WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

VBC/74.7
ENGLISH ONLY

CONFERENCE ON INTOXICATION DUE TO ALKYLMERCURY TREATED SEED

Baghdad, Iraq, 9-13 November 1974

F I N A L R E P O R T

This Conference was supported
by a grant from the
Swedish International Development Authority

PROGRAMME OUTLINE AND INDEX TO CONTENTS

Monday 11 November 1974 — Page

1. INTRODUCTION

WHO participants attended the Conference from Afghanistan, Brazil, Egypt, India, Iran, Iraq (2), Japan, Jordan, Kuwait, Libya (2), Mexico, Pakistan and Turkey. The WHO Consultant and Temporary Advisers were drawn from Poland, Sweden (2), United Kingdom (2) and USA. In addition, 14 foreign observers attended from Egypt, Finland, German Federal Republic, Japan (2), Sweden (2), Switzerland, USA (6) and Yugoslavia. FAO was represented throughout by a Headquarters staff member and the UNDP Deputy Resident Representative attended the opening of the Conference. The Conference was also attended by members of the Iraqi National Scientific Committee and a number of Iraqi observers.

A list of participants, WHO staff, Iraqi National Scientific Committee, representatives of other United Nations bodies and observers from other countries is attached as Annex 1.

Session 1 - 9 November 1974

The Conference was officially opened by H. E. Dr Ezzat Mustapha, Minister of Health, Iraq. Dr A. H. Taba, WHO Regional Director EMR, also addressed the Conference. The text of these addresses is attached in Annex 2. Both speakers were introduced by Dr S. K. Tikriti, Director of Preventive Medicine, Ministry of Health, Baghdad.

The Agenda was adopted without amendments. The following officers were elected by the participants:

Chairman	Dr F. Bakir (Iraq)
Vice-Chairman	Dr W. F. Almeida (Brazil)

2. PAPERS PRESENTED AND SUMMARY OF DISCUSSION

Session 2 - 9 November Moderator: Dr F. Bakir (Iraq)

Papers Presented:

PROBLEMS RELATED TO THE CHEMICAL TREATMENT OF SEED
Dr S. B. Skerfving (WHO Consultant)

Only two types of seed dressing agents have caused major epidemics of poisoning. These are the short-chain alkylmercury compounds methyl- and ethylmercury on the one hand and hexachlorobenzene on the other. In both cases the epidemics have been caused through misuse, by consumption of the dressed seed as such, or in the case of the alkylmercury compounds, by feeding the seed to domestic animals which are later on consumed. Some cases of occupational poisoning have been caused by alkylmercury compounds. Both the alkylmercury compounds and the hexachlorobenzene may give rise to intentional and unintentional pesticide residues in foods and hence exposure in man, but at a level which cannot be supposed to have any toxicological significance at present. The only exception is meat from seed-eating birds which may contain considerable levels of alkylmercury. Mercury waste from plants producing any kind of mercurials as well as from seed dressing stations may cause considerable levels of methylmercury in fish and thus a potential exposure. Hexachlorobenzene waste may also accumulate in fish. Besides these risks for humans, considerable effects on wildlife may be caused by alkylmercury-dressed seed.

CONCLUSIONS AND RECOMMENDATIONS OF A JOINT FAO/WHO MEETING ON THE USE OF MERCURIAL AND ALTERNATIVE COMPOUNDS AS SEED DRESSINGS
Dr J. F. Copplestone (WHO)

In order to consider the problems arising out of the use or misuse of organomercury and alternative compounds as seed dressings, a joint WHO/FAO meeting was convened in Geneva in March 1974. The group of experts approached the subject by weighing the health effects arising from the misuse of treated seed as food against the agricultural need for efficient fungicides. The meeting made a number of recommendations for the control of certain compounds and classes of compounds which, if followed by all concerned, will prevent further large-scale incidents of poisoning arising from the ingestion of treated seed. It also made a number of suggestions for research in order to tighten preventive measures.

The report of the meeting was published in WHO Technical Report Series No. 555 (1974) and the main recommendations are summarized at the end of the report.

THE 1971-1972 OUTBREAK OF POISONING IN IRAQ DUE TO THE INGESTION OF MERCURY TREATED GRAIN
Drs A. W. Al-Mufti and S. K. Tikriti (Iraq)

The cause, geography and course of the epidemic was reported. During the period 15 September 1971 to the first week of December, 73 000 metric tons of mercury-treated wheat and 22 000 tons of treated barley were distributed in Iraq. The first hospital admissions of alkylmercury-poisoned subjects occurred on 21 December 1971. Up to 27 March 1972 a total of 6148 patients were admitted to hospitals. The number of deaths in hospital was 452. It was pointed out that the number of hospital admissions does not represent the total number of cases or deaths. Only farmers were affected, no city-dwellers. The total number of cases was highest in the age interval 1-19 years, but if the age distribution in the rural population in Iraq was taken into consideration, all ages were equally affected with the exception of infants below the age of one year, who were proportionately less affected.

Discussion:

It was mentioned for comparison that the total number of cases in the outbreaks of ethylmercury poisoning in Iraq in 1955 was approximately 200 (70 deaths) and in 1960 was 1000 (200 deaths). Experiments on toxicity are often made on animals under excellent conditions. Animals or humans exposed in reality seldom live under such conditions. Thus extrapolation from animal experiments might underestimate the risks.

A possible combined action of organochlorine and alkylmercury compounds was discussed. A combined action of dieldrin and methylmercury has been shown in the rat kidney. Methylmercury has been shown to inhibit red blood cell delta-aminolevulinic acid dehydratase (ALAD) activity in human subjects exposed through fish eating. Anaemia is not a major effect of methylmercury exposure, but the finding implies a possible effect on haem containing enzymes, e.g. the microsomal drug-metabolizing enzymes of the liver which are also affected by the organochlorines. Effects on these enzymes by methyl-mercury are indicated by animal experiments.

In a discussion of which compounds should be used for seed treatment, it was stressed that alkylmercury compounds should be used only to treat nuclear stocks, i.e. seed of new and improved varieties in quantities used to provide further generations of seed, in amounts suitable for planting by farmers. Treatment of seed does not give rise to toxicologically significant levels of mercury in the grain.

It was pointed out that the numbers of cases poisoned by methylmercury through consumption of contaminated fish in Minamata and Niigata in Japan originally were reported as 121 and 26 respectively. Now the numbers are estimated at 700 and 500 respectively. The reasons were, (i) patients were overlooked earlier, (ii) progress of symptoms, (iii) new cases.

Session 3 - 9 November Moderator: Dr H. A. Shahrastani (Iraq)

FLAMELESS ATOMIC ABSORPTION ESTIMATION OF MERCURY
Drs L. Magos (UK) and A. M. Jawad (Iraq)

Absorption of ultraviolet light of 153.7 nm by atmospheric mercury vapour is the principle for the flameless atomic absorption determination of atomic mercury. In biological samples, the usual procedure is digestion followed by reduction to Hg^{o}. However, digestion takes time and effort and does not enable one to distinguish between inorganic and organic mercury.

These disadvantages were eliminated by using the following procedures. Organomercurials were converted to Hg^{++} by $CdCl_2$ synchronous to the reduction of Hg^{++} to Hg^{o}. These reactions were triggered by a change of pH from strong acid to strong alkaline and mercury vapour was washed from the reaction vessel into the gas cell of a mercury vapour meter by air. If $CdCl_2$ was omitted only inorganic Hg was reduced which made possible the estimation of methyl-mercury by difference.

The practical advantage of this method was proved in the emergency situation in 1972 when data on the extent of contamination of foodstuffs were urgently needed. Within a few hours after a decision had been made to put the method into practice, it was possible to advise the authorities that 3/4 of the kidneys supplied by the abattoir had less than 0.5 ppm mercury and none had more than 1.4 ppm. 10% of the kidney mercury was inorganic and meat on average had 12 times less mercury than the kidneys. The investigation suggested that meat was suitable for human consumption. At the same time a screening programme for wheat and flour made it possible to liberate large quantities of uncontaminated supplies for consumption.

GAS CHROMATOGRAPHIC DETERMINATION OF ORGANIC MERCURY COMPOUNDS IN SAMPLES FROM THE IRAQ EPIDEMIC
Drs F. F. Farris, R. Von Burg and J. Crispin Smith (USA)

The toxicities of organomercury compounds vary widely depending on the particular organic group bound to the metal. Therefore, to accurately evaluate the risk posed by exposure to these compounds, the specific organomercurial involved must be correctly identified. Westöö's developmental work, in the mid 1960's, established gas chromatography as a suitable technique for identification and quantitation of the volatile organomercurials. Since that time, investigators have modified her original method in attempts to maximize sensitivity and accuracy. Analyses of samples obtained during the Iraq epidemic were performed using a procedure (R. Von Burg, F. F. Farris and J. C. Smith, J. Chromatogr. In Press) which introduces a number of improvements over previous methods. Perhaps most importantly, it allows for the correction of individual sample recoveries by spiking each specimen with a small quantity of ^{203}Hg-methylmercury prior to extraction.

Initially, the Iraq poisonings were thought to be due to ethylmercury. However, analysis of a large number of wheat, barley and flour samples obtained primarily from Baghdad, Hilla and surrounding areas showed methylmercury to be the most common form of organomercury. Ethylmercury was also present in most of the grain and flour specimens but only at low levels.

This suggests that it may have been present as a contaminant in the methylmercury used for seed treatment. A limited number of tissue samples from domestic livestock and chickens, as well as from various species of wildlife were also analysed. In most cases, organomercury was either below measurable limits or present only in small quantities as methylmercury, indicating that if the animals had been exposed to significant amounts of treated grain this must have occurred at a time considerably prior to analysis.

In wheat samples methylmercury levels of 2-16 mg/kg were found, the average level was about 7 mg/kg. In barley, methylmercury levels were much lower. Ethylmercury levels were low or not detected in both wheat and barley. In barley comparison between gas chromatography and selective atomic absorption analysis indicated the presence of unidentified non-alkyl organomercurials.

ACTIVATION ANALYSIS: A VALUABLE TOOL IN THE OUTBREAK OF MERCURY POISONING
Drs H. A. Shahristani and M. Abbas (Iraq)

In Iraq during the outbreak of mercury poisoning in the winter of 1971-72, an urgent need arose for a large-scale mercury analysis programme. Activation analysis was employed for analysis of about 11 500 samples of meat, flour, and other food items during a three-month period. Both instrumental and destructive activation methods were used. A large-volume high-resolution Ge(Li) detector and two NaI detectors were used in the measurements. The data were analysed on a small pdp8 computer.

More than 99% of the samples were analysed instrumentally using the isotope ^{197}Hg (half-life 65 hours). The samples were irradiated in the Iraqi Nuclear Reactor. After irradation samples were cooled for one week before measurement to allow the interfering activities of ^{38}Cl, ^{56}Mn and ^{24}Na to decay out. A batch of 500 samples was irradiated daily while another 500 samples were being counted. Sensitivities down to 0.1 ppm were obtained with this technique.

Chemical separations were performed on samples of low mercury concentration. After irradiation the samples were dissolved and mercury precipitated as HgS from a basic solution after addition of a carrier. The mercury activity was counted on a high-efficiency NaI detector. Sensitivities of 0.01 ppm were obtained.

A new activation method for mercury was also developed based on ^{199m}Hg (half-life 43 minutes). The method is quite fast and purely instrumental. The samples were irradiated in a shield of cadmium, sodium, manganese, chlorine, and bromine to eliminate interfering activities. The sensitivity of the method is 0.5 ppm and the analysis time is about one hour. It is well-suited for yes-or-no situations when a quick answer is needed whether or not the sample contains more than 0.5 ppm mercury.

Discussion:

The fact that only 10% of the total mercury in sheep kidneys was found to be inorganic, was discussed. Higher figures have been reported in different species earlier. Possible explanations were species differences and a short time between exposure and slaughter. The low figure seemed even lower in light of the fact that sheep were fed barley and barley was mainly treated with alkoxyalkylmercury and arylmercury compounds and not by alkylmercury. The latter compounds are known to be more stable in the body than in the first two groups mentioned.

At the gas chromatographic analyses a considerable variation in loss of methylmercury during the extraction procedure had been noted and brought under control by the addition of $CH_3{}^{203}Hg$ to each sample. The reason for this variation is not known; absorption in lipid layers has been assumed. It is dependent on the skill and carefulness of the analyst. The addition of the radioactive isotope is more convenient than to use an internal standard in form of non-labelled methylmercury. It was asked whether the mercury levels found in treated seed in Iraq were those expected from other experience of treated seed. No information on this was available, but it is often found that a considerable variation may occur between different batches and in different parts of one batch.

In connexion with activation analysis, there was a discussion on the radioactivity of the shields. It was suggested that a permanent shield can be installed inside the reactor cave when a large number of analyses is to be performed by this technique.

Session 1 - 10 November Moderator: Dr S. F. Damluji (Iraq)

CLINICAL OVERVIEW
Dr S. F. Damluji for the Clinical Committee[1] (Iraq)

Sixty-six in-patients suffering from chronic methylmercury poisoning were examined in Baghdad during 1972. The poisoning was attributed to consumption of home-made bread prepared from seeds treated with mercurial fungicide. The age incidence ranged between four and 70 years.

Of the various clinical features encountered, the neurological symptoms and signs were predominant and included muscular weakness, numbness, unsteady gait, paraesthesia, dysarthria, mental disturbances and in the severe cases blindness, partial deafness, stupor, coma and death. Involvement of the cardiovascular, urinary, gastrointestinal and haemapoietic systems, which was commonly encountered in ethylmercury poisoning in the 1960 outbreak in Iraq, was unusual.

