"If the crew ask, offer your skills. But don't take charge"

always useful to have a medical perspective on board. "Doctor volunteers can be our hands and eyes in any medical situation," he says. "Their professional skills and our experience make a very effective combination, allowing us to make better decisions about when and if to divert, for example."

Should I take a coat hanger?

In 1995, a professor of orthopaedics famously rescued an airline passenger from a potentially lethal tension pneumothorax using little more than a coat hanger, a urinary catheter, and a bottle of Evian water.[11] Fortunately, this type of genuine emergency is extremely rare. There are no industry-wide data describing the precise nature of in-flight medical incidents but various snapshots and anecdotal accounts suggest that faints, vertigo, dizziness, and other neurological problems are relatively common.[12-14] So are diarrhoea and vomiting, asthma, angina, and minor injuries.[15]

People with pre-existing disease were most likely to get ill in one study,[13] although Dr Wilkinson notes that passengers who have been through pre-flight screening rarely become ill during flights. "Incidents usually involve people who don't know they are ill, don't say they are ill, or accidentally pack their medication in the hold," she says. Data from MedLink show that in 2007, more than 40% of calls were about neurological problems, usually faints. About one quarter were gastrointestinal, the rest were cardiac, respiratory, and orthopaedic incidents in roughly equal proportions (figure).

Emergency medical kits vary from airline to airline and can be extensive. The Aeromedical Association's 2007 recommendations are updated regularly by expert consensus (box).[16] Once again, there are no reliable data to inform their decisions. Aircraft registered in the US must carry defibrillators,[4] and many other airlines carry them voluntarily. If you're very lucky, there may even be a telemetry device that transmits a passenger's vital signs, oxygen saturation, end tidal capnography, 12 lead electrocardiogram, and video footage to doctors on the ground. These devices have been on the horizon for several years and a handful of big airlines including Virgin Atlantic are experimenting with them. "Telemedicine is definitely the future for in-flight medical emergencies," says Dr Alves. "We have some experience with these devices and they can be extremely useful." More useful than a real live medical volunteer? "No. Nothing works better than another professional on the other end of the line."

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Despite his emigration to Israel more than 30 years ago, Howard Cedar's voice betrays his New York roots. A senior figure in genetics research, the Hebrew University professor is well placed to give a snapshot of current progress in this complex field, especially its application to cancer. He was an early pioneer in molecular biology, which "started a new era in medicine," he says. Instead of looking just at symptoms, molecular biology delves into the functions of the body and discovers the basis of disease.

Learning how genes are regulated has been long, slow work, and only now, after 25 years, is Cedar seeing the practical application of what he has been studying. Today, he talks about the "unbelievable" pace of genetic research. He is absolutely clear about the direction of travel for basic research to uncover the causes of disease but is frank about the "road blocks" in the way.

Cedar got his introduction to genetics during his Vietnam War draft in the early 1970s. Against that volatile backdrop, Cedar, fresh out of medical school, was "fortunate" to be sent to the National Institutes of Health in Washington, where exploration into DNA and genes was in its infancy. "I got introduced to the study of chromatin, understanding how DNA is packaged in the nucleus. That set the stage for the rest of my career. I saw how important it was in terms of biology."

Ideal research setting

Cedar and his young family arrived in Israel in 1973—just two months before the Yom Kippur war broke out. In Israel, Cedar joined the fledgling department of biochemistry at the Hebrew University, where he is now professor. It has proved a fertile ground for genetics research. "A very high proportion of geneticists are Jewish. I don't know how to explain that," he says. There is also a large number of people who come from a homogeneous source in Israel. "Ashkenazi Judaism is said to have developed from 1000 people that lived in about year 1000. So all Ashkenazi Jews are related to each other from these original 1000 people and for studying genetics that is a very useful thing. In addition, there are uniform Arab populations. A number of new genes have been discovered by studying these populations."

It also makes it easier to screen for certain genetic diseases, such as cystic fibrosis. "It is very difficult to screen for cystic fibrosis because there are about 100 different mutations that cause the disease and it is difficult to develop a test that would pick up all these mutations. But in Israel about 95% of the patients with cystic fibrosis have one of five mutations because of the uniformity of the population."

Is this mere trumpet blowing of Israeli expertise? "I don't think Israel is any better at genetics than anywhere else but there is a lot more use of

THE GENE DETECTIVE

Howard Cedar got sucked into genetics research when it was still in its infancy. He talks to **Rebecca Coombes** about breathtaking progress in oncology and barriers to further advances

genetic testing," claims Cedar. He refers to the sophisticated genetic testing programme that the ultraorthodox population use to screen prospective couples before marriage—before they are even introduced. Or testing for familial dysautonomia, which is an almost uniquely Jewish disease.

