C. L. SHECKLER



A Confidential Condensed Report by

Donald R. Tellefsen, Chairman
Health and Safety Committee on

PERLITE DUST INVESTIGATION

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by

The Saranac Laboratory

of the

Trudeau Foundation
Saranac Lake, N. Y.

Sponsored by

Perlite Institute
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November, 1953

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CLS Copy

June 25, 1971

F. Coda

I have written this letter at J. Siegfreid's request for the purpose of using it, if necessary, at the forthcoming New Mexico hearings.

C. L. Sheckler

cc: Dr. Francis Hutto
P. A. Martinson
E. M. Fenner
J. Siegfried

C.L. SHECKLER

THE BIOTOXICITY OF PERLITE

A review of certain animal experiments and a critique of the report from the Saranac Laboratory concerning them.

SUPPLEMENT

June 19, 1959

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MTC 013973

The Bietoxicity of Perlite

A review of certain animal experiments and a critique of the report from the Saranac Laboratory concerning them.

INTRODUCTION

This supplement to the review and critique submitted June 5, 1959, has been prepared in accord with the request of Mr. Marve Marramore in a letter dated June 11, 1959. The supplement is concerned entirely with a discussion of the suggestions for further research projects as outlined in the final report from the Saranac Laboratory, titled "The Bietoxicity of Perlite" and dated March 19, 1955. These projects were listed as follows:

A. Whether animals nearer in the evolutionary scale to Man are likely to react in the same manner as do guinea pigs. We recommend a study in which Monkeys are to be used.

B. Whether the progressive tuberculosis observed under experimental conditions is amenable to satisfactory treatment by means of modern bio- and chemotherapy.

C. Whether the disabling effects of the ultimate fibrosis may be prevented or minimized through the administration of substances, such as certisone, which are known to be effective against a variety of fibrotic phenomena in Man.

D. Whether the admixture of other commercial substances with Perlite is likely to enhance or reduce its harmful effects.

E. Whether Perlite in a state of finer subdivision would have effects materially different than those of the product we studied.

MTC 013974

DISCUSSION

Brief comments concerning each of the proposed projects follow.

A. It is a widespread rather glib assumption that since monkeys and man are both members of the primate order the results of animal experiments with monkeys will be more closely applicable to the human situation than the results with rodents. There is little convincing evidence in support of this concept, especially in the area of the response to inhaled dust. It is true that there has been a degree of species variation in the response of animals to some materials but usually the responses are consistent and in the case of Perlite dust there was no evidence of such species variation since the dust could be classified as innocuous to normal animals of the two species guinea pigs and rats. If an experiment should reveal that monkeys responded differently from these two species there would still be no evidence upon which to base the belief that monkeys would provide the better indication of future industrial experience.

With regard to the use of monkeys for the evaluation of the effect of dust upon tuberculosis there is absolutely no background experience of previous research upon which to base any interpretation of experimental results. The good correlation with human responses which has previously been demonstrated by the use of guinea pigs infected with the special R_1 strain of tubercle bacilli has no duplicate for any other species. If such studies were to be conducted with monkeys it would be necessary to conduct control experiments with quartz dust and with other substances known not to stimulate tuberculous infection in order to

establish that any correlation between the response of monkeys and man exists. It is thus clear that at best several years of preliminary exploration would be required before the experiment to evaluate the course of tuberculous infection in monkeys exposed to Perlite dust could be conducted.

B. This proposed experiment is concerned with the study of the response of tuberculous infection stimulated by Perlite dust to treatment with drugs. While it is agreed that it would be a neat experiment there seems to be exceedingly little indication for conducting it. It is already clear that quartz dust is considerably more potent in its stimulatory effect upon tuberculosis than is Perlite dust. Therefore, it seems entirely logical to conclude that since "modern bio- and chemotherapy" is adequate to cause healing in the presence of tuberculosilicosis, its effect on tuberculous infection in the presence of Perlite exposure would be equally good if not even better. Furthermore since the experiment has already shown the effect of Perlite upon tuberculous infection to be temporary even without drug therapy, it seems clear that the tendency for tuberculosis with silicosis to relapse after interruption of therapy would not occur in tuberculous individuals exposed to Perlite.

C. The nonvalidity of the assumption upon which this experimental approach is based was explained in the critique submitted on June 5, 1959.

D. With regard to the mixture of Perlite with other commercial substances, one can make no logical prediction as to the result of exposure to such dusts. If any such mixtures were to be prepared and

used in substantial quantities in situations where exposure of personnel to dust might be excessive it would seem logical that the biological activity of such mixtures should be examined by means of animal experiments.

E. As in paragraph D, there is no logical way in which one can predict the results of inhalation of Perlite in a substantially different physical state from that present in the material which has been studied experimentally. With regard to variations in particle size range, however, it is felt that only if particles of an entirely different order of size magnitude should occur would there be indication for further experimental work. Thus in the occasional instances mentioned in the report of March 19, 1955, where materials were damaging to tissue in one particle size range but not in another the size differences were very substantial with the nontoxic range being measured in microns and the toxic range, in Angstrom units. Lesser degrees of particle size range variation in Perlite should be of little significance. Concerning the possibility that the heating of Perlite might produce free silica crystallized in forms other than quartz it would seem that this would be of little significance unless the actual quantity of free silica were also increased considerably above 1 percent by some means. In any case the presence of different crystal structures can be determined by x-ray diffraction studies and only if they actually occurred would there be any reason to consider further experimental investigation in this regard.

