

## DISCUSSION—FOURTH SESSION

Dr. F. W. S. CARVER pointed out that in his introduction Dr. Gadian had said that nitrosamines were so potent that a single exposure could cause cancer. He asked what sort of nitrosamines they were and what did he mean by "single exposure"?

Dr. GADIAN said that one of the most potent was dimethyl nitrosamine and they were formed when nitrites reacted with secondary or tertiary amines. By "exposure" he meant that it could be eaten, as nitrosamine can be formed when nitrites are used as preservatives. Besides this some industrial processes involve the risk of nitrosamine formation.

Dr. CARVER said that secondary amines of the aromatic nature were used in the explosives industry as stabilisers and anybody dealing with explosives would expose themselves to nitrosamines quite frequently.

After Dr. Gadian had pointed out that they were generally accepted to be the most carcinogenic of all substances (the one most of all being dimethyl), Dr. Carver added that he thought that that had not been appreciated in the explosives industry.

The CHAIRMAN said that Dr. Gage had referred to the question of an absolutely new substance coming into a research laboratory. Would the chemical nature of the substance provide any guidance as to its possible toxicological effects?

In general, this was true, replied Dr. GAGE, although it would be possible for a new chemical type to be developed of which one had no knowledge. Carcinogenicity was a difficult subject to deal with experimentally, and it was something of a nightmare in occupational toxicology that one might miss a carcinogen. He thought that if betanaphthylamine was developed today, it would be spotted. There was no doubt, though, that a very innocent looking molecule could occasionally be shown experimentally to be highly toxic.

Mr. P. S. ELLIS asked what the situation was where there were dyestuffs which were derived from betanaphthylamine or similar compounds. Were they likely to decompose into carcinogens?

Dr. GAGE thought that it would be unlikely as they would all be sulphonated. After Mr. Ellis had said that they were not all sulphonated, Dr. Gage added that the amounts absorbed would be very small as they were here dealing with manufacturing risks.

Mr. HUGHES asked about the study of risk in the concept that Dr. Gadian was talking about. He pointed out that Dr. Gadian, in his paper, said that people accepted risks by smoking and by buying bicycles for their children, etc., and that we were living in a world where we accept risk. He talked about several precepts which should be followed when considering cancer cases. Dr. Gadian had said that precaution should be taken to reduce the risk to the very

minimum and later that preventive measures should be taken to such a degree that diseases would be, to all intents and purposes, nil. He thought it was going too far to say on the one hand that we lived in a world of acceptable risk and then saying that the risk should be nil. Should we, he said, say that it should be ten *per cent* of the normal risk or one *per cent*. Or how did Dr. Gadian define his nil concept?

The two, replied Dr. GADIAN, were not inconsistent, because earlier he had said that absolute prevention was, in view of the many factors involved, particularly the human factor, virtually unattainable. It was the duty of the company to make the risk to all intents and purposes nil, when the worker carried out conscientiously all the safety procedures in which he has been fully trained.

The worker's co-operation might make the difference between getting an isolated case or none at all.

Mr. W. G. HUGHES found it hard to accept that companies could make the risk virtually nil; there was always the chance of something going wrong. It was difficult to say the safety factor should be nil. He thought that in practical terms one could define what the risk level should be and there was a need to look at it more so in this manner.

Dr. GADIAN thought that it was almost impossible to quote the risk or benefit of a new procedure in statistical terms as the long latent period of most industrial tumours meant that one would have to wait 20 years or more to obtain meaningful results.

It might well be true that the chance of an odd case occurring was not absolutely nil. Nor is the chance of a taxi driver or a van driver having a serious or fatal accident absolutely nil, however perfect the vehicle he drives. Having taken all the precautions normally used in the process and obeying any Code of Practice which may have been issued, ensuring that the worker is mentally and physically of the right calibre and is fully instructed, there remains one further criterion to be satisfied—one's conscience—and one must ask—would I be happy to work in this process myself as these men are doing?