Genetics and cancer

Cedar talks about genetics as being the "key to life," the route to understanding the basis of cancer and other diseases. In every cancer cell there are genetic changes. "The normal mutations that we see in cancer come about spontaneously; they are caused by the environment, cosmic radiation, carcinogens, or some other form of radiation. But there are also genetic differences between people which make them more or even less predisposed to cancer." The best known of these are the genes predisposing to breast cancer and colon cancer, but there are likely to be many others. "We know there are family histories of certain forms of cancer—leukaemia, brain tumours—that means there is some gene or combination of genes that predisposes you. Even if we haven't isolated those genes yet, we know that they are there."

Although this stage of discovery is exciting, it raises the key question of what to do with the knowledge. "We are identifying those genes that show a predisposition to cancer but many times we don't know what to do with this information. Women with the breast cancer gene face a dilemma—what to do? What can you change so you don't get cancer, or can delay it? That's the next step. We aren't there yet."

There are also other genetic changes at work—a field of study known as epigenetics. "When we are born we inherit genes from our parents. Each cell contains all these genes. But each cell uses only a fraction of these genes. Many times we turn off genes. For example, the gene for eye colour is expressed only in the iris of the eye and everywhere else it is turned off. And one of the things that does this is DNA methylation."

DNA methylation—how genes get turned on and off—is the focus of Cedar's research. "It turns out that if you look carefully inside a cancer cell, which we are now capable of doing to a much greater extent, you see that genes that are normally turned on are somehow turned off, or the opposite. These are changes that are not genetic changes but epigenetic changes. Probably the effect on the cell is much bigger from these epigenetic changes than the genetic changes. But we don't know where these epigenetic changes come from. This process of methylation occurs in every single tumour. It doesn't matter what it is: breast, colon, prostate. It is probably something that occurs very early. Furthermore, this epigenetic change is actually programmed; it is not random like the genetic changes. We can see it in the cell. Something turns on this programme that makes the cell into a more primitive cell—like an embryo cell—which divides very rapidly."

The fact that this change occurs in every cancer cell is good news, says Cedar, because it reveals a "master process." "Now we have a process that has come into every cancer cell. It is very basic, without this you can't get the tumour. That means that DNA methylation is probably a good target for either therapy or prevention—this may be very far down the line but it is good to know." The process has a role in other diseases, such as Prader-Willi syndrome and Fragile X syndrome.

In cancer, the progress in terms of diagnosis and treatment has been breathtaking, says Cedar. "I remember people saying once we understand molecular biology we will be able to devise treatments and new ways of diagnosis. And a long time went by when that was not true. We kept doing molecular biology until it was coming out of our ears but nothing was happening. But now, in the past 10 years, it is starting to come to fruition. In terms of treatment, a gigantic change has happened."

Important advances include smart cancer drugs that target specific cells, such as imatinib for chronic myeloid leukaemia. "Researchers figured out that in this form of leukaemia the genes inside the cell reorganise and make a new product that causes the tumour. They found a drug that attacks that product, which is not present in normal cells or any other tumour. It is a miracle drug and there are a number of treatments like that and more coming every day." He refers to the controversial field of gene therapy as a good approach "in theory" but an area where our ability is still limited. "We have a lot of ideas. We have theoretical ways of turning genes on and off, replacing genes, but getting those things into the cell to do their work has so far proved to be a problem."

Prevention

So what can a family doctor do to help patients avoid cancer? "When I started studying medicine the dean of the medical school got up in our first lecture and said, 'I know that you all think that you are here to cure diseases but that is not true, that is not our goal; our goal is to prevent disease.' I thought this was crazy at first. But over the years, I have come to the conclusion that he is right. We don't have tools to do it yet, but this is the goal." And why do we have no cure for cancer yet? "I think it's not true, there are cures. There are many women who have been cured of breast cancer or of chronic myeloid leukaemia. We know with prostate tumours that if you get it early, cut it out, it's a cure. We have made a lot of progress. It's a misnomer to think of a cure for cancer. I'm not sure that exists. Cancer is not just one disease, it is a lot of diseases."

If the basics of cancer were understood, then doctors could focus on preventing the disease. "Look at diseases caused by vitamin deficiency—you don't cure those diseases, you prevent them by taking vitamins, and that's the way it should be with cancer. OK, maybe not prevention, but delaying the disease until the person is 120 years old. I think it is a reasonable thing if we are able to understand at a basic level what is going on."

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