-rich organ. The blood contains, also in contrast to the opinion of the Hungarian researchers, not more mercury than we previously found in living people (exception again VI). However, the blood values in dead people might not be too important since blood can and will change Hg-level after the cessation of the circulation.

In case VI we find values which differ from the others: more mercury in the cerebellum, spinal cord, thyroid, liver and also blood. This case where the cause of death was veronal poisoning, must be considered pathological. A special uptake of mercury must have taken place and the distribution of mercury in the body has not followed the usual pattern, maybe influenced by the (slow) effect of the poison and also previous disease. It should have been appropriate to exclude this unclear case. I have not done so in order to avoid any conditions but also to show that one has to avoid too general conclusions from a limited material. As really conclusive one can consider cases I to V, in which young, healthy persons had a rapid death. In these cases the results agree to an extent which can be expected from such physiological studies.

An elevated level of Hg is also found in the olfactory bulb and especially in the pituitary gland. The latter is a surprising finding which will be discussed below. The appearance of higher levels in the nose and in the olfactory bulb have already been found in animal experiments and has also almost always been confirmed in the ongoing studies on human material. This can be explained by the fact that also for "mercury-free" persons there is another source of continuous exposure to mercury in addition to food: Dust (for smokers also tobacco smoke which will not be further discussed here). Dust contains, especially in the cities with their soot-containing air, much Hg. We found earlier (Naturw.sch. 22, 1934, 390) in the soot from cooking stove 3500 ng/g, a factory 28000 ng/g, in Karlsruhe street dust 870 ng/g. The dust in Berlin does not differ. A dust sample from an open place in a densely populated area contained in June, i.e. the season without heating, 940 ng/g, another from a street 310 ng/g Hg. The dust on the ground consists mainly of sand and silicate fragments. From the inhaled, more soot-rich dust, Hg must deposit in the olfactory mucosa and then reach the organs with connections to the nose, primarily the olfactory bulb.

The results in group B, the carriers of larger amalgam fillings, do not allow such conclusive results. One must expect less uniformity. The amalgam fillings give off Hg as vapor (as HgCl_2 - vapor, comp. Ber. Dtsch. Chem. Ges. 72, 1939, 1844) which is inhaled and also solubilized or particulate Hg to the gastrointestinal tract. The amounts will be very variable and depend on the composition of the amalgam (Cu- or Ag-amalgam), size, position, age and mechanical load on the filling, pH of the saliva etc. At least in case VII, poisoning by hydrochloric acid, the unusually high amounts of Hg (kidneys 5130 ng/g!) in almost all organs suggest another source of mercury. The often high level of Hg in hydrochloric acid is not a sufficient explanation. Opportunity for "unnatural" uptake of mercury is common: treatment with Hg-containing compounds (ointments, drugs), staying in Hg- or HgCl_2 -containing air (broken thermometers, old amalgam mirrors, open or evaporated HgCl_2 solutions, occupational exposure to Hg or HgCl_2 etc. (In older hospitals the air is constantly more or less Hg-containing). Whether one or more such exposures has happened in a specific case can rarely be determined for deceased people. If the samples originate from people with a violent death (which is certainly better than undoubtedly pathological cases which constituted the material in the work by Bodnar et al and where unnatural uptake of mercury must have occurred), it is mostly very difficult to obtain information on such circumstances.

Despite these uncertainties one can draw some definite conclusions from group B. They agree with conclusions from group A. The general Hg-level in amalgam-carriers is, as could be expected, clearly more than normal. The kidneys are again the principal accumulators of Hg and the level is several times higher than in the liver (because of the size of the liver the comparison of total amounts of Hg in these organs will be different). The spleen is not more Hg-rich than lungs, heart, stomach etc. Especially small amounts are found in the muscles. The Hg-level in blood is only elevated above normal in VII and despite the impregnation of the organism with Hg in this case, only moderately so. A new confirmation that the circulating Hg in blood is rapidly taken up by the

kidneys (and apparently also by the liver). Notable is the high Hg-level in brain and brain stem in cases VIII and IX. The elevated levels in olfactory bulbs and hair have been discussed above.

Also in this group the most conspicuous finding is the accumulation of mercury in the pituitary gland (1580 ng/g in XI, unfortunately we could not obtain the olfactory bulbs in this case) and also -maybe connected with this - in thyroid and lymph nodes.