The severity of symptoms and signs was broadly speaking dose-dependent; the high exposure led to severe clinical manifestation, but variations existed. Judged by clinical manifestations, criteria were set for grading the severity of cases. The series included two asymptomatic cases, 20 mild, 20 moderate, 14 severe and 10 very severe. In the latter group five patients died from central nervous system failure.

The severely poisoned patients died irrespective of medical treatment. After two years of observation, most cases that were graded "mild" or "moderate" lost their symptoms completely. "Severe" cases improved slowly, although ataxia, diminution of visual field and acuity and paraesthesia were still present. Thus the irreversibility of neurological signs previously accepted has been disproved.

---

[1] Members of the Clinical Committee on Mercury Poisoning are: Dr S. F. Damluji (Chairman), Dr M. Murtadha (Secretary), Dr A. H. Al-Abbassi, Dr L. Amin-Zaki, Dr F. Bakir, Dr S. El-Hassani, Department of Medicine, Medical College, Baghdad University, Dr K. Al-Janabi, Dr K. Al-Omar, Karama Hospital, Dr J. Kuwaiti, Al-Shaab Hospital, Dr Fuad Audeau, Kadhimain Hospital, Dr M. A. Majeed, Medical City, Baghdad. The report was prepared by Dr S. F. Damluji.

CHEMICAL TYPES OF MERCURY IN PATIENTS
Drs J. Crispin Smith, F. F. Farris, and R. Von Burg (USA)

A correct toxicological assessment of the outbreak in Iraq required that the chemical form of mercury involved be known. The bulk of the analytical data from Iraq was obtained by atomic absorption spectrophotometry. This method measures total mercury and, selectively, inorganic mercury. A significant number of blood, hair, and post-mortem tissue samples were examined by a gas chromatographic procedure. It was shown that the non-inorganic mercury present could be accounted for as methylmercury. Although the inorganic mercury levels were also elevated, this form of mercury rarely accounted for more than 10% of the total mercury. No other organomercury compounds were detected in the human material. The samples examined were mainly from the provinces near Baghdad but some were from other areas of the country.

The outbreak in Iraq can be attributed to intoxication with methylmercury. Every effort should be made to discuss the toxicological relationships in terms of methylmercury concentrations.

TOXICOLOGICAL ASPECTS OF METHYLMERCURY POISONING IN IRAQ[1]
Drs H. I. Dhahir (Iraq) and T. W. Clarkson (USA)

This study is based on investigations made on hospitalized patients during the outbreak. In this outbreak, methylmercury was identified to be the predominant form of mercury in the grain and the biological materials examined. Total and inorganic Hg were determined by selective atomic absorption spectrophotometry in whole blood, plasma, milk and urine. Inorganic Hg accounted for the following average percentages of total Hg: 22% in plasma, 40% in milk and 73% in urine. Late in the outbreak it was found that the percent of inorganic Hg depended on the level of total Hg in the biological material e.g. in whole blood the percent inorganic was approximately 7% in samples having total Hg in excess of 3000 ng/ml. This percent, however, increased to 30-40% in samples having a total Hg of 100 ng/ml or less. Concentrations of total Hg in plasma and milk correlated well with that of whole blood ($r = 0.8$ and 0.9 respectively). However, concentrations of total Hg in urine did not correlate with that of whole blood ($r = 0.1$).

Clearance of total Hg from whole blood followed a single exponential decay process. The biological half-time averaged 65 days which is close to that reported on human volunteers given trace doses of radioactive methylmercury. However, the values of half-time varied markedly from one individual to another, e.g. in 16 patients studied, the individual half-time ranged from 40-105 days.

A study of the relationship between estimated intake of the contaminated bread and blood levels of Hg, mercury concentrations in samples of whole blood collected soon after the outbreak was related to the estimated total amount of Hg ingested from bread. The slope of the line was very close to that computed on metabolic parameters based on experiments with the radioactive tracer as mentioned earlier. Studies on the dose response relationship indicated that the toxic manifestations of methylmercury become detectable when individuals have accumulated 0.5-0.8 mg Hg/kg body weight. Data on the kinetics of methylmercury in individuals exposed to the poison in Iraq were presented.

Discussion:

The cause of the gastrointestinal (GI) symptoms seen in the 1971-72 Iraqi epidemic was discussed. Such effects were not seen in Japan. GI disturbancies were very severe in the 1955-56 and 1960 outbreaks of ethylmercury poisoning in Iraq and had also been noted in other cases of poisoning from alkylmercury

[1] See also Science, 181: 230-241, 1973).

treated seed. There was some speculation whether diarrhoea was a primary or contributory cause of death outside hospitals. However in 1971-72 the GI symptoms were slight. Possibly the GI symptoms in Iraq would be due to the fact that methylmercury is loosely bound on the seed and much of the mercury could actually be washed away. In fish methylmercury is bound to proteins. Also the dose may be important.

No information was available on the background frequencies of different neurologic symptoms in an Iraqi population.

The reason for levels of inorganic mercury of 5-20% of total mercury in wheat samples was discussed. A possible presence of small amounts of other organic mercury compounds than alkylmercury might have come out as inorganic mercury on analysis.

It was also assumed that the methylmercury preparation might have contained impurities of inorganic mercury, and that breakdown during storage might possibly have occurred. In barley, low methylmercury levels were found. Analyses of about 60 samples at the Swedish Institute of Water and Air Pollution Research indicated the presence of methoxypropylmercury and phenylmercury in barley. Little exact information was available on compounds or amounts used for treatment of the wheat and barley.

Session 2 - 10 November Moderator: Dr S. F. Damluji (Iraq)

NEUROLOGICAL STUDY
Drs H. Rustam, T. Hamdi (Iraq) and R. Von Burg (USA)

Fifty-three patients were examined neurologically and followed for two years. Multiple system involvement was evident in the majority of the patients and cerebellar deficit was the most common and most disabling symptom. Seventeen patients suffered diffuse brain damage similar to encephalopathy with suggestive evidence of lesion of the hypothalamus. Clinical pictures resembling decortication, decerebration, and akinetic mutism were seen in some of the encephalitic patients. Sensory impairment clinically resembled peripheral polyneuropathy but this was not confirmed electrophysiologically. Visual field constriction of different severity with sparing of central vision pointed to cortical lesion while reduction of visual acuity was possibly due to reversible retrobulbar optic neuritis. Six patients had optic atrophy, in three it was bilateral and one patient had blurred discs. Twenty patients showed definite pyramidal tract defect but in none of them was this the only system involved as in motor neuron disease. Seventeen patients had involuntary movements of various types and only four had clear signs of extrapyramidal lesion.

No correlation could be obtained between the severity of poisoning and mercury blood levels. Some patients were almost asymptomatic with mercury blood levels higher than some of the encephalitic patients. Individual variations in sensitivity to mercury appeared to be a decisive factor.

The severely poisoned patients either deteriorated rapidly and died within two to three weeks or survived totally incapacitated. The mildly and moderately affected patients recovered remarkably with or without treatment by mercury binding agents. Early administration of these agents seems to be of crucial importance. Improvement was most evident in cerebellar function, superficial sensation, and visual acuity.

ELECTROPHYSIOLOGICAL OBSERVATIONS OF METHYLMERCURY POISONED PATIENTS[1]
Drs R. Von Burg, (USA), H. Rustam, L. Amin-Zaki and S. El-Hassani (Iraq)

The earliest signs and symptoms associated with methylmercury intoxication suggest a neurological dysfunction similar to peripheral polyneuropathy (1). Classically, such a condition is amenable to electrophysiological confirmation. However, this technique failed to confirm such a disorder in the patients of the Iraqi methylmercury epidemic of 1972. Instead, the data suggest two alternative sites of damage.

One of these areas could be the lower brain stem since intoxicated patients demonstrated lower thresholds for eliciting the H reflex as well as clinical signs normally associated with this type of damage.

The other site of damage could be at some point in the neuromuscular linkage. Some of the patients exhibited myoneural transmission failure similar to that seen in myasthenia gravis. This failure responded to intramuscular injection of neostigmine. Subsequent neostigmine therapy significantly improved the clinical condition and clinical strength of the patients tested during the course of a procedure that was interspersed with placebo administration.

Although the exact mode of action of methylmercury in this regard is still unknown, preliminary investigations on isolated rat phrenic nerve-diaphragm preparations indicate that methylmercury can hasten muscle fatigue and increase the tolerance to a fixed dose of neostigmine.

TISSUE LEVELS IN ORGANOMERCURY POISONING
Dr T. Saleem for the Clinical Committee (Iraq)

Tissues from eight autopsies of patients with organomercury poisoning were studied: two still-born twins and their mother who died a few hours after delivery, one one-month old baby, and four more adults. Tissue levels (including the central nervous system) in the mothers and the still-born infants were similar, indicating a free trans-placental transfer. In all cases, more mercury was deposited in the grey matter of the brain than in the rest of the central nervous system. The mercury in the kidneys was mostly inorganic. High levels were noted in the bile of the gall bladder but low levels in the cerebrospinal vitreous and pericardial fluids. Histologically, there was marked degeneration of the nerve cells in the central nervous system in all cases and nerve cells were virtually absent in sections of the central nervous system of the still-born infants.

Discussion:

In the discussion it was pointed out that paraesthesia of the extremities is a highly nonspecific symptom. Numbness periorally, in tongue and in mouth, is more specific to methylmercury poisoning. Disturbances of deep sensation might be more reliable. In published estimations on dose-response relationships (*Science*, 181: 230-241, 1973) the "background" of paraesthesia had been considered in the evaluation. It was obvious that some non-symptomatic subjects or mild cases had mercury levels in blood and hair which were much higher than severe cases. On a group basis, however, there was a good relationship between blood and hair levels (extrapolated back to the time of the known end of exposure) and severity of the disease.

---

[1] See also Bull. Environm. Contm. Toxicol., 12: 81-85, 1974 and EEG Clin. Electrophysiol., 37: 381-392, 1974.

In Japan histopathological studies recently have shown peripheral nerve to be effected in all cases studied. Seven years after the Niigata epidemic the motor nerve conduction velocity was reduced in patients and there was a negative correlation with the hair mercury levels measured at the time of the epidemic. The studies made in Iraq did not show any changes in conduction velocity. A study of some of the patients has been reported earlier (Leguesne et al., J. Neurol. Neurosurg. & Psych., 37: 333-339, 1974). The results were very similar. The findings did not exclude an effect on the central nervous system, but rather indicated a possible effect on central cholinergic neurons. The latency period between exposure and onset of symptoms in single dose methylmercury exposure might be explained by slow distribution of methylmercury to the site of action. It was pointed out that diphenylhydantion caused myoneural blockade and cerebellar effects but no sensory symptoms. Thus an effect on central cholinergic neurons by methylmercury did not seem likely.

The gall of the common bile duct in methylmercury exposed monkeys contains less mercury than bile of the gall bladder.

The two still-born infants were exposed for 4 to 5 months during gestation. It was pointed out that the exfoliative dermatitis observed in some of the Iraqi patients might be due to hypersensitivity to mercury, perhaps to inorganic mercury. The eosinophilia observed in many patients may support the idea of an allergic reaction. No cutaneous tests had been made. There was a definite recovery of the Iraqi patients both in regard to sensory and motor function (regarding vision, see below). It was discussed whether this was due to non-damaged neurons taking up the functions of the damaged ones or if it was due to transient neurons tissue oedema. Other possibilities were also mentioned, such as the recovery of protein synthesis. The great value of and strong need for rehabilitation facilities, even at this time, was stressed (in next discussion).

Session 3 - 10 November Moderator: Dr S. F. Damluji (Iraq)

PSYCHIATRIC ASPECTS OF METHYLMERCURY POISONING
Dr H. I. Maghazachi (Iraq)

In 1972 an outbreak of mercury poisoning took place in Iraq. The present study was concerned with the psychiatric manifestations exhibited by the poisoned patients.

Forty-three patients are included, 21 males and 22 females ranging in age from 2 to 70 years. 74% showed some degree of depression; their mercury levels were higher than the average values for the whole group, and considerably higher than the levels of the non-depressed patients. Irritability was observed in 44% of the patients, all except one being under 30 years of age.

There was general improvement in the mental states of the patients who were hospitalized. Mercury binding compounds did not seem to have a significant effect in enhancing the recovery from the depressive state.

Some of the relevant experimental studies dealing with the biochemical changes in animals exposed to various mercurial compounds were reviewed. It is possible that there may be two distinct syndromes, due to organic and inorganic mercury poisoning.

OPHTHALMIC MANIFESTATIONS OF METHYLMERCURY POISONING
Drs S. Sab El Aish and G. Hilmi (Iraq)

About 100 patients suffering from organomercury poisoning were hospitalized in the Medical City of Baghdad University, where they received thorough ophthalmic study in the period between March and December 1972, and were reviewed again some 10 months later.

Onset of visual loss was usually early, though not the earliest sign of poisoning. Only occasional cases stated that blurring of vision was the signal and it occurred at the same time as numbness, ataxia and other neurogenic symptoms. A few patients mentioned xanthopia as the beginning of the visual disturbances; some had experienced recurrent attacks of blackouts that eventually culminated in persistant visual loss. The severity of the visual loss was variable, even between the patients from families who seemed to be exposed to the same dose. There was no close correlation between the degree of visual disturbances and the amount of blood mercury as estimated in the early weeks in hospital: most of the patients who suffered from visual disturbances had blood mercury above 1000 ng/ml before any treatment was started. No visual disturbances could be detected or reported in victims who had a blood mercury value of less than 500 ng/ml before any treatment.