MTC 013977

SUMMARY

1. The further research projects suggested in section 6 of the final report to the Perlite Institute from the Saranac Laboratory, dated March 19, 1955, and titled "The Biotoxicity of Perlite" have been specifically reviewed.

2. On the basis of information already available there seems to be little or no indication for pursuing the studies identified as A, B, and C.

3. Studies D and E might be required if the special industrial conditions upon which they are postulated should occur.

MTC 013978

THE BIOTOXICITY OF BERYLITE

A review of certain animal experiments and a critique of the report from the Saranac Laboratory concerning them.

SUPPLEMENT

June 19, 1959

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MTC 013979

The Biotoxicity of Perlite

A review of certain animal experiments and a critique of the report from the Saranac Laboratory concerning them.

INTRODUCTION

This supplement to the review and critique submitted June 5, 1959, has been prepared in accord with the request of Mr. Marve Narramore in a letter dated June 11, 1959. The supplement is concerned entirely with a discussion of the suggestions for further research projects as outlined in the final report from the Saranac Laboratory, titled "The Biotoxicity of Perlite" and dated March 19, 1955. These projects were listed as follows:

A. Whether animals nearer in the evolutionary scale to Man are likely to react in the same manner as do guinea pigs. We recommend a study in which Monkeys are to be used.

B. Whether the progressive tuberculosis observed under experimental conditions is amenable to satisfactory treatment by means of modern bio- and chemotherapy.

C. Whether the disabling effects of the ultimate fibrosis may be prevented or minimized through the administration of substances, such as cortisone, which are known to be effective against a variety of fibrotic phenomena in Man.

D. Whether the admixture of other commercial substances with Perlite is likely to enhance or reduce its harmful effects.

E. Whether Perlite in a state of finer subdivision would have effects materially different than those of the product we studied.

DISCUSSION

Brief comments concerning each of the proposed projects follow.

A. It is a widespread rather glib assumption that since monkeys and man are both members of the primate order the results of animal experiments with monkeys will be more closely applicable to the human situation than the results with rodents. There is little convincing evidence in support of this concept, especially in the area of the response to inhaled dust. It is true that there has been a degree of species variation in the response of animals to some materials but usually the responses are consistent and in the case of Perlite dust there was no evidence of such species variation since the dust could be classified as innocuous to normal animals of the two species guinea pigs and rats. If an experiment should reveal that monkeys responded differently from these two species there would still be no evidence upon which to base the belief that monkeys would provide the better indication of future industrial experience.

With regard to the use of monkeys for the evaluation of the effect of dust upon tuberculosis there is absolutely no background experience of previous research upon which to base any interpretation of experimental results. The good correlation with human responses which has previously been demonstrated by the use of guinea pigs infected with the special R_1 strain of tubercle bacilli has no duplicate for any other species. If such studies were to be conducted with monkeys it would be necessary to conduct control experiments with quartz dust and with other substances known not to stimulate tuberculous infection in order to

MTC 013981

establish that any correlation between the response of monkeys and man exists. It is thus clear that at best several years of preliminary exploration would be required before the experiment to evaluate the course of tuberculous infection in monkeys exposed to Perlite dust could be conducted.

B. This proposed experiment is concerned with the study of the response of tuberculous infection stimulated by Perlite dust to treatment with drugs. While it is agreed that it would be a neat experiment there seems to be exceedingly little indication for conducting it. It is already clear that quartz dust is considerably more potent in its stimulatory effect upon tuberculosis than is Perlite dust. Therefore, it seems entirely logical to conclude that since "modern bio- and chemotherapy" is adequate to cause healing in the presence of tuberculosilicosis, its effect on tuberculous infection in the presence of Perlite exposure would be equally good if not even better. Furthermore since the experiment has already shown the effect of Perlite upon tuberculous infection to be temporary even without drug therapy, it seems clear that the tendency for tuberculosis with silicosis to relapse after interruption of therapy would not occur in tuberculous individuals exposed to Perlite.

C. The nonvalidity of the assumption upon which this experimental approach is based was explained in the critique submitted on June 5, 1959.

D. With regard to the mixture of Perlite with other commercial substances, one can make no logical prediction as to the result of exposure to such dusts. If any such mixtures were to be prepared and

MTC 013982

used in substantial quantities in situations where exposure of personnel to dust might be excessive it would seem logical that the biological activity of such mixtures should be examined by means of animal experiments.

E. As in paragraph D, there is no logical way in which one can predict the results of inhalation of Perlite in a substantially different physical state from that present in the material which has been studied experimentally. With regard to variations in particle size range, however, it is felt that only if particles of an entirely different order of size magnitude should occur would there be indication for further experimental work. Thus in the occasional instances mentioned in the report of March 19, 1955, where materials were damaging to tissue in one particle size range but not in another the size differences were very substantial with the nontoxic range being measured in microns and the toxic range, in Angstrom units. Lesser degrees of particle size range variation in Perlite should be of little significance. Concerning the possibility that the heating of Perlite might produce free silica crystallized in forms other than quartz it would seem that this would be of little significance unless the actual quantity of free silica were also increased considerably above 1 percent by some means. In any case the presence of different crystal structures can be determined by x-ray diffraction studies and only if they actually occurred would there be any reason to consider further experimental investigation in this regard.

MTC 013983

SUMMARY

1. The further research projects suggested in section 6 of the final report to the Perlite Institute from the Saranac Laboratory, dated March 19, 1955, and titled "The Biotoxicity of Perlite" have been specifically reviewed.

2. On the basis of information already available there seems to be little or no indication for pursuing the studies identified as A, B, and C.

3. Studies D and E might be required if the special industrial conditions upon which they are postulated should occur.

MTC 013984