The observation that the pituitary gland, which despite its small size, is of such importance for the regulation of the hormonal status, accumulates mercury to levels similar to the kidneys, should be of extreme importance for the mechanism of chronic mercury poisoning. If an above normal Hg-level disturbs the functioning of the pituitary gland as it is known to do with the kidneys (inflammation, anuria, uremia etc), then almost all symptoms of the up to now quite mysterious chronic mercury(- vapor) poisoning can be explained. Before this is discussed more in detail, more material will be studied. Our current, because of the difficult analyses rather time-consuming, studies might answer the following questions: How does mercury enter the pituitary gland; from the general circulation or (as it appears) from the nose? Where does it go from the pituitary gland? Into the brain and in which parts of the brain? Is there a connection between the Hg-level in the pituitary gland and in certain other glands? What is the level of mercury in the organs in various pathological cases? What diseases causes the elevated mercury levels?

The answer to these questions might, in addition to mercury poisoning, be of value also for the treatment of other types of poisonings.

We are, in addition, also studying the changes in blood mercury levels during the course of mercury ointments. No values have up to now been published.

My gratitude to the German Research Council and the Schering AG for supporting also this study, to Helene Heintze, Ruth Lehmann and Elisabeth Grube for careful analytical work.

Summary

The "normal" Hg-level, i.e. the level not originating from nonnatural sources has been determined in a large number of human organs (with about 250 micro-Hg determinations). As study material we used bodies from persons who had died a violent, fast death in order to avoid pathological complications.

The general level of Hg in the human body is similar to that in the organic world, in animals and plants and in general in the range 1-10 ng/g wet weight. In carriers of amalgam fillings it is -often considerably - higher.

In some organs Hg accumulates, especially in the kidneys, to some extent also in the liver and conspicuously so also in the pituitary gland. This unexpected finding is of utmost importance for understanding the mechanisms of chronic mercury poisonings especially and probably also for medical understanding of poisonings in general. If the functioning of the pituitary gland is disturbed by elevated levels of Hg in similar ways as that of the kidneys, something which must be presumed, then almost all symptoms which so far have been difficult to interpret, can be explained. Maybe also directions for therapy can be inferred. The studies will be continued in various directions.

According to our findings, the higher levels for the normal Hg- content, reported by others, can only be explained by other sources of exposure for the pathological material which was used.

In addition to food, also inhaled dust is a source which continuously exposes the organism to traces of mercury.

GALVANIC BURNS OF THE ORAL MUCOSA

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In a recent contribution, Everett S. Lain called the attention of American dermatologists to an important and what might appear as a relatively frequent cause of lesions of the oral mucosa (1).

Three patients have come under my observation recently in whom annoying lesions of the oral mucous membrane disappeared on the removal of amalgam and gold dental fillings and other gold appliances in accordance with the principles outlined by Lain. Each instance can be considered clinically to have been a galvanic burn of the oral mucous membrane.

REPORT OF CASES

CASE 1. Mrs. A. P., aged 28, was examined, March 10, 1930, on account of multiple, recurrent and exquisitely painful ulcers of the oral mucosa, resembling the clinical picture of aphthous stomatitis. The ulcers first appeared about two years before and usually numbered from fifteen to thirty at various times, being always decidedly worse just before her menstrual periods. A routine examination revealed little of importance.

Mouth smears were negative. Gastric analysis showed a low content of hydrochloric acid. The pharynx and the cornea were in a condition of anesthesia, as one at times finds in hysteria.

Testing of sensitivity to foods both by intradermal injections and by the trial method proved nothing. When the patient was given dilute hydrochloric acid in doses of 30 minims (2 cc.) the lesions of the mucous membrane increased.

Slowly the patient was so much worse that she found it extremely difficult to masticate her food. She was then placed at absolute rest in bed, on a milk diet, for a period of six weeks. There was some improvement, but the ulcers continued to recur.

Shortly after Lains communication, all the amalgam fillings were removed from her teeth and replaced with temporary (cement) fillings. Within ten days there was a great change and since then there has been no recurrence of the ulcers, though two menstrual periods have passed.