Visual field defects have been more striking than impairment of visual acuity. The most common finding was concentric contraction or depression of the visual fields. The central vision was almost always spared. On following up the patients, some showed slight improvement and enlargement of the visual fields. A few patients improved from perceiving only light to just seeing hand movement or counting fingers. The majority of the cases are still seriously disabled; none of the seriously affected people improved to normal vision.

The corneal changes observed did not seem to be definitely related to mercury, apart from the loss of corneal sensation in severely affected patients. Slight (5% of cases) or no changes were noticed in the lens, even in severe cases. The anterior chamber always appeared clear and healthy. A semi-dilated pupil with sluggish or no reaction to light was seen in children totally blind or with only perception of light. Adults had normally functioning pupils.

On fundoscopy, most of the patients showed slate pigmentation around the optic disc. The disc itself showed little change. Ten per cent of the cases who had badly affected vision had a hyperemic disc with an ill-defined margin and with swelling ranging between one-and-a-half and two diopters.

Discussion:

In the discussion it was pointed out that it was wise to be cautious in attributing depression to a toxic effect of methylmercury on the brain. It might very well be caused by the social and medical situation of the patients.

Note: All discussion on visual disturbances has been summarized under Session 4, 10 November.

Session 4 - 10 November Moderator: Dr A. Khalidi (Iraq)

NOTES ON THE CLINICAL PROGRESS OF METHYLMERCURY POISONING
Dr L. Amin-Zaki et al. (Iraq)

Fifty-four children, all of them with a history of ingestion of bread made from methylmercury treated wheat, and all of them falling into the same range of very high exposure, were studied. The patients were classified according to their clinical severity into asymptomatic, mild, moderate, severe and very severe and the definitions were given. The clinical manifestations observed on admission were discussed. Progress of the various groups and of the major neurological manifestations after one year and two years of the onset show that the clinical picture improved greatly. All of the mild cases, seven of 10 moderate cases and one out of 13 severe cases recovered normal physiological function. Seven children were left with complete physical and mental incapacitation. The rest of the cases made various degrees of improvement of physiological function.

EPIDEMIOLOGY OF ANTIBIOTIC AND HEAVY METAL RESISTANCE IN BACTERIA
Dr A. J. Thewaini et al. (Iraq)

Staphylococci were isolated from rural and urban populations in Iraq, who were not known to be exposed to either heavy metals or antibiotics. The antibiotic and heavy metal resistance patterns of these strains were analysed in both mannitol-fermenting and non-fermenting strains. Over 90% of the strains were resistant to at least one of the following antibiotics: penicillin, chloramphenicol, erythromycin, tetracycline, cephalothin, hincomycine or methicillin. In general, mannitol-fermenting strains were resistant to penicillin and cupric ions. Mannitol negative strains were more frequently associated with mercuric ion and tetracycline resistance.

The possibility of selection of heavy metal resistant strains due to exposure to severe poisoning by methylmercury was examined. No significant increase in mercuric ion resistant strains of staphylococci or Escherichia coli were detected in exposed populations as compared to control groups. The possible reasons for this result are discussed.

Intestinal and water E. coli were found to differ markedly in their resistance to antibiotics and heavy metals. The frequency of resistance was more common in the E. coli of intestinal origin than in the E. coli of water origin.

Antibiotic resistance as well as mercury resistance was uncommon in non-agglutinable vibrios of water origin. However, cadmium resistance was common in these organisms.

CHROMOSOMAL STUDIES
Dr N. Farman

5741 cells from lymphocyte cultures grown from 65 methylmercury-poisoned subjects (blood mercury 300-4500 ng/ml) and 30 "non-exposed" controls (blood mercury levels 1-20 ng/ml) were analysed cytogenetically. Isochromatid-type aberrations were found in 6.5% of the metaphases in the poisoned subjects and in 5.4% of the cells from controls. This was not a statistically significant difference. There was no difference between the groups in frequency of aneuploidia, nor was there any correlation between blood mercury levels and frequency of aberrations. A statistical analysis showed a non-random distribution of the chromosome breaks, the frequency of aberrations in some chromosomes being higher than in others.

Discussion:

An extensive discussion on visual findings took place in the discussion on four papers. Blurred vision was described in many cases. The prognosis of this was very good. Optical atrophy was reported in some children in one series but was reported as not present in another. Retrobulbar optical neuritis was suspected in some cases but was considered unlikely by other speakers as no central scotomas were observed. Constriction of visual fields was present in many patients and also blindness. Disturbances of eye movements were present in some cases in one series but not at all in another. In some patients a very dramatic improvement occurred from total blindness to some degree of vision. In some of these patients a constriction of the visual fields remained. In one case a constricted visual field had become normal. In some additional cases some improvement might have occurred but was not certain. It was recognized that it might be difficult to distinguish between actual improvement of vision and improved ability to manage with impaired vision. In Japan many patients had disturbances of eye movements. Also, improvement of visual fields was observed in a few cases, but it was followed by progressive impairment in a few years.

The social situation of the patients and their families was discussed. Most of them took the disaster in a quiet way but of course many were anxious.

Regarding the lack of effects on lymphocyte chromosomes, it was pointed out that lymphocytes may live for decades and that thus the exposure time might be of major importance. An increased frequency of aberrations had earlier been observed in Swedes exposed to methylmercury through consumption of contaminated fish. In those subjects the exposure had lasted for at least three years, in many of them 20 years or more. In Iraq the exposure time was short, a few months.

Session 1 - 11 November Moderator: Dr F. Bakir (Iraq)

SIGNIFICANCE OF MERCURY LEVELS IN HAIR[1]
Drs T. Giovanoli-Jakubczak (Poland) and G. Berg (USA)

Sequential measurements of total and inorganic mercury in 1 cm segments from bundles of human hair have been used as a convenient method for tracing the history of exposure of people to methylmercury compounds. One key item of information sought in epidemiological studies of this kind is the time of initial uptake of high doses of the mercurial derivatives. Extrapolation of the accumulation curve back to the background level have, however, been ambiguous because the curves were sigmoid, although the history of exposure indicated a linear accumulation in hair after initial acute exposure. This discrepancy was explained by postulating that the distribution of mercury in individual hair fibres was in accord with theory, but the fibres were displaced in relation to each other in the tested bundle. The hypothesis was confirmed by analyses of 1 cm segments of individual hair fibres and two models were investigated to account for the displacement.

Data on the distribution of mercury in hair were converted by a mathematical model into information about the key indices of exposure, including times of onset and termination, peak concentration in hair, and half-time of retention in blood. A computer simulation of a displacement due to differential rates of growth of individual hair was demonstrated (first model). In the second model the consequences of disturbing the alignment of hair before cutting the bundle into segments was measured.

Conventional methods of hair sampling and fitting the resulting data to a curve were shown to introduce systematic errors underestimating peak concentrations and overestimating retention times. These errors were minimized by practical modification of hair sampling procedures and by a new graphic method for deriving the measurements of distribution of the trace mercury in hair.

MERCURY IN HAIR AS AN INDICATOR OF TOTAL BODY BURDEN[2]
Drs H. A. Shahristani, K. Shibab and I. K. Al-Haddad (Iraq)

Hair is known to concentrate mercury and in general the concentration of mercury in hair is proportional to and many times higher than its concentration in the blood.

In this work the variation of the mercury concentration in human head hair was used to follow the history of poisoning in people who ingested grain treated with methylmercury. Instrumental neutron activation analysis technique was used for mercury determination.

---

[1] See also Arch. Environm. Health, 28: 139-144, 1974.

[2] See also Arch. Environm. Health, 28: 342-345, 1974.

The initial rising slope of mercury concentration along the hair was shown to be proportional to the daily intake of methylmercury per kg body weight.

The ratio of the concentration of methylmercury in human head hair to the average body concentration was found to be about 200. Using this ratio and measuring mercury concentration in hair the total body-burden can be calculated. In patients studied, the maximum body-burden ranged from 0.6 to 3 mg/kg in persons showing mild symptoms, from 1 to 4 mg/kg in persons with moderate symptoms, and from 2 to 8 mg/kg in people with severe symptoms.

The curve of the variation of mercury concentrations along the hair was also used to calculate the biological half-life of methylmercury in man. Forty-eight persons were studied and it was found that the frequency curve (population distribution curve) is grouped into two distinct regions. About 90% of the population had a biological half-life for methylmercury of 35-100 days and 10% showed high values of 110-120 days.

TISSUE LEVELS OF MERCURY IN AUTOPSY MATERIAL
Drs L. Magos (UK), T. W. Clarkson (USA), F. Bakir, A. M. Jawad and M. H. Al-Soffi (Iraq)

Fifty autopsy specimens of liver conserved in ethanol were analysed for total mercury with the method of Magos (1971). 26% of the specimens contained less than 10 µg/g mercury with a minimum value of 1.4 µg/g indicating that death in suspected cases was not always due to lethal exposure to methylmercury. The methylmercury concentration in 54% of the livers was between 10 to 30 µg/g and in 20% of the specimens more than 30 µg/g with a maximum of 76 µg/g. In the majority of livers the mercury level was the same as that reported in the Minamata cases but time elapsing between the onset of symptoms and death was most likely shorter and the exposure of those who died without hospitalization may have continued until death. However, the maximum liver concentration in fatal cases in Iraq was lower than the maximum value based on the extrapolation of the data of the Minamata victims. In Iraq the dressed wheat was consumed within a relatively short time compared with the prolonged intake of methylmercury with fish in Japan. In methylmercury poisoning of occupational origin where death occurred only 30 days after the onset of symptoms, livers contained only 14 and 20 µg mercury (Swensson, 1952). Limited additional estimations have shown that 71% of the liver mercury was organic, kidneys accumulated 4 times more mercury than livers and the level of mercury in the liver of a 7 months old foetus was only 25% of that in the liver of the mother. In a patient who died in hospital with a blood mercury level of 4.1 µg/ml, the liver contained 16.5 µg/g mercury.

Discussion:

It was pointed out that hair sample sections in excess of 1 cm of length give a considerable margin of error when used for analysis of mercury in order to estimate peak body burdens. One half-time of methylmercury corresponds to about 2 cm growth of hair. It takes about one month after ingestion of a dose of lead before the lead level rises in hair. The same should be expected in methylmercury exposure. Experience in cats indicates one month time lag.

The subjects who eliminate methylmercury slowly were discussed. There were no indications that age, sex, diet or rate of hair growth influence this, nor had they abnormal standard liver function tests. In spite of this a biliary factor was proposed. The slow eliminators did not belong to a special group in regard to severity of symptoms and signs. It was also queried whether slow elimination rates should be used when recalculations are made of mercury levels in blood or hair measured after the end of exposure to levels expected to have been present at the date of the end of exposure. That way of calculation would have added an extra tail on the dose-response curve based on the Iraqi experience that had already been published in Science, 181: 230-241, 1973. In recalculations of groups of subjects, average values of elimination rates had been

used. The inter-individual variation could then be accounted for by a greater safety margin in estimations of acceptable daily intakes, etc. In individuals, however, the individual rate should be used.

It was pointed out that the Minamata liver mercury levels were higher than the Niigata ones, and that the latter levels fit well with those found in Iraq. Differences in exposure - chronic in Minamata versus acute or subacute in Iraq - could perhaps explain the difference. In Niigata the exposure was probably shorter than in Minamata. Also, possible differences in selenium intake was discussed, as selenium has been shown to protect experimental animals from methylmercury poisoning. Levels of selenium in fish are high - in grass they vary very much. Selenium analyses were being made in Iraq. It was also pointed out that analytical problems may account for some of the differences between mercury levels in certain tissues in Minamata and Iraq. Also the possibility that the exposure was not due to the same organomercury compounds was mentioned.

Session 2 - 11 November Moderator: Dr A. W. Al-Mufti

TREATMENT I
Drs F. Bakir and A. Khalidi for the Clinical Committee (Iraq) and T. W. Clarkson and M. Greenwood (USA)

D-penicillamine, N-acetyl-DL-penicillamine and unithiol were given to patients. After an initial increase in mercury levels in blood, there was a decrease of 10-20%. An increase of mercury in urine was seen. There was no clear-cut effect on the clinical picture. Mild cases did improve, severe cases did not, as was the case in untreated controls.

TREATMENT II - MOBILIZATION OF METHYLMERCURY FROM PATIENTS BY THE USE OF BINDING AGENTS
Drs L. Amin-Zaki, S. El-Hassani, M. A. Majeed (Iraq), L. Magos (UK), T. W. Clarkson and M. Greenwood (USA)

Patients were treated with one of the following mercury binding agents: a polythiol resin, D-penicillamine or N-acetyl-DL-penicillamine. The dosage for the polythiol resin was from 40 to 160 mg/kg and for the penicillamines 20 to 40 mg/kg. The treatment period was usually nine days, but in some cases, was extended to 21 days. Several conclusions were drawn from these studies. First, blood levels of methylmercury could be dramatically reduced but the extent of the reduction varied from patient to patient. Second, the penicillamines produce an elevation in blood levels lasting one to three days before a reduction takes place. Third, a second period of treatment was always less effective than the first period of treatment at the same dosage. Fourth, the penicillamines are more effective in mobilizing methylmercury when given at a dosage of 2 g/day/adult, than at a dosage of 1 g/day as previously reported for treatment of inorganic mercury poisoning. Fifth, the mercury binding agents should be given daily until the blood levels have fallen to an acceptable value. In the past, the usual practice has been to intersperse periods of treatment with periods when treatment was withdrawn. This procedure resulted in slowing the rate of clearance of methylmercury from blood as compared to continued administration.

