September 10, 1968

P.S.I. Barry, M.D.
The associated Octel Company Limited
Ellesmere Port, Cheshire
England

Re. M.A.3.1.

Dear Pat:

I am most grateful for your comprehensive letter of July 30th. It came after I had left Cincinnati on my vacation in Montana. I had made no attempt to have mail forwarded to me, except in emergency, and since this did not fit in that category, I actually received it in person on my return some days ago.

It is plain to be seen that the views, or, at least, the practices, of most of the participants in the conference do not correspond to our own. The reason for that in this instance, or so it seems to me, is that they are in no position to handle their wards - the employees in their lead plants - on a strictly preventive program in which they put dependence on the analytical findings for lead in the blood, but rather must undertake to recognize toxic manifestations in sufficiently early stages to enable them to ward off the more serious disabilities associated with plumbism. It may be that this will turn out to be feasible, in that the removal of men from exposure to lead when they develop minimal abnormalities in the levels of A.L.A. or of porphyrins in the urine. However, in my opinion, this is not only a faulty procedure, in principle, but it is highly unlikely to work out practically, not only because systemic intoxication (as contrasted with chemical signs of impending? /actual?/ intoxication) may appear concurrently in some instances, but also because managers will not be willing to remove a man from his work simply because he has this potential threat, while the employees, themselves, will protest. This raises the entire issue of whether and when a man is ill, and it lacks the specificity and therefore the significance of the concentration of lead, per se, in the body. I am sorry that I was not present to combat the apparent consensus, and to support, vigorously, the concept of preventive medicine that is involved in the concentration of lead in the blood.

However, there is to be a conference in Amsterdam in November on the subject of the maximum allowable concentration of lead in the air of industrial plants (it does not appear at present, that the lead in the ambient air is an issue, but it is bound to come up). Zielhuis has written to me (received yesterday) urging me to attend, and I think I should do so. I am not much interested in the main issue, although I have some pertinent experimental results to present on it. However, the matter needs to be ventilated thoroughly, and in addition the tolerable concentration in the ambient air will be discussed, I am sure, by some one, if only for the deliberate purpose of keeping this issue alive.

This is to be a "closed conference" which means, I suppose, that it will be open to invited persons. Beritić, Djurić and Stanković, it seems will be there from Yukoslavia, and I should find it possible to talk to them, as will Teisinger from Prague (if he is permitted). The intention seems to be to thresh this out, under the auspices of the Permanent Committee, International Association of Occupational

Health, before the meeting in Tokyo. I may be taking on a foolish mission, but I have a feeling that these conferences have potentialities for mishandling these matters.

It is likely that I shall go to Amsterdam via London, or that I shall return via London. In any case, I shall certainly have a chance to see and talk with you and my friends at 20 Berkeley Square. If you have any purpose in mind that I can serve on your behalf, let me know promptly. I'm writing to Ray Bevan also, to let him know of the prospects.

With all the best,

Sincerely,

Robert A. Kehoe, M.D.
Professor Emeritus of
Occupational Medicine

RAK:wp

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OUR REF. M.A.3.1.

YOUR REF.

Dr. R.A. Kehoe,
University of Cincinnati,
Department of Environmental Health,
Kettering Laboratory,
Eden Avenue,
CINCINNATI, Ohio 45219, U.S.A.

30th July, 1968.

Dear Dr. Kehoe,

I returned from Jugoslavia on 24.7.68, also having spent 2 days in Germany at our plant at Biebesheim on the way back.

I travelled from London with Jim Stopps (Haskell Laboratory, Dupont) on July 14th and we were met by Prof. Beritic and his wife at Dubrovnik airport, together with Waldron and his wife, who were on the same 'plane. Don Fowler and wife had arrived at Dubrovnik the previous day and we were also joined by Prof. Saric and his wife. Prof. Saric is the titular head of the Institute for Medical Research, including the Institute of Industrial Hygiene, at Zagreb; Prof. Beritic works under him, although he is really the more senior of the two. This, I gathered, is because Saric is a member of the Communist Party and Beritic is not. However, they were both obviously very good friends. We were also joined in Dubrovnik by the only German who had accepted to attend the Conference, Dr. Schlegel, Medical Director of the Mercedes motor manufacturers.