Mr. HUGHES said that it went back to the discussion on toxic substances. Companies did take great precautions but there was always a risk. But he still did not think that the chance was nil. Perhaps it was small and that it was only, say, ten *per cent* but there was a risk.

The words replied Dr. GADIAN, "to all intents and purposes nil" meant the occurrence of, at the most, an isolated case in very many years of exposure of a large number of men.

Dr. J. C. GAGE commented that the Standard established by the British Occupational Hygiene Society for exposure to chrysotile asbestos, accepted that there might be a one *per cent* incidence of asbestosis in men exposed to the recommended limit for asbestos fibres in air. It must be assumed that management and men were prepared to accept that controlled

risk. It appeared that there was a small proportion of individuals who were, through some metabolic or physiological peculiarity, unusually sensitive to certain toxic substances, and they should be excluded from occupations where they were a bad risk.

It is necessary, said Mr. P. GRANTHAM, to consider that type of approach in respect of the possible consequences of handling radioactive materials—leukaemias, tumors, *etc.* He thought that the only possible standard which could be set for this was that the incidence amongst persons involved should not be any higher than in the community at large.

Mr. M. KNEALE referred Dr. Gadian to his expression "exposure to a considerable amount over a long period" which was used in connection with mineral oil. He remembered that in a previous paper Dr. Gadian had given some years ago he had said that cancer due to asbestos was due to an inhalation of a single fibre many years before.

Was the lengthy exposure a proven prerequisite for this cancer?

Dr. GADIAN replied that the mesothelioma tumour due to asbestos could occur from the inhalation of relatively small amounts of fibres over a fairly short period of time.

In the case of cancer of the scrotum due to oil it is generally accepted that a man had to have his scrotum repeatedly soaked in oil, from splashing, or from keeping oil-soaked rags in his pockets day after day. This is averted now by many precautions, including improved plant design to eliminate splashing, the wearing of pocketless trousers, and the use of less or non-carcinogenic oils. But the ordinary man who may occasionally get a bit of oil on his trousers, and so on to his scrotum is not, nor was in the past, at risk.

In reply to a question from Mr. M. KNEALE asking whether the physics of this repeated exposure had ever been explained, Dr. GADIAN supposed it was the principle of repeated trauma.

In certain parts of India, he said, there was an increased incidence of cancer of the thigh and lower abdomen because in the winter they carried hot coals inside a metal container covering that area, and that eventually resulted in cancer. In other parts of India they got cancer of the palate because they were in the habit of smoking cigarettes with the lighted end in the mouth.

Cancer due to repeated trauma was very well known and he thought this applied to repeated soaking.

Mr. A. D. CRAVEN asked whether in view of the complexity of the subject of toxicology, Dr. Gadian thought that the normal medical officer in a small works—who was probably a G.P. from around the corner—was sufficiently qualified to advise the factory in the event of a suspected outbreak

Dr. GADIAN replied that there is very little training in occupational medicine in the medical student's curriculum and so many doctors—consultants as well as G.Ps.—were not in a position to advise on industrial toxicology.

If a G.P. acting as medical officer to a factory came across a problem on which he required advice, he could get it from a number of sources including, in Manchester, the School of Occupational Medicine. Many private companies advise on such problems on a fee-paying basis.

Was there a requirement, asked The CHAIRMAN, that doctors took special training in relation to the effects of chemical exposures?

There was not, replied Dr. GADIAN, and that was quite wrong. The last government was going to alter this but it

had been put a bit further back on the Statute Book. He thought that it would still come in but only many years later. An appointed factory doctor might have no specialised knowledge whatsoever to start with.

The CHAIRMAN invited Dr. Gage to enlarge a bit on the correlation between animal testing and application to humans.

This was difficult, said Dr. GAGE, but there is no alternative to animal experiments. They did, on rare occasions, do experiments on man but only after extensive experiments on animals first.

Having found the no-effect level on an animal, on more than one species, one could apply an appropriate safety factor but establish a threshold limit for man.