No adverse symptoms or signs attributable to the drugs were noticed throughout the treatment. It is felt that the greatest benefit comes when these agents are given as soon as possible after exposure, to reduce mercury levels in the body before the onset of irreversible damage to the central nervous system.

EXTRACORPOREAL COMPLEXING HAEMODIALYSIS SYSTEM FOR THE TREATMENT OF METHYLMERCURY POISONING II: IN VIVO APPLICATIONS IN THE DOG
Drs P. J. Kostyniak, T. W. Clarkson, J. J. Vostal (USA) and A. H. Abbassi (Iraq)

Greater than 99% of the methylmercury in blood is protein bound, probably as a result of its high chemical affinity for sulfhydryl groups. The binding of methylmercury to protein sulfhydryl groups can be reversed by the addition of sulfhydryl containing complexing agents. For example, the sulfhydryl containing amino acid, cysteine, added to blood in sufficient concentrations will convert over half of the methylmercury in whole blood to a non-protein bound diffusible form. This information is applied to the in vivo use of a standard haemodialyzer (for description see abstract by Abbasi et al. next paper) for the removal of methylmercury from dogs dosed with methylmercury chloride.

At an extracorporeal cysteine concentration of 10^{-2}M in whole blood, it was possible to achieve a 40% reduction in whole blood mercury concentrations during a single pass through the dialyzer using a blood flow of 30 ml/min. The blood compartment showed a biphasic exponential decline in methylmercury with time during dialysis. More mercury was removed during dialysis than could be accounted for by the reduction in blood concentrations alone indicating that mobilization must also have taken place from tissue compartments. The reduction in whole body methylmercury during a five-hour dialysis period was as high as 14% of the original dose administered 18 hours previously. Animals dosed with methylmercury labelled with the gamma ray emitting isotope ^{203}Hg, exhibited a reduction in radioactivity in the head region suggesting that methylmercury had been removed from the brain, the principal target organ.

EXTRACORPOREAL REGIONAL COMPLEXATION DIALYSIS IN PATIENTS WITH MERCURY POISONING
Dr A. H. Abbassi (Iraq) et al. Read by Dr P. J. Kostyniak (USA)

An outbreak of methylmercury poisoning occurred in Iraq in late 1971. Exposure was due to the consumption of home-made bread prepared from seeds dressed with fungicide containing methylmercury. The number of cases and the seriousness of the exposure in some, posed a therapeutic challenge.

In view of the severe damage which methylmercury can cause to the nervous system, it was obvious that rapid elimination of the methylmercury from the body was vital if tissue damage was to be minimized.

Chelation therapy using complexing agents containing free sulfahydral groups or the use of non-absorbable polythiol resins, do not seem to be adequate even at their best in the face of dangerously high methylmercury ingestion.

A new approach to the problem was described, utilizing extracorporeal regional complexation dialysis, using the Travenol RSP 145 twin coil dialyzer. Essentially this consists of a blood compartment and dialysate compartment, separated by semi-permeable dialysis membrane. Using an infusion pump, arterial blood from the patient is mixed extracorporeally with the complexing agent before it enters the dialysis coil, where redistribution, complexation and diffusion of the complexated methylmercury and free complexing agent occur. The blood is then returned to the patient having lost (as estimations indicated) an important part of its methylmercury and the infused complexing agent. N-acetyl penicillamine was used early in the project, but cysteine which is devoid of side effects was substituted later. The amount of methylmercury depleted was found to be related to the dialyzer blood flow and the concentration in the blood of the infused complexing agent. These parameters can be manipulated to achieve the optimum results.

The well-known rapid equilibration of methylmercury in the blood and other parts of the body ensures a constant decline of tissue levels with falling blood levels. As far as one can tell, no harmful effects are encountered using this procedure. It was difficult to tell if clinical improvement was obtained as these cases were received very late and had sustained widespread organ damage.

Discussion:

The rationale of treatment was queried and it was emphasized that this could not be reflected since there is little information on the nature of damage to the nervous system and the rate at which this develops. It is known from animal experiments that there is a delay in distribution of methylmercury to the brain. Also, in man there is a latency period between a single exposure and onset of symptoms. It might be that a certain mercury level must be present in the brain cell for some time before damage occurs. In that case, cells may be spared by mercury mobilization. Although the general impression of some clinicians was that improvement in some cases occurred after treatment (as compared to untreated patients) no data proving this were presented. Other clinicians had not noted improvement by treatment (penicillamine, unithiol, polythion resin). The statistical treatment of blood decay curves in treated subjects was questioned, as it was claimed by several speakers that the penicillamines, unithiol or polythiol resin, did lower the blood mercury level. Some effect on blood levels seemed likely but no information on effects on total body burden were available. The fact that the blood mercury decay curve did not after treatment return to the track which could be expected from extrapolation from the pretreatment slope, but on a lower level, might however indicate a possible effect on the total body burden. It was stressed that a possibly way of treating methylmercury poisoned subjects should be a gall bladder fistula.

Session 3 - 11 November Moderator: Dr A. Khalidi

Papers Presented (Short Presentations)

EFFECTS OF COOKING AND BAKING ON FOOD CONTAINING ORGANOMERCURY
Drs A. Khalidi (Iraq) and J. Crispin Smith (USA)

Mercury levels in foods were studied before and after different kinds of preparation. No change in mercury concentration was found before and after baking of bread. In cooking, frying and roasting of meat there was a considerable decrease in the mercury levels, the levels after preparation being only about 20% of the pre-preparation levels.

PATHOLOGY OF THE LIVER
Drs M. Hassani and T. Saleem (Iraq)

In autopsy cases the levels of mercury in brain and liver were comparable. Some changes were found on light microscopy of the liver, but were inconclusive. They might well be explained by malnutrition. In electron microscopy very large lysosomes and inclusion bodies were noted.

ALKYLMERCURY POISONING - HAEMATOLOGICAL OBSERVATIONS
Dr A. M. Al-Hilali (Iraq).

Some haematological investigations, including a haemogram, prothrombin time and ESR, were performed on most of the cases with proven mercury poisoning included in the clinical study. Other tests, like bone marrow cytology, RBC osmotic fragility, platelet count and reticulocyte count, were performed on some of the cases randomly.

Positive findings included prolonged prothrombin time in 80% of the cases tested and eosinophilia in 43%. ESR was raised significantly in 20% of cases tested and there was leukopenia in 10% and leukocytosis in 8%. Only one out of six marrows examined was hypoplastic while no other case showed peripheral pancytopenia, leukopenia and thrombocytopenia.

Results other than eosinophilia and prolonged prothrombin time were not considered as significant since they did not represent a consistent picture in relation to mercury poisoning. High ESR was commented upon and a small experiment was performed on rabbits later to elucidate the exact coagulation factor deficiency leading to prolonged prothrombin time.

ELECTROCARDIOGRAPHIC FINDINGS
Drs M. Murthada, A. H. Abbassi, K. Hilmi and J. Kuwaiti (Iraq)

A group of 50 patients admitted to hospital after ingestion of methylmercury in the form of home-made bread prepared from treated seeds was studied with 12-lead electrocardiograms, in addition to detailed clinical and laboratory examinations, including blood mercury levels.

Various changes were noted in the electrocardiograms of 25 of the patients studied. ST-T changes formed the major abnormality, noted in eight patients (16%).

These results were contrasted with the findings in the earlier outbreak in Iraq in which the incidence of electrocardiographic changes was much higher. Possible reasons for this discrepancy were discussed. No strict correlation was found between the electrocardiographic changes and the blood mercury level.

METHYLMERCURY KINETICS DURING EXCHANGE TRANSFUSION
Drs S. El-Hassani, L. Amin-Zaki, M. A. Majeed (Iraq) and T. W. Clarkson and R. A. Doherty (USA)

Early in the outbreak, four patients with blood total mercury concentrations above 1500 ng/ml were treated with exchange-transfusion as an emergency measure. During the transfusion period, blood levels were observed to fall dramatically. However in the post-infusion period, the concentration of mercury in blood slowly rose to values close to pre-exchange levels. For example, in one patient, the blood level at the start of the experiment was 1500 ng/ml and fell to 750 ng/ml two hours later at the end of exchange. In the ensuing 10 hours, the blood levels slowly rose to a maximum close to 1400 ng/Hg/ml. A slow decline was then observed. It may be calculated that approximately 3 to 7% of the body burden is removed by this procedure.

Discussion

As regards the experiments on levels of mercury in foods before and after treatment, it was pointed out that the lack of effect on levels in bread was in agreement with experience on cooking and frying of methylmercury-contaminated fish in Sweden and USA. On the reason for the decrease in the levels in meat, the possibility that the meat might have contained other organomercurials than methylmercury was suggested.

In the discussion of the paper on morphologic liver changes, it was mentioned that lysosome changes had also been noted in Japan.

As to effects on the heart, it was discussed whether ethylmercury affects the heart while methylmercury does not do so. The experience from the 1955-56 and 1960 Iraqi ethylmercury poisoning outbreaks, as well as some animal experiments, seems to support this assumption.

In the discussion on exchange transfusions it was pointed out that one postnatal case did improve, while one prenatal case did not. One non-symptomatic child did not develop any symptoms, possibly because of the exchange transfusion treatment.

Session 4 - 11 November Moderator: T. W. Clarkson (USA)

Papers Presented (Short Presentations)

ERYTHROCYTE SURVIVAL STUDIES AND HAEMATOLOGICAL ASSESSMENT
Drs L. Amin-Zaki, T. Al-Hitti, M. A. Majeed (Iraq) and R. A. Doherty (USA)

Red blood cells from four patients with blood total mercury concentrations above 2000 ng/ml were tagged with ^{51}chromium using the standard sodium chromate labelling procedure. Red cell survival half-times of ^{51}Cr-erythrocytes in self-transfused patients were determined, as well as half-times of survival when the same ^{51}Cr-erythrocytes were transfused into normal volunteers. In addition the survival half-time of ^{51}Cr-labelled erythrocytes from a normal volunteer transfused into a methylmercury patient was also determined.

The red cell survival half-times were correlated with haematologic indices including haematocrits, haemoglobin concentrations, reticulocyte counts and haptoglobin levels in these as well as other methylmercury-poisoned patients.

No conclusive effects of methylmercury exposure on red blood cell survival time were noted.

CLINICAL STUDIES ON HOSPITALIZED AND OTHER PATIENTS IN NORTHERN IRAQ
Dr A. R. S. Dabbagh (Iraq)

The Arbil district was seriously affected during the methylmercury poisoning catastrophe. Two hundred and sixteen persons were admitted to Arbil Republic Hospital (109 males, 107 females) aged:

1-5 years	5-10 years	10-15 years	15-20 years	over 20 years
29	45	24	8	110

Sixteen had no signs or symptoms of poisoning.

Most of the cases were admitted late. Only 15 (7.5%) had gastrointestinal symptoms on admission. Twenty-nine (14.5%) had only paraesthesia, numbness and generalized weakness. Seventy-nine (39.5%) had ataxia, 26 (13%) had loss of or impaired vision and 19 (9.5%) impaired hearing or complete deafness.

There was only one hospital death (0.5%), but this was not the only death as 14 (74%) of our patients left hospital without notice and some were seriously ill.

These patients were traced to their villages where they were also studied by the Rochester University team, sampling 10 of these villages with an overall population of 3627. One hundred and thirty five had signs and symptoms of mercury poisoning, i.e. (3.7%) of the population.

It was curious to note that most of the cases came from the plain area around Arbil and only a few from the mountains. This is probably due to the fact that people living on the plain depend mostly on wheat as their main diet, while mountain people take a more mixed diet.

CORRELATION OF BLOOD MERCURY LEVELS AND CLINICAL PICTURE IN MOSUL
Drs M. A. Mahmood, S. Sabbagh, A. T. Saigh (Iraq)

Clinical findings in a group of patients were presented. Aphasia, in this case inability to speak, was noted in some cases, improvement of blindness to some degree of vision was seen in one case. BAL treatment caused deterioration in symptoms. Blood and hair was analysed for mercury. No correlation between severity of symptoms and levels was found. Two cases of nephrotic syndrome found incidentally had 45 and 54 ng Hg/ml blood.

NORMAL MERCURY LEVELS IN IRAQ
Drs A. Khalidi, F. Bakir, S. F. Damluji and A. W. Al-Mufti (Iraq)

In November 1972, 429 blood samples were obtained from subjects with no known exposure to mercury. About 80% had levels of 0-20 ng Hg/ml, 6 over 100 ng Hg/ml. In a second series of non-exposed subjects, 30 (approx.) samples with levels of 0-30 ng Hg/ml were reported.

LETHAL LEVELS OF MERCURY IN HUMANS
Drs M. I. Hilmy, R. A. Rachim and A. H. Abbassi (Iraq)

Thirteen tissue specimens of humans who died of mercury poisoning in hospital were analysed for total content of mercury. Solutions of the specimens were prepared by a modified wet ashing technique and the total mercury level was determined using the flameless method of atomic absorption spectroscopy. Loss of mercury vapour was minimized by using a closed system with proper cooling. The kidney content of mercury was the highest (8-9 ppm) followed by the liver and the cerebellum, while the lethal blood level of mercury was about 15 ppm. The above values were compared with controls obtained from humans who died from various accidents and showed no signs of mercury poisoning.

