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CLINICAL

An oracle on drugs safety

David Potterton talks to leading cancer consultant Dr Francis Roe about his work

DRUG companies concerned about safety, especially from the viewpoint of possible cancer risk, may well seek the advice of Dr Francis Roe.

For he is a member of the DHSS Committees on Toxicity and Carcinogenicity and of the WHO Expert Advisory Panel on Food Safety. Dr Roe has an established reputation for interpreting results of laboratory data on potential drugs.

'For every potential drug that is deemed to be adequately safe, there are many others which have to be given the thumbs down on grounds of inadequate efficacy or safety. These never proceed as far as the regulatory authorities,' he told *Doctor*.

'I try to give the companies or organisations that come to me an insight into the results of the work they have done.'

Dr Roe is not just concerned with drug safety, but also advises on the toxicity of other agents such as food additives, industrial chemicals and pesticides. Like anyone else who serves as both an adviser to industry and sits on government committees, Dr Roe jealously guards the name he has built up for absolute scientific integrity.

Dr Roe . . . keeps a keen eye on drug safety and advises industry on products' toxicity

It was ten years after he qualified at Oxford that Dr Roe made a deliberate decision to devote his life and work to the prevention of cancer.

'In the late 1950s almost the whole of cancer research was geared to finding therapeutic cures, but I never believed that there was any rational basis for thinking that one could kill off cancer cells selectively without at the same time seriously damaging normal, healthy tissue. I was convinced that the right way ahead was via prevention,' he said.

He was appointed reader in experimental pathology at the Chester Beatty Research Institute in 1961 and was in charge of that department for ten years under the late Sir Alexander Haddow. Dr Roe was co-author of a book on cancer prevention together with Mr Ronald Raven, the well-known cancer surgeon, and Chairman of the Marie Curie Memorial Foundation.

Later with Professor Ernest Cotchin of the Royal Veterinary College Dr Roe wrote what is still regarded as one of the most important standard text books on the pathology of rats and mice.

'It was evident that basic knowledge available for those undertaking animal experiments to find out if chemicals are carcinogenic was extremely deficient. Researchers were floundering because they had inadequate knowledge of the natural diseases of laboratory animals,' he explained.

'Many experiments on mice, rats and hamsters were poorly designed and poorly carried out. All sorts of wrong deductions were being made from badly collected and inappropriately analysed data.

'Until the 1960s it was assumed that the results of animal experiments for cancer were equivalent to humans dying from cancer. Then it was realised that most of the tumours arising in laboratory animals were non-fatal. A failure to appreciate the significance of this important difference led to miscalculations in correlating animal experiments to man,' said Dr Roe.

It is perfectly clear that some animal experiments are full of flaws. The most important and

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most common flaw is that animals are grossly overfed.

A few years ago there was a welcome move to reduce premature death from a wide variety of infections and infestations by the use of pathogen-free animals, but their use makes it necessary to sterilise diets with consequent destruction of certain nutrients and vitamins and a tendancy for food pellets to crumble.

To compensate for these changes more minerals, vitamins and fats were added with the result that many widely used diets contain too much calcium, too much phosphate and too much fat.

Apart from this, caged animals tend to eat too much because they are bored and some become grossly obese. They are also sex-starved. The males are segregated from the females but the sexes are kept in the same room where they can smell each other.

Sex

'Partly through over-feeding and partly through sexual deprivation they develop a wide variety of endocrine disturbances including numerous tumours of endocrine and sex glands,' said Dr Roe.

'The bladders of frustrated males become plugged with coagulated protein from the seminal vesicles or prostate, and sex-starved females spend half their lives in a state of pseudo-pregnancy because they can smell the males.

'I am sure there are human parallels to some of these problems but clearly the size of the overall problem is far greater in the laboratory then it is in human society. There is evidence that over-feeding increases the cancer risk in humans, but the effect is much less obvious than it is in laboratory rats and mice.

'Compared with laboratory animals eating *ad libitum*, animals restricted in food intake by about 15 per cent, develop far fewer tumours — in some experiments only an eighth of the number of tumours — while looking healthier and living longer.'

Risky

Dr Roe now has long-standing connections with several companies that make or use chemicals, such as food additives, pesticides, drugs or domestic products, or expose their workforce to such chemicals. He advises them on whether their products are risky or whether they are safe and how to test them for carcinogenicity.

In his opinion there has been rather too much carcinogenicity testing of food additives which are clearly not toxic. There is still research work to be done on food colours, he says, but he doubts very much whether anyone has come to any harm from any of the colours in current use in this country.

'I sleep easily at night and do not go out of my way to avoid any particular colours in my food, unless the appearance is aesthetically distasteful. However, I do not like substances being put into food just for the convenience of the manufacturers.

Mistake

'One has to be very careful when dealing with the safety of mass-produced foods because one mistake can affect a large number of people. With drugs, a mistake will affect only a relatively small number of people, and if they are receiving some benefit from the drug at the same time, then unmitigated large-scale tragedy is unlikely,' he said.

Dr Roe believes that the results of tests for toxicity and safety should become public property and not be locked away in researchers' files. But he is against instant public disclosure of undigested and unconfirmed data because half-baked information getting loose causes a quite disproportionate amount of trouble and wastes resources.

This was the situation with nitrites he believes. Because of the scare created by premature disclosure of muddled data, scientists are time and time again being summoned from numerous countries to international conferences to discuss the results of essentially uninterpretable experiments.

Spinach

Of course nitrites should, on the whole be discouraged, but many foods, like spinach, naturally contain nitrate which can be converted into nitrite. Such foods cannot be banned. The reason nitrite is added to bacon and meats is to prevent botulism.

Taking this and other factors into account, Dr Roe believes that regulatory bodies worldwide are making essentially correct decisions with regard to the use of nitrites in foodstuffs.

The public, he said, tend to get the impression that everything is toxic. This is partly because toxicology journals rarely publish results of studies showing that chemicals are safe, and partly because for lay journalists, 'toxic effects' are news but 'safety' is not.

To black all products as dangerous in the eyes of the public is counter-productive because people end up by ignoring all warnings on the grounds 'you can't win'. For this reason Dr Roe is opposed to 'scary' labels on everything.

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