The magnitude of that factor would depend on the nature of the last toxic effects seen. It did not mean that man would be more sensitive than animals; it may well have been that man was less sensitive.

The majority of carcinogens have been so termed because of the results of animal experiments, and there is no knowledge of their effects on man. He did not think there was any case of cancer with nitrosamines yet. It might be that man was totally insensitive to nitrosamines, though this seemed unlikely.

Dr. GADIAN added that this applied to dichlorobenzidine. He did not think there had been an authenticated case where a person had been exposed to dichlorobenzidine alone as opposed to benzidine as well, and had developed a bladder tumour.

Nevertheless, it was one of the controlled substances in the Carcinogenic Substances Regulations, and the precautions taken were very stringent. These very stringent precautions which were taken with a substance which was a doubtful carcinogen in man did not mean it was a proven man carcinogen.

Mr. J. S. MERCER wondered whether there could be any correlation between different species of animals. Was there anything which could give Dr. Gage an idea as to what the correlation would be with man?

Dr. GAGE replied that if there was a difference in metabolism, which could be an important difference, the toxic effects could be correlated with that. It was possible to study the metabolism in man and then assess whether man was likely to be nearer to the species investigated.

If it was a case of greater sensitivity at the receptor site it was more difficult and, so far as he knew, there was no means of tackling that.

He was unable to add how variable the receptor site might be in different species including man.

Asked for the names of references by a delegate, Dr. Gage said that Hygienic Guide Series were very good. They did attempt a summary of conclusions. There were similar ones produced by the American Petroleum Institute. But when it was published, the ILO (International Labour Organisation) Encyclopaedia should be a very good volume. It was expected in the near future.

A SPEAKER said that, although there were a number of consultancy organisations which carried out tests and gave an interpretation of the meaning of them in terms of toxicological effects on man, and some organisations which would do tests on effluent, it seemed to him that he could not find an organisation which was able to interpret those tests.

They had the River Board Authority's definition which said the materials which were not specified had a maximum permissible level of nil in general, but they seemed to be entirely in the dark as far as being able to find an authoritative consultancy service which would interpret Fish toxicology tests and state how they related to actual practice and what the attitude of the River Board was likely to be to these effects.

Dr. GAGE could not really comment on this but referred him to the I.C.I. Laboratories at Brixham who were concerned with pollution.

The CHAIRMAN asked Mr. Green to give a little more information about the service provided by the Systems Reliability Service Industry. How was it available?

Mr. GREEN said that the services offered by the SRS were of four types—confidential project service, reliability data bank, Associate Membership, and training. Quantified reliability techniques were utilised and available for all kinds of applications both for plant systems and equipment. The full services of the Authority in this field were channelled through the SRS and were available on a commercial basis. The applications of the techniques were both in the fields of safety and availability and were of particular value where there were high risk situations involving consequences which could lead to large loss of money or human life or national prestige.

The SRS came into being by the demands of technical personnel who wanted to combine their efforts in some way in order to assist one another in the field of reliability. It may be obvious that certain switchgear, for example, used in the chemical industry, the generating industry, and the nuclear industry may be the same. Therefore, by pooling the resources in some way from these industries we are able to derive information from larger populations of equipment and also to do it more economically. This also applies to reliability analyses of large systems where perhaps some large computer program needs to be developed which may be applicable to systems from different industries. Essentially this is what the SRS is all about, it is a pooling of resources and co-operative effort at a technical level to assist industry. A very valuable attribute of this service has been the ability to offer to industry independent assessments on the reliability of systems and equipment.

The general details of the services are described in brochures giving information which could be obtained from the General Manager of the SRS at UKAEA Risley.

Asked by the The CHAIRMAN to what extent the data was published, Mr. GREEN replied that information received was generally circulated amongst the associate members or by special arrangement where a job was being done *ad hoc*. It was entirely a co-operative effort which was the only way.