Discussion

In the Japanese outbreaks, total inability to speak was not observed. In Iraq, BAL treatment had been observed to cause deterioration in symptoms. In the 1960 Iraqi outbreak of ethylmercury poisoning the outcome of a patient seemed unaffected by BAL treatment. Some side effects of BAL had been seen. Animal experiments suggest that the reason for the deteriorative effect of BAL is a faster and/or increased distribution of methylmercury to the brain. A possible combined action of malnutrition and methylmercury poisoning was suggested. Although one speaker had an impression that there might be an additive effect definite data was lacking. It was pointed out that the cases of nephrotic syndrome were probably not due to methylmercury. The combination of nephrotic syndrome and slightly increased blood mercury levels could very well be accidental. As to other observations on kidney lesions, an exposure to phenylmercury (which causes renal damage in rats) was a possibility. Differences in biological half-lives, mercury exposure, or analytical errors may be reasons for some high mercury levels among presumably non-exposed Iraqis. Testicular atrophy had been observed in only one case out of three studied. An exposure to phenylmercury in this case was proposed as a possibility, as that compound does accumulate in the testes in animal experiments. The possibility of a post-mortem redistribution of mercury within or between tissues was discussed, but no information was available.

Alternative Session 3 - 11 November Moderator: Dr W. F. Almeida (Brazil)

Papers presented (short presentations)

OCCURRENCE AND LEVELS OF METHYLMERCURY IN ORGANS OF NON-EXPOSED HUMANS
Drs J. Kosta and V. Jelenko (Yugoslavia)

A method has been devised covering concentrations of the order of a few nanograms of methylmercury per gram of biological tissue, 0.5 ml of blood were analysed.

Using this method levels were measured in human hair, blood and post-mortem samples of several organs including liver, brain and kidney.

The area covered in the survey is characterized by somewhat elevated levels of inorganic mercury, due to mining and processing of the ore and to production or use of certain mercurials. The fraction of fish in the average diet of humans taken into consideration in this investigation however is practically negligible. Concentrations found could therefore be regarded as contributed from natural, transformations of inorganic mercury in the methyl form and/or the uptake of the latter, thus representing typical background concentrations. Only hair appears to contain a considerable fraction of total mercury as methylmercury. Concentrations in other organs are in the range of one to ten nanogram per gram of fresh tissue. Some other species, primarily amphibians, have been analysed for comparison, as well as certain fungi in which a minor, and varying, fraction of mercury was present in the methyl form.

DIFFERENTIAL EFFECTS OF MERCURIAL COMPOUNDS ON EXCITABLE TISSUES - CLINICAL IMPLICATIONS
Dr A. E. Shamoo (USA)

Sarcoplasmic reticulum controls the contraction-relaxation mechanism of muscle by regulating the concentration of free Ca^{++} in the sarcoplasm. We isolated sarcoplasmic reticulum and Ca^{++} + Mg^{++}-ATPase from rabbit white skeletal muscle, and studied four parameters: (a) Ca^{++} uptake by SR vesicles; (b) Ca^{++} binding by SR vesicles; (c) Ca^{++} + Mg^{++}-ATPase activity; and (d) Ca^{++} ionophoric activity. It has been shown that Ca^{++}-dependent and selective ionophore is part of the Ca^{++} + Mg^{++}-ATPase (Shamoo & MacLennan (1974) Proc. nat. Acad. Sci. (Wash.)) (In press). Methylmercury was found to inhibit 50% of parameter a, b and c at 2×10^{-5} M and 100% at 7×10^{-4} M. No inhibition of Ca^{++} ionophoric activity was observed with up to 10^{-3} M methylmercury. This is the first evidence that the Ca^{++} ionophore has no sulfhydryl groups essential for its activity. Mercuric chloride at 2×10^{-5} M showed no inhibition of Ca^{++} transport, Ca^{++} binding and Ca^{++} ionophore, but approximately 45% of the ATPase activity was lost, and at 7×10^{-4} M $HgCl_2$ inhibited all four parameters 100%. The inhibitory effect of $HgCl_2$ for Ca^{++} ionophore is not due to inhibition of sulfhydryl groups, but rather is similar to the observed inhibition of the Ca^{++} ionophore by Hg^{++}, Zn^{++}, La^{+++} and Mn^{++} according to their order of affinity to the ionophore.

The Ca^{++} + Mg^{++}-ATPase was shown to be a single protein by SDS gel electrophoresis. The finding that 50% of that activity can be inhibited by $HgCl_2$, without inhibition of active transport of calcium, indicates that the enzyme which is not coupled to transport is selectively susceptible.

The observation that methylmercury did not inhibit the Ca^{++} ionophore but $HgCl_2$ did, indicates that the inhibition of Ca uptake, Ca^{++} + Mg^{++}-ATPase and Ca^{++} binding by $HgCl_2$ is due to inhibition of the Ca^{++} ionophoric site. In the case of $HgCl_2$ poisoning, chelating agents could be used to remove Hg^{++} from the ionophore and restore that function. In the case of methylmercury, removal of the toxic agent would be expected to reverse the inhibition of the active transport of calcium.

BRAIN MERCURY CONCENTRATIONS IN RELATION TO DOSE AND DIAGNOSTIC METHOD FOR EARLY NEUROLOGICAL SIGNS IN METHYLMERCURY POISONED MONKEYS
Drs M. Berlin, C. Grant, J. Hellberg (Sweden)

Squirrel monkeys have been found to react to methylmercury exposure similarly to man. Mercury concentration in blood and brain increases linearly with a dose up to 1000 ng/g mercury in blood. Above that level, a significant increase in mercury accumulation in relation to dose occurs in brain and, less pronounced, in blood. The earliest objective neurological sign by some months is an impairment in scotopic vision, which can easily be diagnosed by testing critical fusion intensity at 10 cycles per second. Studies are under way to establish normal values and variation of critical fusion intensity at low frequencies in man.

EFFECTS OF DIMERCAPTOSUCCINIC ACID AND D-PENICILLAMINE ON MERCURY RETENTION IN RATS FOLLOWING A DOSE OF MERCURY BICHLORIDE AND METHYLMERCURIBROMIDE
Drs E. Freidheim and C. Corvi (Switzerland)

Rats were injected with $HgCl_2$ and CH_3HgBr and later given penicillamine and dimercaptosuccinic acid (DMA) orally. In $HgCl_2$-animals the mercury levels in the kidney decreased. In CH_3HgBr-exposed animals decreases were noted in the kidney, liver and possibly in brain.

Discussion

It was mentioned that methylmercury levels of 0.5-1 hg/ml blood have been found in "non-exposed" subjects in USA. As to effects on myoneural junction, it was pointed out that physiological concentrations of mercury were used in the in vitro experiments.

The same levels did affect in vitro cholinergic receptors in rat diaphragms. Normal muscle biopsies had been found in Iraqi patients. This could possibly be due to the fact that the effect of methylmercury was exerted on the calcium metabolism of the cells. In regard to the non-linear relations between dose - blood levels - brain levels in monkeys, differences in distribution may occur at increasing tissue levels, perhaps as a result of saturation of tissues. No such redistribution had, however, been observed in monkeys, and excretion pattern was not significantly altered at increasing levels. Sex differences in distribution have been seen in mice, the most affected organ being the kidney. It was discussed why DMA has decreased tissue mercury levels more than unithiol. It might be a matter of absorption.

Alternative Session 4 - 11 November Moderator: Dr W. F. Almeida (Brazil)

Film: "THE PROGRESS OF RESEARCH ON MINAMATA DISEASE"
Producers: R. Takagi and N. Tsuchimoto (Japan)

Session 1 - 12 November Moderator: Dr A. Khalidi (Iraq)

ENVIRONMENTAL CONTAMINATION WITH MERCURY IN IRAQ
Dr A. Jernelöv (Sweden)

In order to get an idea about environmental mercury contamination in connexion with the outbreak of mercury poisoning, a series of wild life samples were collected from different provinces (Anbar, Babil, Biala, Kirkuk and Nineva). A total of 192 samples were analysed of small mammalians, birds, reptiles and fish.

A. Aquatic environment

Analyses were performed on different fish species (not typical predatory ones) and a few specimens of water living birds (not fish eating). With a few exceptions the fish samples contained concentrations in muscles ranging from 0.01 to 0.15 ppm. The concentrations are within the range found in tropical rivers like the Congo and the Amazon and somewhat lower than those mostly found in Europe and North America. Somewhat higher figures, 0.3-0.5 ppm were found downstream from a caustic soda plant south of Baghdad (samples collected by Hamilton and Rissner). A few cases of very high mercury concentrations (25-30 ppm) were reported from an area where fish-kills had occurred. Aquatic birds (ducks and waders) contained low concentrations of mercury - similar to those found in migratory Swedish birds returning after having spent the winter in Ethiopia (900-2750 ng/g).

B. Terrestrial environment

Tail feathers of seed-eating birds were found to contain 13.500-21.000 ng/g of mercury which is about ten times higher than values reported from Ethiopia and within the range found in Sweden and Canada. A few insect-eating birds that were caught contained 1.850-5.200 ng/g which also is thought to be slightly elevated. Extremely high concentrations of mercury were found in muscle tissue of dead seed-eating birds (15.000-40.000 ng/g) while feathers contained similar concentrations (9.000-52.000 ng/g). (In equilibrium the feather ought to be 7-8 times higher than the fresh muscle, according to Johnels and Westermark.) The extremely high concentrations were only found in vicinities of storage houses where returned seed was kept. No birds of prey could be caught and analysed

Discussion

An extensive discussion took place on the chemical forms of mercurials in barley. At analyses in Sweden of about 60 samples from Iraq the dominating compound was methoxy-propylmercury. This compound is unstable chemically. Phenylmercury was found in many samples, in some up to 40%. Only traces of methyl- and ethylmercury were found. As the organic compounds listed did not make up for the total mercury content, presence of inorganic mercury was assumed. In wheat samples only methylmercury was found with varying degrees of inorganic impurities. It was pointed out that four batches of barley were distributed and that differences might have existed between the batches. However, the picture obtained from the barley samples could explain why in some cases much higher mercury levels were found in kidneys of barley-fed sheep than in muscle. The need for a proper labelling of sacks with the compound used was emphasized.

METHODOLOGY OF EPIDEMIOLOGICAL SURVEYS
Drs J. F. Copplestone (WHO), G. Kazantzis (UK) and A. W. Al-Mufti (Iraq)

This paper discussed some aspects of the design of field studies and the extent to which known but unavoidable inaccuracy may be acceptable.

The success of any field survey is decided before the survey actually begins by an exact formulation of the questions that the study is to answer. Most field surveys are prevalence surveys. The first two points to be decided are the size of the survey group required and the selection of the control population. In a longitudinal study there should be no hesitation in excluding study subjects who no longer fit the characteristics of the population.

If sampling is to be used, it may be preferable to sample in clusters of subjects, than to attempt to do random sampling over a wide area. There is much advantage to be gained in selecting survey subjects according to pre-determined criteria based on their relevance to variable being studied, and then matching each subject with a control subject. Errors in estimated age can be minimized by using a few wide age cohorts in analysis of data rather than quinquennial cohorts.

When taking histories it must be remembered that the period of accurate recall of the average person may not exceed six months and may be as short as a few weeks. Processing of data can be facilitated by using a self-coding form. Great care must be taken to make each question as objective as possible.

As regards field laboratory methods, provided that the field method has no bias itself, the greater the difference in the means of the factor being studied, between the survey group and the control group, the greater the experimental error that can be allowed in the test.

It is better to plan surveys from limited objectives on a realistic scale than to try to mount one massive survey. The finding that two results may be significantly associated does not necessarily mean that they are interdependent since they may both separately be dependent on a third factor. On the other hand, surveys may show up trends even if these are only bordering on or not quite achieving statistical significance.

These trends may indicate the need for further surveys. If decisions are to be made on a basis of fact instead of opinion, a lot more field surveys than are at present carried out will be needed in the future.

EPIDEMIOLOGY I: OUTLINE OF STUDY
Drs A. Al-Mufti, R. M. Mahmood, M. A. Majeed (Iraq) and G. Kazantzis (UK)

A study was performed in an area severely affected by alkylmercury poisoning to determine the extent of the outbreak, the clinical pattern with regard to symptoms and signs, the likely intake of mercury and the level of mercury in the population surveyed. An area reported to be free from cases of poisoning was surveyed in the same way. Both were rural areas inhabited by farmers with their families. In the absence of a suitable sampling frame an attempt was made to survey the whole population of a limited area, and for this Hillali in the Greater Mussayeb Project Area was chosen as the affected region and Saglawiya as the non-affected or control region.

Nine hundred and twenty-six persons were seen in Hillali and 1014 persons in Saglawiya. An additional 207 persons were seen who were living in the neighbourhood of Hillali making a total of 2147 persons altogether. The survey was performed by a small team of doctors and health assistants who visited each household to apply a questionnaire, perform a limited clinical examination and collect blood and hair samples for mercury analysis. Apart from basic demographic data, the questionnaire elicited information on the dietary pattern, the approximate quantity and duration of consumption of mercury contaminated bread, and symptoms and signs considered to be relevant to a diagnosis of organomercury poisoning. The survey commenced about six months after the end of the epidemic and was completed in a further six months. Subsequently, 348 persons from the original survey were re-examined and further blood and hair samples were taken. Baseline data will be used for continuing studies with special reference to children.

The incidence of organomercury poisoning in the affected area was estimated at 283 per thousand with a mortality of 59 per thousand and a case fatality of 21%. Of those persons who were seen, 150 per thousand had subjective symptoms only, 41 per thousand had mild or moderate signs and 32 per thousand had clinical evidence of severe organomercury poisoning. No cases were diagnosed in the control area.