CASE 2. L. W. O., a man, aged 31, was examined, June 16, 1931, on account of a sore tongue of four months duration. The sore complained of was a whitish-gray elongated patch about 2.5 cm. long and 1 cm. wide, affecting the under and lateral surface of the right side of the tongue opposite, a gold fitting of a so called hygienic fixed bridge, which occupied the space of an extracted lower right first molar. There were two other similar patches on each side of the buccal mucosa. The patient complained of a metallic taste. He smoked about twenty cigarets a day.

Smears of the mouth, and general and serologic examinations, proved nothing.

On account of the appearance of the lesions and the history of a fair amount of smoking, I considered the lesions as smokers patches, but the discontinuance of the use of tobacco had no effect on the lesions.

Further questioning proved that these lesions began shortly after the hygienic fixed bridge was placed in the mouth.

Examination also showed a number of amalgam fillings in the teeth. On removal of the gold bridge, all the lesions disappeared. In January, 1932, the same gold bridge was replaced and within one week the same lesion of the tongue and on the right buccal mucous membrane and also the metallic taste reappeared. Within a week after the second removal of the gold bridge the lesions and the metallic taste disappeared, and the patients mouth since then has remained well.

CASE 3. N. K., a man, aged 41, consulted me, Dec. 15, 1931, on account of painful and recurring ulcers of the mouth, which clinically resembled those of aphthous stomatitis. This condition had been recurring for a period of eighteen months. There were eight lesions in the patients mouth, each one oblong and sharply defined, with an inflammatory halo around a necrotic center, which was covered by a yellowish pyogenic membrane. He did not complain of a metallic taste. He had many amalgam fillings in his teeth and also a gold crown over the lower left incisor tooth. After the removal of this crown, the ulcers disappeared and have not recurred since.

Comment: Each instance seems to fit to the fact that the principle of Lain is correct and that two dissimilar metals suspended in normal saliva, which is a fair electrolyte (Hodgen, quoted by Lain) complete a galvanic battery.

Summary: One case of so-called smokers' patches (leukoplakia) and two cases of aphthous stomatitis-like ulcers of long standing were cured when the metals producing the galvanic burns of the oral mucosa were removed, after all sorts of other therapy failed.

1. Lain, E. S.: Chemical and Electrolytic Lesions of the Mouth Caused by Artificial Dentures, Arch. Dermat. & Syph. 25:2131 (Jan.) 1932.

ACRODYNIA OR HOW TO FAIL TO RECOGNIZE MERCURY POISONING FOR MORE THAN 100 YEARS

Mats Hanson

How many physicians have heard the story of how medical science eradicated the disease called acrodynia? Very few probably since the discovery and cessation of a major poisoning is hardly anything to be proud of. However, medical science ought to learn an important lesson from a disease which cost numerous children's lives - completely unnecessarily. Unfortunately the sentence under mercury in Casarett & Doull's Toxicology seems to be true: Man is apparently a poor student of history.

Anyone who has experienced the toxic effects of amalgam fillings and has compared the symptoms with those reported in the mercury literature, is amazed that the poisoning has not been recognized at any of numerous visits to doctors during years or decades. The oral symptoms (salivation, ulcers, metallic taste, bleeding gingiva and general irritation of mouth and upper airways) directly indicate mercury poisoning and in addition there are usually numerous other typical symptoms: psychic, neurologic, gastrointestinal etc.

Damage from medicines is called iatrogenic and it is certainly not an easy task to bring dentists to admit that a practice they thought was beneficial for the patients in reality caused damage. It appears to be even harder to get the medical profession to recognize that numerous patients with symptoms indicating anyone of a number of diseases are mercury poisoned.

The problem is certainly not new, especially not regarding mercury. The metal and its chemical compounds have been used widely; in numerous medicines, for disinfection, electrical apparatus, thermometers and barometers, photographic purposes, toys, cosmetic preparations, paints etc. There are several cases described where children have played with mercury and distributed the metal at home.

The ignorance is still baffling. In a recent electronic magazine I found a description of experiments with lasers to produce holographic pictures. The hologram was obtained by having the laser beam reflected from a drop of mercury towards the object to be photographed and a film. "The drop of mercury can be obtained from a broken thermometer... The high voltage is directly life-threatening to touch and looking into the laser beam can give irreversible eye damage." Not a word about mercury giving off toxic vapor, especially if heated by a beam of light.