Large firms were unable to solve the problem on their own as there is a difficulty in getting sufficient population sizes. The data scheme described operating on a "club" basis tended to be available only to clients of SRS. This pooling of information enhances population sizes.

Mr. M. KNEALE asked whether Mr. Green would like to give an example of small but successful co-operation with some more practical detail.

Mr. GREEN replied that it will be well known the work that has been done on various systems and chemical plant but an interesting example of co-operation is that in the field of high pressure diecasting machines. Concern has been expressed on certain aspects of defect rates and availability of

machines in a particular factory and a combined effort was mounted between SRS, the factory, and the Department of Trade and Industry who had experience of such machines. The SRS mounted an investigation whereby a data bank collected information on failures of machines on all shifts and analysed them using the existing facilities. In parallel, a theoretical prediction of the various reliability characteristics for machines was undertaken, such as failure rate and availability. In this case the reliability data were drawn from the SRS data bank which was not set up originally for the purposes of predicting the reliability of diecasting machines but, as has already been suggested, contains certain component parts which may be found in different industries and, taking into account the environmental and stress factors, it is possible to utilise such data in a meaningful way for the start of such an investigation. The results of the field data collection exercise and theoretical prediction were then compared and there was reasonable agreement. In addition, certain areas were revealed which required further detailed investigation. A method of prediction was shown to exist such that in the event of designing a new machine, theoretical analysis could be undertaken in the early design stage and, furthermore, meaningful reliability specifications could be prepared for such a new machine. Obviously, a by-product of this exercise was the start of a data bank which was particularly applicable to diecasting machines in their own environment. The end products of the exercise were, therefore, to enable the optimisation of maintenance and operation of the existing machines and to lay the foundations of the design techniques of a new machine if it is required.

A SPEAKER said that he did not want to decry the sort of work described but asked what fraction of accidents were really accountable to hardware and what fraction to the human element.

In an aeroplane there were safety mechanisms and there was a pilot. Until recently one would not have thought about a physical attack by a hijacker. There were many things which could not be anticipated before you started.

With reference to the human element, replied Mr. GREEN, generally it will be appreciated that in any accident it would be expected that the human element will occur because people are involved in the system somewhere. For example, they design, operate, maintain, test, build, manufacture, and carry out various functions. Hence, it is necessary to consider what hierarchical level in the system is to be considered, for example, piloted aircraft would be expected to be more susceptible to the human element than a type which is completely automatically controlled. The question is wide but in various types of accidents studies show that about 50% involve the human element and the rest involve hardware and other factors.

In the Atomic Energy Authority, analyses have been carried out on data collected on various types of events occurring on plant, with a view to investigating the human factors involved. It has been found that in the case of unscheduled shutdowns of particular types of reactor plant that about 14% of unscheduled shutdowns of the plant involved the human factor. Obviously, there will be variations from plant to plant depending on particular conditions.

It is an interesting point the speaker raises with reference to a hijacker and to things that could not be anticipated before you started. It is necessary to decide whether the policy is going to be along that of causal analysis because the analysis of causes will go on till the end of time and the hijacker is just a particular instance. This means that any situation which is now viewed and requiring a decision is not one that would be deterministic. Therefore, one is faced with a

probabilistic situation which introduces the idea of risk. It may be argued that if one knows what one is doing, one does not need statistics, but this is another argument. The main point is that it is possible to harness the experience to date and quantify the risk on that experience without knowing the cause. For example, it is fairly clearly known that if human error occurs in a particular task, it may be possible to quantify the error rate for that task undertaken by human beings without knowing the causes as to why the human being fails to undertake the task.

In practice, the engineering of a design or the operation of

plant tends to utilise both methods of causal analysis and risk analysis and the basic problem is how to harness our experience to date such that we use it in the best possible way to predict the future and the more the subjectiveness can be removed from the argument the more objective a decision can be.

The speaker may be interested to note that active work in this area, for example, of probabilistically modelling a man failing to press an emergency button in a given time, is being studied and is one of the joint co-operative topics being dealt with in the SRS.