EPIDEMIOLOGY II: SIGNS AND SYMPTOMS IN RELATION TO INTAKE OF MERCURY
Drs A. W. Al-Mufti, R. M. Mahmood, M. A. Majeed (Iraq) and G. Kazantzis (UK)

The pattern of organomercury poisoning over the country as a whole as revealed by hospital admissions showed that all the known cases without exception had occurred in rural areas and had followed the eating of bread made from mercury-dressed wheat.

In the survey of the severely affected area, all persons over the age of five years were asked how much bread they usually ate per day and whether they had eaten contaminated bread. The average number of loaves eaten per day in this areawas 3.2 although some persons had eaten up to 10 loaves per day. Four hundred and seventy-three persons admitted to having eaten contaminated bread. Fifty persons who had started eating before the end of Ramadan (19 November) did so for a mean of 39 days and 420 who had started eating after this date did so for a mean of 32 days although some people had eaten for up to 90 days. For the 426 persons for whom the data was available, the mean number of loaves eaten over the entire period was 121, with a range of six to 480 loaves. Few meals had been eaten away from home, and meat and fish were eaten by the large majority of persons on an average of less than one day in the week. The mean intake of mercury from contaminated bread was estimated at approximately 150 mg but some people may have ingested up to 600 mg over this period.

One-half of the persons who had eaten contaminated bread, and just over 1% of those who claimed they had not done so, reported symptoms which could have been related to organic mercury poisoning. The diagnosis of mild cases in a population-based study can be more difficult than in the more severe cases presented in hospital, for the symptoms and signs are not specific and require careful evaluation. The commonest symptom was paraesthesia, present in 38% of 415 people who had eaten contaminated bread and in 2% of 1012 people who had not done so. Other frequently occurring symptoms in the exposed group compared with their frequency in the control group were: some difficulty with walking 31% and 0.2%; persistent pains in the limbs 26% and 1%; persistent headaches 22% and 1%; visual disturbance 22% and 1%. The most frequently occurring signs were: ataxic gait 11%; visual field defect 9%; astereognosis 7% and ataxia 5%. These signs were not found in the control groups. Other signs were less discriminating, for example dysarthria, emotional instability, apathy and deafness.

Discussion

In the discussion on techniques of epidemiological surveys, the importance of taking into account social and economic factors in the areas to be studied was stressed. The interviews should be done by nationals; sociologists are often suitable. The design of the form is important. The size of the form was discussed. On the one had there is a need for comprehensive forms to get reliable information, but on the other it might be difficult to convince people to answer detailed inquiries. The importance of check-questions was stressed. Also, the advantages of using the same forms in similar studies in different countries was emphasized as such a procedure would make possible comparisons of results. The size of the groups and of the area to study was discussed. It was pointed out that a small but well designed study is far better than an extensive but poorly designed one. Also, the size of the groups is dependent on the expected differences between the exposed group and the control one. To demonstrate a large difference, only small groups are needed. It was mentioned that WHO is preparing a multipurpose analytical field kit which will be useful for estimations of pesticide exposure.

On the epidemiological studies carried out in Iraq, it was stressed that paraesthesia was the first symptom of poisoning, just as was reported in the paper in Science by Bakir et al. (181: 230-241, 1973). Objective signs occurred only later. It was discussed whether a subjective symptom like paraesthesiawithout any objective findings should be used in the establishment of dose-response relationships. Such symptoms are common in depressed patients and many of the Iraqi subjects had reason to be depressed. It is rather common in any population, whether exposed to methylmercury or not. One speaker preferred to use only objective signs. On the other hand it was pointed out that this may lead to an underestimation of risks. In occupational health, subjective complaints were often used to obtain a basis for establishing threshold limit values. The Iraqi study was made 6-12 months after the end of the outbreak. Many of the patients who had only subjective complaints might well have had objective neurologic symptoms earlier since many authors had stressed the improvement in the Iraqi cases. In fact, evidence of such an improvement was found also in the epidemiological survey. In the Japanese cases of methylmercury poisoning from fish consumption, paraesthesia without objective symptoms was found only in few cases.

Attempts were made to calculate the total number of cases and deaths in Iraq, by extrapolation from the figures found at the survey of the severely affected Hillali areas. However, it was pointed out that the situation did vary so much between different areas that the total error at such calculations would be considerable.

The authors pointed out that if they had selected a less affected area, the small number of positive cases should have reduced the chance to establish correlations and hope for a follow-up study.

In the papers it was mentioned that although it seemed that the intake of bread in relation to weight might be higher in the children than in the adults, the incidence of poisoning was higher in the latter. No attempt had been made to compare blood or hair mercury levels in individuals of different ages in the same family. In Sweden, no difference was present between children and adults in fishermen's families exposed through consumption of methylmercury-contaminated fish. It was pointed out that paraesthesia, weakness, etc., are symptoms more frequent in adults than in children. It was supposed that this might explain the different incidences in children and adults in the Iraq epidemic.

An extensive discussion took place on the estimation of methylmercury exposure from the number of loaves consumed per day and the period of consumption of bread baked from treated seed. It was questioned whether the farmers could recall these facts 6-12 months after the end of the epidemic. It was assumed that the estimation of the number of loaves per day was more reliable than the period of consumption.

Session 2 - 12 November Moderator: Dr N. Al-Rawi

EPIDEMIOLOGY III: MERCURY LEVELS IN BLOOD AND HAIR. THE RELATIONSHIP TO EXPOSURE AND TO THE CLINICAL PICTURE
Drs G. Kazantzis (UK), A. W. Al-Mufti, A. Al-Jawad, R. M. Al-Shahwani, R. M. Mahmood and M. A. Majeed (Iraq)

In the survey of the severely affected area described, the total mercury concentration in whole blood was determined by the atomic absorption method described by Magos and Jawad. Hair samples, which were obtained by cutting bundles of hair close to the scalp were cut into segments, dissolved, and estimated for total mercury in the same way as the blood samples. The mean mercury concentrations were calculated for the survey population divided into four groups; (1) those who had been hospitalized for organomercury poisoning; (2) other household members of the above, all of whom would have eaten contaminated bread; (3) other people living in the heavily affected area who claimed they had not eaten contaminated bread and (4) people living in the control area. Mean blood mercury levels for these groups were respectively 42, 25, 7, 5 ng/ml. Mean hair mercury levels were respectively 275, 71, 12, and 1 µg/gram. The means for hair were based on the maximal value in one inch segments in each subject. Those persons who had estimated they had eaten a total of less than 50 loaves of mercury-containing bread had a mean maximal hair mercury level of 90 µg/gram whilst those who had eaten more than 200 loaves had a mean maximal hair mercury concentration of 259 µg/gram.

The variation in mercury concentration in hair strands with distance from the growing end could best be shown in the long hair of female subjects. In those who had eaten contaminated bread, the mercury concentration rose steeply to its maximal value from a level similar to that seen in those who had not eaten and then declined again. Those who had not eaten showed a small rise with a maximal value of 22 µg/gram coinciding in position along the hair with the peak shown by those who had eaten. An explanation for this small rise could be mercury absorption from sources other than bread. The distribution of mercury along the hair shows that accumulation began in most cases in November 1971 which agreed with the time given when the persons in the survey said they had started to consume the contaminated bread.

The blood and hair samples were taken between six months and one year from the end of the epidemic as measured by the last recorded hospital admission. Both blood and hair mercury levels reflected well on previous exposure in groups, for the group results the ratio of mercury level in the first inch of hair to the level in blood was within the range found in other series. At this period in time, however, the relationship to the clinical picture of poisoning in individuals was less close. The reason for this may have been due to differing susceptibility or to differing clearances of mercury from the body between individuals.

EPIDEMIOLOGY IV: CHANGES IN SYMPTOMS AND SIGNS AND THEIR SIGNIFICANCE
Drs G. Kazantzis (UK), A. W. Al-Mufti, R. M. Mahmood, and M. A. Majeed (Iraq)

While none of the symptoms or signs elicited in the survey could be regarded as specific for organomercury poisoning, their onset in relation to the time of ingestion of mercury-contaminated bread was relevant. Twenty persons described symptoms which could have been due to poisoning but which occurred before Ramadan (19 November) at a time when significant mercury accumulation was unlikely to have occurred. Thus eight out of 179 persons (4.5%) had paraesthesia involving the limbs and 15% of those with persistent headaches had this symptom before Ramadan, but by contrast only one person in 90 complained of repeated falling before this date, so that this symptom had considerable specificity. Nevertheless such non-specific symptoms as persistent headaches and persistent pains in the limbs were also found to be important symptoms in organomercury poisoning.

An attempt was made to match symptoms by means of objective signs, although the absence of signs does not necessarily invalidate the symptom. The match ranged from 30% for the presence of ataxia in those who complained of weakness or unsteadiness of the legs to 75% in those who complained of being unable to see. The assessment of vision was difficult, especially in children and under field conditions.

Those with symptoms which could be due to organomercury accumulation were asked if their status at the time of the interview was (a) unchanged, (b) better, or (c) worse than it had been previously. The majority considered they had improved, although such answers could not be assessed objectively. However, when the proportions showing improvement for the various symptoms were compared, some interesting differences were seen. Ninety-four per cent. of those with difficulty in walking claimed to have improved, but only 79% of those with symptoms related to their sight did so. Of 20 persons who claimed they were unable to see, 12 or 60% thought they had improved. Eighty-eight per cent. of those complaining of paraesthesia also claimed to have improved. Paraesthesiae were also complained of by a small number of people in the control group, but in contrast none of those in the control group claimed to have improved, suggesting that the underlying cause was different in this group.

In a group of 75 persons with a clinical diagnosis of organomercury poisoning, a broad assessment in terms of severity made on the initial visit was compared with that made on a second visit approximately six months later, without knowledge of the first assessment. The assessment was unchanged in 52 cases, 17 persons (23%) had improved their category and six (8%) had deteriorated. However 13 persons in whom no evidence of mercury poisoning was found on the second occasion had only subjective evidence the first time they were seen. It was concluded from the evidence that in the current context, with relatively short-term accumulation of mercury to high levels, considerable improvement in the clinical status of the cases was possible some months later.

Discussion

The hair peak concentrations found were unexpectedly low. This might be explained by the fact that authors estimated mercury in one inch segments instead of 1 cm. This could possibly decrease the true peak value by a factor 2.

The considerable improvement in most cases was emphasized by many speakers and was documented by a film and a demonstration of patients from the Medical City, Baghdad. In the discussion the importance of rehabilitation was stressed.

Session 3 - 12 November Moderator: Dr F. Bakir (Iraq)

MERCURY IN FOODSTUFFS DURING OUTBREAK
Drs F. Bakir, N. Al-Rawi, H. Shahristani, A. W. Al-Mufti and A. Kaddori for the National Scientific Committee (Iraq)

Results from a nationwide sampling of foods were presented. No data indicates that any other food than bread contributed to the outbreak. A national survey on sheep showed that with few exceptions the mercury concentration in kidneys and meat was low (< 0.5 mg/kg, up to 5 mg/kg in very few samples)

ABSORPTION, DISTRIBUTION AND METABOLISM OF ORGANOMERCURY IN SHEEP
Drs N. Al-Rawi, T. Dhahir and A. Kaddori for the National Scientific Committee (Iraq)

Feeding experiments on sheep were carried out with barley for 30 days. Tissue concentrations of mercury were measured during and after exposure. Biological half-time was approximately 10 days in kidney, liver and muscle. Poisoned animals had intestinal disturbances but no neurologic signs. They were not blind.

EXPERIMENTAL STUDIES ON ORGANOMERCURY POISONING IN CHICKENS IN IRAQ
Drs M. Al-Folloji, T. A. Makkawi, I. M. Abou-El-Azim, I. M. Sekkar, A. M. Al-Darraji (Iraq)

Dressed wheat was given to chickens for up to 39 days. Total mercury levels in organs and eggs were studied. Levels in egg white up to 150 ppm were found, the levels in egg yolk being lower. Also, high levels of mercury were measured in muscle and other organs. High mercury levels were found in egg white for a long time after the end of exposure; levels in yolk decreased much faster. Only two birds died, both with non-specific symptoms. Some histological changes were found in liver and kidney. Other organs were not studied.

Discussion

In the discussion it was pointed out that as levels of mercury in mutton and sheep kidney as a rule were low, it could be assumed that not much barley was actually given to sheep. The authors of the paper on the sheep feeding experiment had no information on the organomercury compound present in the barley feed. However, data from another laboratory indicated that the main compounds probably were methoxypropylmercury and/or phenylmercury. This could explain the absence of neurological signs and the rapid elimination of mercury after the end of exposure. As methylmercury was the principal compound in all wheat samples analysed, it could safely be assumed that the chickens were exposed to that compound. One speaker reported that foetal resorption had been observed in sheep and rats fed barley.

Session 1 - 13 November Moderator: Dr L. Amin-Zaki

PRENATAL METHYLMERCURY POISONING: A TWO YEAR FOLLOW-UP
Drs R. A. Doherty, M. Greenwood, T. W. Clarkson (USA), L. Amin-Zaki, S. El-Hassani and M. A. Majeed (Iraq)

Mercury is known to cause damage to the central nervous system in children and adults. It was also shown to be foetotoxic to human beings in retrospective studies in Japan. Clinical manifestations were observed on the first examination of 29 infant-mother pairs known to have been exposed to methylmercury during various trimesters of pregnancy were reported. Nine infants showed evidence of gross impairment of the motor and mental development with cerebral palsy, deafness and blindness in eight. Thirteen mothers showed one or more clinical manifestations of methylmercury toxicity.