The whole party set off in three cars on the 15th July spending the night en route at Bijelo Polje and arriving at Trepca on the evening of July 16th, having travelled through some amazing country including a mountain pass to Pec which went to an altitude of 6,000 ft. and at times provided hair raising moments. Apart from the mountain pass, which was a dust road, all other roads we travelled were tar-macadamed. Although it was a very interesting experience, I think Lucille would have found the journey somewhat trying.

The accommodation at Trepca was very good, all of us staying at a hotel which appeared to belong to the Trepca Mining people and within a mile or so distance of the mine itself. The conference was held in a more than adequate hall which was part of a recreation centre for the Trepca workers. Simultaneous translation of the papers was laid on in Russian, Serbo-Croat, English and French, although only one speaker, Dr. Zurbo from Prof. Vigliani's group, gave his paper in French and no French delegates were present at the meeting.

After the meeting was officially opened on the morning of 17.7.68 by Prof. Beritic, who was the prime organiser, we all proceeded to the battery plant and ore smelting plant for a tour.

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The battery plant was operating with new equipment and seemed to be in good condition, with the exception of the drying and storage rooms for the battery plates, where ventilation was poor, and a high level of lead in the room atmosphere was evident.

The ore foundry really belies description; the conditions of work were quite appalling with a powdery lead dust forming a thick carpet on the floors and yard area. Lead dust and fume was issuing from roasting furnaces into the building atmosphere to the extent that a constant fog haze was present. There did not appear to be a ventilating system operating and employees did not wear respiratory protection, apart from the occasional one who wore a form of leather face-piece with no filter which appeared to me to be somewhat useless. Smoking was permitted anywhere on the plant, but I believe a canteen was available for meals, although I got the impression that there was no objection to the men eating on the job. I was not sure if bathing facilities were available or were used. As sanitation generally in Jugoslavia was most primitive, I would doubt it.

The Conference proper started on the afternoon of July 17th and it became apparent during the course of the proceedings that there was some cross-misunderstanding between the views of the Balkan delegates and the Western group. Whereas the papers delivered by the Western delegates were concerned with the prevention and early detection of lead poisoning in Industry, those from Jugoslavia and the other Balkan countries were concerned more with the diagnosis of established lead poisoning. As Prof. Beritic pointed out lead poisoning is a common disease in Jugoslavia and their concern was the effective diagnosis of the disease, rather than its prevention or early recognition of pre-clinical states. At the present time they were unable to effect a reasonable control towards prevention. He indicated the two main sources of poisoning: (a) from lead glazed wine pots and (b) from lead ore foundries. As there appeared to be a difference of view as to the interpretation of terminology such as "pre saturnism" and "lead absorption", he pleaded for a recognition of the meaning of such terms so that we could all understand what was meant.

Much of the argument with respect to biological aids centred around the relative values of ALA and coproporphyrin as opposed to the blood lead. Prof. Cramer and Dr. Selander from Gothenburg, Sweden, considered ALA determination to be the most sensitive test and indicative of early interference with haem synthesis, whereas they considered lead in blood determinations only indicated a level of absorption and did not provide an indices of damage. Neither did they accept a level of 80 ug.Pb/100gm. blood as a safe limit. Waldron, who incidentally has a B.Sc. and is now studying medicine at Birmingham University, advocated the semi-quantitative coproporphyrin test as the single diagnostic aid of choice. Although he did not bring this out in his paper, he believes that there are people who develop a true sensitivity to lead and that blood lead estimations in these cases are of little value.

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Stopps indicated that ALA levels may remain elevated after levels of lead in blood and urine have reduced to normal. Don Fowler in his paper indicated that the lead level in blood was the best parameter for use in the control of Industrial lead exposure, but this view appeared to be in the minority, most of the speakers being more in favour of ALA and coproporphyrin estimations.