CALOMEL

A mercury compound which was earlier much in use was calomel, monovalent mercury chloride (mercurous chloride), Hg_2Cl_2 . The substance which has a low solubility, was considered harmless despite a large number of reported cases of poisoning. It was commonly used as a medicine for gastrointestinal irritation. A large dose caused diarrhoea and the patient got rid of both the medicine and the possible problem-causing bacteria. However, an apparently common practice was to take much smaller doses which made the medicine pass the gastrointestinal tract slowly, allowing time for absorption. There have been cases of severe brain degeneration after several years of calomel use (dementia, erethism, colitis and renal failure) (Davis et al, 1974)

Calomel was, however, used in many preparations, often without any indication on the label of the calomel content. A popular use was as worm-chocholate against intestinal parasites. Another use, mainly in english-speaking countries, was to treat irritation when the teeth of small children broke through with teething- powder, containing calomel. "wherever the British flag waved, teething powders were almost a nutrient of infants." According to several early publications calomel had sedative properties and that might have added to its popularity (Bayles, 1879, Hatchett, 1884). The powder was sold in groceries and drug-stores. One of the manufacturers in England reported in 1954 that 30 million packages were sold each year. Studies showed that about 50% of all british mothers used such powders to treat their children.

In Sweden and on the european continent teething powders were little used but instead calomel in worm-chocholate, a variety of mercury compounds, in medicines made up at pharmacies and in chemical-technical preparations, e.g. "germicidal soaps", 5 grams of mercuric chloride in the bathtub for eczema etc. Everyone has been exposed to mercury in vaccines and other preparations. Absorption and side effects from calomel treatment of children should have been anticipated from earlier experience, early warning were not lacking, eg. Cruickshank, W., Remarks on the absorption of calomel from the internal surface of the mouth; accompanied with a preliminary sketch of the history and principal doctrines of absorption in human bodies. London 1779; And what happened to the children's teeth after mercury exposure? Hutchinson J., On the malformation of the teeth, caused by giving mercury to infants (Edinburgh Med J 1897). Warkany (1966) cites Underwood (1865) who suspected the harmless calomel, prescribed in small amounts, as the villain that caused ptialism, ulceration of the gums, sloughing of the palate, and falling out of the teeth. He knew of several such cases which resulted in the death of the patient.

ACRODYNIA

What were the consequences of this human mercury impregnation? What are the consequences of mercury exposure from amalgam today? A clue to the magnitude of the problems caused by mercury might be obtained by studying the medical records of the disease called acrodynia. This is quite rewarding since there are careful descriptions from both before and after the mercury etiology was recognized. Even the psychosomatization was not missing. Spitz and Wolf (1946) described under the title "Anaclitic depression" a syndrome among children in a nursery (5-11 months of age). Several of the children died and arrested development was noted in others. The authors considered the illness to be comparable to melancholia in the adult and caused by "withdrawal of the love object". The psychic diagnosis is discussed (and rejected) in a review paper by Leys (1950) where these cases were considered typical of acrodynia.

The first appearance, at least in a sufficient number of cases to be recognized as something special, was in a building-block at rue del'Orsay in Paris in sept. 1828. In the house a number of children but also adults fell ill. An infectious agent was suspected. The epidemic was described in medical journals and subsequently cases were reported from other places, often isolated cases among children but sometimes groups of children and also adults were affected. Epidemics from prisons and military camps were reported.

The disease spread during the 19th century and at the end of the century it had spread to large parts of the world; In England, Australia, the southern USA and other english-speaking countries mainly children below 2 years of age were affected. The peak was at 9 months of age. On the continent the peak was at 2 1/2 years and continued up to 9 years. In England 585 deaths because of acrodynia were officially registered between 1939 and 1948. In the year 1952-3, acrodynia cases constituted 3.6 % of all visits to the children hospital in a british city. In Australia the disease had epidemic forms. The responsible virus was discussed and its mode of transmission from person to person. Epidemics could occur in isolated, rural areas. The cause was unknown.