Follow-up examination throughout two years revealed neurological effects in infants previously thought to be free from methylmercury poisoning. These manifested themselves in

the form of brisk tendon jerks and developmental retardation.

Methylmercury evaluation in blood samples of mothers and infants indicated that it passes readily from mother to foetus. The infants' blood levels of mercury were higher than their mothers' during the first four months after birth. The level is maintained through the ingestion of methylmercury in mother's milk.

PHARMACOKINETIC ASPECTS OF PRENATAL AND POSTNATAL METHYLMERCURY EXPOSURE THROUGH BREAST MILK[1]
Drs R. A. Doherty, A. H. Gates, T. W. Clarkson, M. Greenwood (USA), L. Amin-Zaki, S. El-Hassani and M. A. Majeed (Iraq)

Evidence to date suggests that foetal and neonatal developmental stages are the most susceptible portions of the mammalian life cycle to methylmercury poisoning. A detailed examination of mercury secretion in milk was presented. It was shown that milk mercury concentration is highly correlated with plasma mercury concentration ($r = 0.89$) throughout a wide range of blood mercury levels and that the plasma/milk ratio does not vary with mercury dose or during depletion of total body mercury by excretion.

Discussion

A discussion took place on difficulties in making a diagnosis of prenatal methylmercury poisoning. This is dependent on lack of development as compared to non-exposed infants and thus in turn depends on what is considered to be a normal development in terms of when the deadlines for the normal infant to sit, walk, etc. are set. In Iraq the deadlines were deliberately set rather late in order not to include late-developing non-poisoned infants in the group of poisoned. As the follow-up has only been made for two years there is a possibility that additional prenatal cases might occur in the group studied.

From the data from the outbreak in Japan, it seemed that the foetus was more susceptible to methylmercury than its mother. In Iraq in most cases, both the mother and the foetus did get poisoned if heavily exposed. There were a few cases in which the mother showed no symptoms or signs of poisoning while the infants did so. There were also cases in which the mother was poisoned but not the infant. It must be kept in mind that the observation time of the children was only two years. It was also stressed in the discussion that the lowest blood level in a damaged infant was 560 ng/ml while it had been assumed from extrapolation from the Niigata data that adult subjects may get poisoned at a blood level of 200 ng/ml. The general impression was that the most heavily poisoned infants had been exposed in the third trimester of pregnancy. There seemed to be little improvement in the prenatally poisoned infants. A study on a greater number of mother/child pairs was under way. It was also mentioned as a general impression that abortion and still-birth was common in the women who had been heavily exposed. Out of 25 women, nine had suffered such losses during the two years after the epidemic. However, it was stressed that reliable data on abortions and still-births are not easily acquired in any country.

On the matter of mercury in milk, it was considered that the protein and/or fat content of the milk might influence the mercury levels. Such determinations on human milk had not been carried out in Iraq, but there would appear to be no reason why it should differ from other areas. The samples analysed for mercury were obtained "mid-stream" during a breast feed. The percentage of inorganic mercury in milk decreased as the total mercury levels increased. Also, the data indicated a breaking point in the blood mercury/milk mercury relation at a blood level of

[1] See also Science, 181:230-241, 1973

about 1000 ng/ml, an interesting fact as in monkeys a change in the dose/blood level/brain level relationship had been observed at that level.

Session 2 - 13 November Moderator: Dr A. W. Al-Mufti (Iraq)

STUDY ON SCHOOL PERFORMANCE IN RELATION TO SUBCLINICAL MERCURY CONCENTRATIONS IN HAIR
Drs A. Jernelöv (Sweden) and H. A. Shahristani (Iraq)

In the village Khallawiya in the province of Kirkuk, 482 persons were hospitalized out of a population of 1200. By the end of May 1972 81 had died and 94 remained blind and/or paralysed.

The village had a school with 80 boys, 60 of whom lived in Khallawiya.

School records from previous years and the year ending June 1972 were collected together with hair samples from available symptom-free children. The boys were grouped in four classes according to mercury levels in hair and a correlation was found between mercury levels in hair and failure rate in school during 1972. No such correlation was found for previous years. No conclusion can be drawn whether the observed correlation is due to toxic effects at a subclinical level or to a psychosociological effect connected with the fact that boys with high mercury levels in their hair were more likely to have severely affected family members at home, thus drastically affecting their whole life and study situation. No doubt the latter explanation might contribute to less successful studies.

SUMMARY AND FOLLOW-UP OF EFFECTS OF ALKYLMERCURY POISONING
Dr S. B. Skerfving (WHO Consultant)

A summary was given of the 49 papers presented so far at the Conference.

From the analytical work it was obvious that the dominating mercury compound present in wheat, was methylmercury. It was also clear that no losses of mercury occurred during baking. The methylmercury level in the bread was 5-10 mg Hg/kg. In barley the situation was less clear. In most samples, methoxypropyl- and/or phenylmercury dominated. Alkylmercury was present only in a few samples and then mostly in low concentrations. Barley was not eaten as such, but was fed to sheep. In experiments sheep have been shown to accumulate considerable levels of mercury in different tissues. However, extensive analytical work had shown mercury levels in mutton and sheep kidney on the market in Iraq under 0.5 mg/kg, in a few cases up to 5 mg/kg. Other foods were always well below 0.5 mg/kg. Surveys of the environment had shown no signs of contaminations of food chains leading back to man. The grain was distributed to farmers. The epidemiological survey indicated that these ate meat and fish only once a week or less, but ate several loaves of bread each day. There is thus no doubt that the exposure was entirely due to methylmercury in bread baked from treated seed, an assumption which was also supported by the demonstration of methylmercury in tissue samples. Different data presented indicates exposure times of 1/2 - 3 months in different subjects.

There are no data which allow an estimation of the total number of cases or deaths in Iraq. It is obvious though, that data on hospital admissions and deaths under-estimates the numbers. The outbreak only affected rural areas. In one such area, which was among those most heavily affected, an epidemiological survey indicated a morbidity rate of 25-30% and a case mortality rate of about 20%, but these data can by no means be applied to Iraq as a whole.

The clinical picture was mainly the same as that reported in previous outbreaks: sensory, motor and visual disturbances (subjective and objective). It was demonstrated by electrophysiological studies that there was no peripheral nerve damage. However, there were some differences from the well known picture of Minamata disease: gastrointestinal disturbances occurred in many cases, a few cases of exfoliative dermatitis, possibly some cases of optical atrophy and a lack of eye movement disturbances. Also the course of the disease

with regard to sensory and motor disturbances, was quite different; mild cases in Iraq did recover, moderate cases either recovered or improved, severe cases either died or in most cases made some improvement. "Blurred vision" had a good prognosis. A few blind cases were reported to regain some sight and a few exceptional cases with concentric constriction of visual fields possibly improved.

The only effect found in subjects without the usual symptoms or signs of poisoning ("subclinical" effect) was a reported dose-related impairment of school performances, although further studies have to be done to ascertain that this is really a toxic effect of methylmercury.

Treatment with BAL (British Anti Lewisite) caused deterioration in severe cases. D-penicillamine, N-acetyl-DL-penicillamine, unithiol and a polythiol resin caused some decrease of blood mercury levels and increase of urinary mercury. No data showing an effect on the body burden was presented nor was there any study showing a clinical improvement of the treated subjects as compared to non-treated controls. However, extracorporeal dialysis with addition of cysteine no doubt did decrease the body burden of mercury. It is at present the method of choice if the equipment is available.

In accordance with earlier findings, a considerable individual variation in the biological half-time of mercury in hair and blood was demonstrated. This means a considerable variation in accumulation of methylmercury at a certain exposure level. Also, several authors demonstrated a variation in sensitivity to the same tissue level of mercury.

However, several studies showed beyond any doubt that when means of tissue levels were employed, there was a definite relationship between levels, the presence of symptoms and signs, and their severity. Also it was shown by recalculation of blood levels (Science, 181, 230-241, 1973) and hair levels into body burden at the onset of symptoms, that symptoms may occur at a body burden of about 40 mg mercury as methylmercury. This is in remarkably good accordance with estimations made from data from Niigata. Also, estimations on basis of bread intake as recorded in the epidemiological study seem to confirm this.

Although a high proportion of inorganic mercury is present in breast milk of methylmercury-exposed mothers, the infant may suffer a considerable exposure to methylmercury. However, the peak mercury level in blood of the breast-fed infant is considerably lower than that in the mother.

It is well known from Minamata that in utero exposure of the foetus may cause severe brain damage. In the Iraq outbreak this was confirmed. Little or no improvement has occurred in the prenatal cases during the two year follow-up. From the Minamata data it was supposed that the foetus is more susceptible than the mother. The Iraqi data does not support this concept; at least the foetus is not considerably more susceptible. However, caution in making conclusions is necessary because children exposed in utero have only been followed for two years. The few data presented indicate similar levels in brain tissue of mother and foetus.

As to genetic effects, no statistically significant increase of aberrations in peripheral lymphocyte chromosomes could be demonstrated in poisoned Iraqis as compared to controls. However, it must be remembered that the exposure time was short.

For further studies the following proposals were made: more samples of wheat and especially barley should be analysed for presence of non-alkyl organomercurials. A more extensive analysis of combinations of symptoms and signs should be made. Objective methods to register effects should be developed. Cases of different rehabilitation facilities should be employed and results evaluated in a controlled study. Methods of treatment should be studied. The possible "subclinical" effects on school performances should be followed up in a fully controlled way. The possibility of obtaining more data on dose-response relationships should be considered. Bread consumption patterns could be used. The possibility of

re-analysing inch-cut hair samples in 1 cm. pieces should be considered. Subjects who excrete methylmercury rapidly and slowly should be studied further. It is important to find more prenatally exposed children and to follow these for many years. More data on levels in the foetal brain should be published, if available. A cytogenetic follow-up for several years seems worthwhile.

Some conclusions were drawn from the experience of the Iraqi outbreak on how to prevent further outbreaks and on how to limit the effects if an outbreak does happen. Short chain alkylmercury compounds should not be used for seed treatment with the exception of nuclear stocks, and the compounds should then be used under strict control. The control measures in all countries should be reviewed. There should be rules for permission to use pesticides and registration of approved compounds. Import and usage should be controlled. Rules for handling (central seed treatment by trained personnel, rules for labelling, addition of colours, and possibly of distasteful compounds) should be enforced.

The users of all pesticides should be educated. Facilities for analysis of pesticides should be established.

Central plans should be worked out ahead on how to handle an outbreak. Resources for carrying out epidemiological surveys should be established. The medical service should be prepared to handle an outbreak in the best way in terms of distribution and treatment of patients, etc.

International cooperation is essential in regard to rules for the transportation of pesticides and of treated seed. Emergency facilities to assist rapidly a country which has suffered an outbreak should be continuously reviewed.

Discussion

The importance of a follow-up study of school performances and other factors in exposed but "non-poisoned" children was stressed. The considerable improvement of most of the postnatal cases was underlined by several speakers as was the need for rehabilitation facilities and controlled follow-up studies of the achievements by such programmes. The difficulties encountered in rehabilitation programmes were however great, as cases were scattered all over Iraq. The remarkably consistent picture between different estimations of the dose-response relationships in methylmercury poisoning was discussed. The great value of international cooperation in an outbreak of the Iraqi type was obvious. It was stressed that a major outbreak may strike any country at any time, not only developing countries. Thus, every country has to be prepared.

Session 3 - 13 November Moderator: Dr F. Bakir (Iraq)

THE PRINCIPLES OF MANAGEMENT OF A COMMUNITY POISONING OUTBREAK
Dr S. B. Skerfving (WHO Consultant)

The requirements for detecting a community poisoning outbreak, to establish the cause and size, to limit the effects and to prevent further outbreaks were presented together with examples from different outbreaks that have occurred.

How can it be ascertained that there is an outbreak? The alertness of the local medical and health organization to report cases - especially if they occur in clusters - is to be encouraged. The health statistics must be detailed with regard to the clinical picture and geography on a time basis. In spite of this, some types of outbreaks will not trigger the alarm system at an early stage, for example those giving rise to teratogenic, mutagenic and carcinogenic effects.

What should be done when an outbreak is indicated but before the size and cause is known? Two actions are crucial: (i) information to the health service, hospitals, and the general

public, and in some cases also to other countries and to international organizations, (ii) an epidemiological survey to find out the size and cause of the outbreak. An epidemiological team (director, clinician, sanitarian, epidemiologist, and laboratory personnel) is formed. A survey form (main items: sex, age, place of living, and recent absence, occupation, time of onset of disease, clinical picture, food intake, water supply, potentially affected contacts), is made and employed on a suitable population sample (and sometimes also in controls) together with a clinical examination. Extensive samples are taken of food, containers in which food has been kept, water, blood, urine, hair, gastric content, faeces, autopsy tissue. Sampling is carried out at an early stage with guidance from informed guesses on the vehicle of the noxious agent. Laboratory analyses are started. Sometimes considerable cooperation between different laboratories with special capacities will be needed. As infectious diseases are often the main differential diagnosis to poisoning, laboratory activities may need to include both chemical analyses and bacteriological and virological work. Studies of dose-response relationships are often crucial for the establishment of a firm conclusion on the cause.

When the epidemiological group has reached conclusions on the size of the outbreak, the vehicle and the agent responsible, rapid measures are taken to limit further effects. The public, the health service, hospitals, other countries and international organizations are informed. The treatment of choice can now be established. Measures are taken to confine the cause.

What must be done after the outbreak is under control? Measures to prevent further outbreaks should be taken on local, central and international basis. Laws and regulations have to be re-examined, information and education improved, etc. The actions taken during the outbreak must be scrutinized and emergency plans changed to get a more efficient organization. Finally, it is very important to publish a full account of the outbreak in an international scientific journal to spread information on the danger and especially to make available the data on human toxicology which has been collected during the outbreak. Data on toxicity in humans are rare and thus of great interest.