Beritic, as a clinician, considered that the reticulocyte count and basophilic stippling provided a sound confirmation of lead poisoning and that these investigations should not be ignored. This opinion was held by other Jugoslav representatives, who also considered coproporphyrins and the ALA test to be of more value than blood lead level, partly because they were simpler and cheaper to undertake, but also because they represented a direct indication of the action of lead on haem synthesis. Dr. De Bruin from Holland supported the use of coproporphyrins and ALA tests.

The Russian contingent was interesting in that their speakers generalised without providing statistical details. Prof. Kokorov told the audience that lead poisoning in Russia was very rarely seen as factory control was now excellent. However, this statement hardly matched up with the rest of his paper, in part of which he mentioned the prophylactic use of EDTA, which he later indicated was at present under review. Another Russian speaker spoke of gastrointestinal motility in lead colic which was diagnosable radiologically.

A speaker from the Zagreb Institute discussed the work they had undertaken on lead in blood and bone marrow, showing a close correlation between the two.

Papers on the effect of lead on liver and kidney function were given by Jugoslav authors, indicating that normal function was deranged. A Russian delegate (I think Prof. Sancevic) however did not accept that lead caused renal disease as she had never seen evidence of this in cases of poisoning. Dr. Malcolm discussed the work of Prof. Lane with respect to pensioners from the Battery works in Manchester and this caused a fair degree of discussion on the effect of lead on the cardio-vascular system as a cause of hypertension. It was noted that transient hypertension was seen to occur in cases of lead poisoning with colic and it was suggested this phenomenon may be a result of either muscle spasm or reflex stimulation of the autonomic nervous system.

With regard to the treatment of lead poisoning Prof. Cramer compared EDTA with penicillamine and advocated penicillamine as the drug of choice, as it can be given by mouth effectively and has no side effects when given therapeutically over short periods. All agreed that oral EDTA was of very limited value, but some delegates considered EDTA intramuscularly or intravenously was more effective than penicillamine and did not cause side effects. The effect of chelation therapy on coproporphyrin excretion was discussed, and the point made that the porphyrins tended to increase in the urine during the early stages of therapy.

To sum up, the conference was attended by 55 delegates from Jugoslavia, Russia (6), Bulgaria (2), U.S.A. (3), Britain (4), Italy (1), Germany (1) and Sweden (2). Holmquist from Sweden failed to turn up. It was well organised and conducted in a friendly spirit, with an element of informality largely engendered by Prof. Beritic, who was himself a most hospitable and congenial individual. The problem of lead poisoning is a serious one in

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Jugoslavia and results in a somewhat different approach to the subject than would be our own. At the present time aspects of diagnosis and treatment predominate over considerations for prevention and it looked to me likely that this approach would continue indefinitely. The diagnostic tests most favoured were the ALA, coproporphyrins and Reticulocyte count, including Basophilic stippled cells. The estimation of lead in urine and blood was less favoured. Pre-saturnism, or the pre-clinical picture, was discussed on the basis of abnormal laboratory findings indicating pre-symptomatic disease, but no reasonable accord was reached on what constituted a disease picture in these terms.

No reference was made to air pollution with respect to Public Health and neither was any mention made of lead alkyl compounds.

We each received a set of copies of the papers that were delivered at the Conference and if you would like me to do so I would be happy to ask Prof. Beritic to forward you a set, although perhaps either Fowler or Stopps may be able to let you have one.

As I have mentioned earlier, on my way back I visited our plant at Biebesheim, which has undergone a dramatic improvement in the past year. It is now operating very satisfactorily and a firm control is being exercised in respect to housekeeping and safety factors. This is reflected in the urinary lead excretion figures which are really very good at the present time. One man is on alternative work with some suspicion that he may be absorbing lead from a source other than from his work. After the troubles we experienced earlier at Biebesheim it is a relief to have the plant operating so satisfactorily.

Incidentally, Prof. Beritic was very sorry you were unable to make it to Jugoslavia, but I think Lucille would have found the trip somewhat trying. I hope that her troubles are clearing. Anne sends her regards as also do I.

Sincerely yours,

Pat Bamy

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