SYMPTOMS

The disease had other names besides acrodynia. Because of the swollen, painful hands and feet with peeling skin and a reddish color, it was called pink disease. Skin problems in other parts of the body was also common. After physicians who described various features, it was also called Feer's disease, Selter's disease and Swift's disease. More symptom-describing was erythema arthriticum epidemicum, vegetative neurosis of childhood, vegetativ encephalitis, erythroderma polyneuritis, throphodermatoneurosis, primary emotional disorder. A physician wrote: ".. it is difficult to imagine anything more pathetic than a baby suffering from pink disease with complete apathy and loss of interest in his his surroundings."

The children had pains in hands and feet and these were often swollen, damp, sensitive to touch and felt cold. Demyelination was noted in nerve biopsies. There were disturbances of blood circulation and temperature regulation; in severe cases fingers and toes could be lost by gangrene. Blood pressure and catecholamine levels were often high. The victims exhibited extreme weakness of muscles; they usually stopped standing and walking. Loss of weight, tremor and shaking, cramps and uncontrolled movements, abdominal tenderness and gastrointestinal troubles belonged to the clinical picture. Also conjunctivitis and fever was reported in earlier descriptions; fever was apparently very common in Germany and Switzerland where the most common misdiagnosis was scarlet fever. In a considerable number of cases there was salivation, swollen gingiva, loss of teeth and necrosis of the jaws.

WHAT CAUSED THE DISEASE?

Guesses were numerous. Vitamin deficiency, neurosis, endocrine disturbance, adrenal insufficiency, electrolyte imbalance, allergy, hysteria, trikinosis, rye fungus. The similarity to pellagra (vitamin B3-deficiency) was pointed out several times. There were studies to assess possible contacts with animals; unknown viruses and a variety of microorganisms were suspected.

The similarity to arsenic poisoning was noted in 1889. Mercury poisoning and the similarity in symptomatology to effects of mercury treatments with grey ointment was first suggested in 1846 and again in 1922. A physician wrote that year " For a while I had the idea that it could be a metal poisoning. Several of my patients had been treated with large doses of calomel at the onset of the disease. There were, however, cases where no calomel treatment could be found and this drug could be eliminated."

Why did he think about mercury? The reason was the oral changes. "A symptom which is almost unknown in every disease except poisoning with mercury or phosphorous." In the USA the idea of poisoning also appeared. Bilderback described a number of cases 1920 and noted that the disease " was more like a low-grade poisoning or a deficiency disaese than an infection. The children were, however, well-fed. low-grade toxemia remained."

In 1945 an americal physician, Warkany, got the idea to send an urine sample to a laboratory for metal analysis because of the similarity with arsenic and thallium poisonings. The urine contained 360 micrograms Hg per liter and no other metals. Additional measurements demonstrated mercury in most urine samples, however not in all. Careful studies showed mercury exposure in every case, most often from teething powders. Warkany wrote that "its seems rather odd that one could not detect the injurious mercury at

only a negligible fraction of the population is allergic to mercury, based on useless tests. A more true statement would be that only a small fraction of the population can not tolerate amalgam on the skin without local allergic reaction.

The sometimes severe neuroallergic reactions in acrodynia and his own observations on neurologic patients, led Baash (1966) to the conclusion that multiple sclerosis was an adult form of acrodynia, a neuroallergic reaction, in most cases caused by mercury from amalgam fillings. The hypothesis seems to be a perfectly logical one which can explain every puzzling feature of MS. Our experience in the patient organization certainly verifies Baasch observations. Apparently Baasch had contact with Fanconi, one of the first researchers to adopt and clarify the mercury etiology of acrodynia.

Pseudo-acrodynia with some features of the real disease was produced in animals by various treatments. Today relapsing allergic encephalomyelitis is produced in animals by injection of brain tissue and is considered a model for MS. However, a much more rewarding approach would be to look at the role of mercury. It might then turn out that exactly the same happens as with acrodynia. "A subtle, complicated, and no doubt molecular disease was eradicated by such a prosaic measure as removing calomel from oldfashioned teething powders and worm medicines." (Warkany, 1966). "There were data on electrolyte changes explaining the symptoms of acrodynia and their alleviation by subtle saline treatments. But these data did not take into account the one electrolyte that mattered, namely mercury." (Warkany, 1966).

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- The papers by Warkany are highly interesting and recommended. They also contain many further references.