ASSISTANCE OFFERED BY WHO IN COMMUNITY POISONING OUTBREAKS
Dr J. F. Copplestone (WHO)

Community poisoning outbreaks are fortunately not a frequent occurrence. However, when an outbreak does occur, the national health authority is faced with the immediate problem of ascertaining the cause, defining the extent of the outbreak, taking measures to limit it and to provide effective treatment for the victims. Following this early phase comes a period of inquiry into the chain of events that led to the outbreak and consideration of the clinical course of poisoning and the rehabilitation of the survivors. WHO can assist in all these matters, but, as in all its activities, the Organization only participates at the request of a government and assists in a spirit of cooperation with national authorities. It is essential that the government should request assistance early in the outbreak so that the resources open to the Organization can be mobilized. WHO, through its contact with its collaborating laboratories and with experts throughout the world, is in a position to add to the resources of the national administration the best facilities and brains available. No country should ever feel that any blame will attach to it for allowing an outbreak to occur. The involvement of WHO in a poisoning outbreak also means that it is able to take steps on an international level to prevent similar outbreaks in the future. The implications of assistance pass far beyond the immediate outbreak and help to bring to all peoples a means of preserving health.

Session 4 - 13 November Moderator: Dr F. Bakir (Iraq)

In private session open only to the invited participants, representatives of United Nations organizations, WHO staff and temporary advisers, and members of the Iraqi National Scientific Committee, the following recommendations of the Conference were approved.

1. Having considered the report of the Joint WHO/FAO Meeting held in Geneva in March 1974, "The Use of Mercury and Alternative Compounds as Seed Dressings",[1] the Conference urges all governments to study the recommendations made and to apply them strictly in their own countries, in order to avoid any chance of the misuse of treated grain. Particular attention should be given to labelling in the local language or dialect and with locally understood warning signs. Every effort should be made by governments to discontinue the use of alkylmercury compounds as seed dressings.

2. The Conference considers that:

(a) rules for the strict control of treated grain should be part of a system of regulation of all pesticides in every country, in order to prevent misuse and accidental cases of poisoning.

(b) the environmental pollution aspects of pesticide use should always be considered and there should be adequate monitoring of the environment.

(c) Public Health Authorities should be informed before the large-scale use of pesticides occurs.

3. The Conference urges WHO and FAO to give assistance on request to countries in the establishment of pesticide control programmes, including laboratory facilities and the distribution of information. The establishment of national poison control centres should be encouraged.

4. The Conference notes that WHO can provide emergency assistance in cases of outbreaks of poisoning and recommends countries to make use of this assistance when necessary. WHO should continue its assistance to countries in carrying out epidemiological surveys.

5. The Conference considers that each country should hold stocks of antidotes, where these exist, and have available information on therapeutic procedures for poisonings that might arise within the country, so that treatment of cases of poisoning might commence at the earliest possible moment.

6. The Conference recognizes the considerable amount of research that has been carried out in Iraq on the toxicology, both human and animal, of organomercury poisoning, and its contribution to scientific knowledge on the subject. It recommends that this research should continue with particular attention to the following of affected people in order to define accurately their future development, and that of prenatally and postnatally exposed children and other high risk groups.

7. The Conference urges that rehabilitation and retraining activities for severely affected patients might be intensified.

CLOSURE OF THE CONFERENCE

The Conference was closed with acknowledgements and thanks to H.E., The Minister of Health of Iraq, the Ministry of Health, and the Scientific Committee for the arrangements made; to the Broadcasting and TV service of Iraq for the provision of interpretation equipment, to the Iraqi Red Crescent for refreshments, to H.E. The Minister of Health, the Regional Director, WHO, the Ministry of Tourism, the University of Baghdad, Drug Establishments, and the Iraq Medical Society for social functions arranged, and to the Chairman and Vice-chairman.

The special contribution of the Swedish International Development Authority to the holding of the Conference was gratefully acknowledged.

---

[1] Wld Hlth Org. techn. Rep. Ser., No. 555.
FAO Agricultural Studies No. 95

ANNEX 1

LIST OF PARTICIPANTS

AFGHANISTAN	Mr Mohamed Rahim Ali Zadah Pharmacist Department of Toxicology Institute of Public Health Kabul
BRAZIL	Dr W. F. Almeida Director Division of Animal Biology Biological Institute of São Paulo São Paulo
EGYPT	Mrs Farida Abou-Hamda Chief of Division Drug Analysis and Control Laboratories Department of International Health Ministry of Public Health Cairo
INDIA	Dr C. M. Bhandari Physician S.M.S. Medical College and Hospital Jaipur (Rajasthan)
IRAN	Dr Kazem Yazdi Technical Inspector Ministry of Health Teheran
IRAQ	Dr F. Bakir Chairman, Scientific Committee Medical City Baghdad
	Professor Salem Al-Damluji Chairman, Department of Medicine Medical College Baghdad University, Baghdad
JAPAN	Professor Tadao Tsubaki Department of Neurology Niigata University Niigata
JORDAN	Mr Seifuddin M. Irani Chief of Toxicology Section Public Health Laboratory Ministry of Health Amman

Annex 1

List of participants (continued)

KUWAIT	Dr Noori Z. Al Kazemi Head of Preventive Section Ministry of Health Kuwait
LIBYA	Dr Abdul Gader A. Sherif Director General of Research Centre Ministry of Agriculture Sidi Mesri, Tripoli
MEXICO	Dr Habib Nasser Quinones Chief, Department of Technical Advice Secretaria de Salubridad y Asistencia of Mexico Mexico
PAKISTAN	Dr Khalilur Rahman Chemical Examiner Government of Punjab, Health Department Lahore
TURKEY	Dr Nadir Tekirli Directeur général du Centre d'Education et de Recherches sur la Santé publique Ecole de la Santé Publique Ankara
OBSERVER FROM LIBYA	Dr Essed Abdallah El Tomi Officer in charge of Toxicology Section Central Laboratory Ministry of Health Tripoli

WHO SECRETARIAT

Dr A. H. Taba	Director	WHO Regional Office for the Eastern Mediterranean Alexandria, Egypt
Dr J. F. Copplestone	Medical Officer/ Toxicologist (Secretary to the Conference)	Vector Biology & Control WHO Headquarters Geneva, Switzerland
Dr Staffan B. Skerfving	Consultant	University Hospital Department of Internal Medicine Lund Sweden
Dr A. Jernelöv	Temporary Adviser	Head, Biological Dept. Swedish Inst. Water & Air Pollution Research Stockholm Sweden

Annex 1

Dr G. Kazantzis	Temporary Adviser	Middlesex Hospital Dept. Community Medicine London, England
Dr L. Magos	Temporary Adviser	MRC Toxicology Unit Medical Research Council Laboratories Carshalton Surrey, England
Dr. T. W. Clarkson	Temporary Adviser	University of Rochester Dept. Pharmacology and Toxicology Rochester New York United States of America
Dr T. Giovanoli-Jakubczak	Temporary Adviser	Department of Inorganic and Analytical Chemistry Medical Academy Warsaw Poland
Miss C. Cartoudis	Conference Officer	WHO Regional Office for the Eastern Mediterranean Alexandria Egypt
Mrs N. Abdel Fattah	Interpreter	WHO Headquarters, Geneva
Miss Abdel Latif	Interpreter	WHO Headquarters, Geneva
Mrs A. Yoakim	Interpreter	WHO Headquarters, Geneva
Mr M. Yacoub	Interpreter	WHO Regional Office for the Eastern Mediterranean Alexandria Egypt
Mr J. Bornet	Technician	WHO Headquarters, Geneva
Miss J. H. M. Carter	Secretary	Vector Biology and Control WHO Headquarters Geneva

REPRESENTATIVES OF OTHER UNITED NATIONS BODIES

UNDP	Mr O. Adeel Resident Representative United Nations Development Programme Baghdad, Iraq
FAO	Dr E. E. Turtle Pesticides specialist Pesticides and Post-Harvest Control Group Plant Production and Protection Division Rome, Italy

Annex 1

IRAQI NATIONAL SCIENTIFIC COMMITTEE

Dr Farhan Bakir (Chairman)
Professor of Medicine
Medical College
Baghdad University

Dr Aladdin Al-Khalidi (Secretary)
Assoc. Professor of Pharmacology
Medical College
Baghdad University

Dr Salem F. Al-Damluji
Professor and Chairman
Department of Medicine
Medical College
Baghdad University

Dr Abdul Wadood Al-Mufti
Director-General of Scientific Affairs
Ministry of Health
Baghdad

Dr Sadoon Al-Tikriti
Director of Preventive Medicine
Ministry of Health
Baghdad

Dr Najib Al-Rawi
Director of Veterinary Services
Ministry of Agriculture
Baghdad

Dr Ali Atia
General Company for Vegetable Oil
Baghdad

Dr Hussain Al-Shahristani
College of Engineering
Baghdad University

Dr Hashim I. Dhahir
College of Pharmacy
Baghdad University

Annex 1

OBSERVERS FROM OTHER COUNTRIES[1]

H. M. Younis	Egypt	R. Von Burg	United States of America
P. Sumari	Finland		
E. A. Stähler	Germany	B. M. Hackley	"
T. Tajagi	Japan	P. J. Kostyniak	"
P. de la Pina	Mexico	T. M. Murad	"
M. Berlin	Sweden	F. J. Al-Bazzaz	"
S. Dahlberg	Sweden	D. Marsh	"
F. Freidheim	Switzerland	Dr Horner	"
R. Gramoni	Switzerland	Y. Sugata	"
F. F. Farris	United States of America	M. R. Greenwood	"
		J. Kosta	Yugoslavia

[1] Based on list provided by the National Scientific Committee who made all arrangements for the observers.

ANNEX 2

ADDRESSES AT THE OPENING SESSION OF THE
CONFERENCE ON INTOXICATION DUE TO
ALKYLMERCURY TREATED SEED
Baghdad, Iraq, 9-13 November 1974

ADDRESS BY H.E. EZZAT MUSTAPHA
MINISTER OF HEALTH, IRAQ

I would like to welcome you all to Iraq and thank you for coming, Dr Taba, WHO experts and the distinguished participants.

Following on from the foundation of a developed society, one of our guidelines has been the radical development of a programme for the realization of change in all spheres of life for all people. The Government has given special attention to the provision of good health facilities and we have seen that the rule of nationalization has improved sanitary services for the people. We have promoted the pharmaceutical industry to meet the medical needs of the people. These pharmaceuticals are of good quality and in accordance with international regulations and with the recommendations of international organizations. The programme in the field of health goes side by side with other radical changes with scientific and cultural programmes, in a broad and vast plan to create an advance for social and scientific progress. What happened in 1972 in the outbreak of poisoning in our country has proved the efficiency of our health services in following up and containing these losses and controlling them. For the sake of preventing other countries from suffering as our citizens, we hope this programme will be of benefit to all the countries of the world, and the experience from this incident will be valuable to scientific research. There is no doubt that your assistance has contributed much and we are sure you will share this scientific experience for the benefit of mankind and the progress of science.

I cannot on this occasion participate in this Conference but I wish our guests a pleasant stay in our country and I wish the Conference much success.

ADDRESS BY DR A. H. TABA
DIRECTOR
WHO EASTERN MEDITERRANEAN REGION

Your Excellency, Ladies and Gentlemen,

It is with pleasure that I welcome all the participants to this Conference. I do so in the certainty that there will be much mutual benefit to be gained from the exchange of knowledge and experience amongst such a distinguished group of participants. We certainly look forward to sharing their knowledge and experience and hope that they can carry back to their countries the newly acquired knowledge of others.

Our gratitude must go to the Ministry of Health of Iraq and to the National Scientific Committee for the important and strenuous efforts they have made to bring this Conference into being, and also for their unfailing and generous hospitality.

I would also like to express the gratitude of the Organization to the Swedish International Development Agency who have provided the funds for this Conference, and for the WHO/FAO Meeting on the Use of Mercury and Alternative Compounds as Seed Dressing. The willingness of this Authority to contribute to these activities illustrates well that this is a problem which actually occurred in Iraq but is a matter of international concern.

Annex 2

The Constitution of WHO charges the Organization to furnish technical and material assistance to countries in emergencies, either upon the request or acceptance of their respective governments and also to promote cooperation among scientific and professional groups which contribute to the promotion and protection of health.

This Conference is the result of the exercise of the first of these functions and in furtherance of the second.

While the primary task of the Organization is assistance to countries to establish and improve basic health services, we are always ready to assist when a major unforeseen incident strikes a community, and we try to ensure that the opportunity is not lost of studying the cause of the incident. We must seek to prevent any recurrence in the future, wherever in the world a similar or related set of circumstances may arise.

The outbreak of organomercury poisoning in Iraq in early 1971 and early 1972 was just such an incident. The Government of Iraq sought and received at that time both international and bilateral assistance. As a result of the continuing investigations, both clinical and epidemiological, much new information on the effect of organomercury on man has been obtained and the Organization is pleased to be able to organize this Conference, in collaboration with the scientists concerned, in order to ensure that this information may be made available to the scientists of the world in a coherent form. WHO has also played an active role on the preventive side and is confident that if governments will adopt the recommendations of the Joint WHO/FAO Meeting, the chances of recurrence of such an outbreak of poisoning will be negligible.

I wish you success in your deliberations, assuring you that the Organization will study with care your recommendations made in concluding this Conference.