Logical Changes – a look at the changing face of cancer research

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The word cancer provokes a fearful response and people often see the diagnosis as a death sentence. It conjures up such an emotional response that people, who normally treat animals in a humane and caring way, will condone animal testing or vivisection, believing that it will bring about a cure.

Animal testing for scientific reasons has been happening since the days of Aristotle around 300BC (when they didn't have access to the vast technology we have today). Strangely, it began ramping up in the early 1900s and increased even as great advances were made in imaging, communication and research techniques. Cancer has been documented since the dawn of civilisation and still we don't have a cure. Could it be that the chance of finding a cure for cancer is not related to the number of animals we genetically modify, maim, make sick and kill?

Cancer is one of the leading causes of death in Australia accounting for more than 28% of deaths in 2004. But there is some good news and that is that Australia has one of the highest survival rates in the world and over the last two decades, cancer related deaths have dropped by about 14% between 1986 and 2004.

The bad news is that the number of new cases more than doubled between 1982 and 2007. Projections by Australian Institute of Health and Welfare state that the number of cases of cancer diagnosed in Australia will increase by 40% from 2007 to 2020. The increases are to a certain extent, brought about by ageing of the population, but even with age standardisation the rates are on the rise.

Animals are used for testing new drugs, researching and exploring the biology of cancer cells and also the causes of cancer. There are a huge variety of tests performed on these often genetically modified animals. Many species are used, but the mouse is often preferred because of the high level of genes in common with humans.

Researchers readily admit that in-vivo, or animal tests are unreliable and that results often cannot be extrapolated to humans. And there are varying reactions to drugs even between human siblings, different genders, and different races, because people don't necessarily metabolise drugs the same way even though we share many genes. So it is obvious that there will be huge differences between species.

In the human body drugs go through a complex range of processes involving its absorption, distribution, metabolism and elimination. When animals are tested, the tumour has been implanted into an immunocompromised animal. It has not occurred spontaneously and this creates differences in the tumour microenvironment and therefore its response to drugs. Thus drugs that have been approved for trial ultimately fail, and ones that may have succeeded are eliminated early. In an article in Nature Reviews the success rate for new development projects in phase II trials is said to have dropped from 28% to 18%, stating 'insufficient efficacy' as the reason for failure and so, cancer treatment still relies heavily on drugs that were developed decades ago.

The global oncology market is estimated to be worth US$42billion, with 2292 anti cancer products in development. But only a fraction of those will reach the market and only one out of 10,000 compounds tested on animals and showing potential is successful and allowed to enter clinical trials.

Meanwhile, there is increasing acceptance in research arenas that non-animal tests provide a superior technique and are quicker and cheaper than their animal counterparts. There are lists of alternatives available such as microdosing, body on a chip technology and microfluidic chips and many more. However, looking at the bigger picture provides more answers to the reasons that cancers are on the increase; reasons that are applicable to humans, not monkeys who are forced to take up smoking, not mice who have been modified to make them more like humans, but our own species. The answers are there, and after taking a look at two of our biggest cancer institutions it is apparent that research is turning more to our own kind and fields such as epidemiology, pathology, early screening and prevention are coming to the fore.

Two of the major cancer institutions in Australia, the National Breast Cancer Foundation and Cancer Council Australia, show that although researchers are still clinging to animal models, there have been other changes which make use of the fact that we have a large resource of humans to test on. No genetic modifications are needed. We can study our own species with tumours that have developed spontaneously and we can compare those findings to the rest of the population. The aim of this research is to prevent cancer from occurring and limiting its spread within the body in a way that is efficient and causes the least amount of side effects.

Prevention

The World Health Organisation estimated that a third of all cancers are preventable and that the incidence in developed countries is more than twice as high as in developing nations. Professor Ian Frazer of the Cancer Council Australia believes that in Australia the percentage of preventable cancers is closer to the 40 to 50% mark.

Meanwhile the Australian Institute of Health and Welfare has recently reported that most people are not adopting a healthy lifestyle and have at least one risk factor, with the majority of people not eating enough fruit and vegetables, a well known risk for chronic diseases such as cancer. More than half of the population doesn't exercise enough, many are obese and still smoking and 17% of men and 11% of women have five or more risk factors (2012).

A healthy lifestyle does not guarantee freedom from cancer because there are other factors such as genetic makeup and environmental carcinogens that are less controllable than how we treat our bodies. However, it does help to tip the balance and if a diagnosis of cancer is made then someone with good health habits is more likely to cope with the treatment and make a favourable recovery.

Here is an overview of research being conducted at the NBCF and the CCA that does not require animals:

Population Studies

- **Register 4** is a register of women prepared to provide information about themselves and their lifestyle. They will be given the choice to take part in research. The register

will eventually cover a range of health issues, enabling research to 'move from the lab to humans'.
- Australian **Ovarian Cancer Study** collecting patient histories, blood samples and biological samples from over 3500 women with cross study of factors such as folate intake and alcohol use.
- The **45 and Up** study is Australia's largest study into healthy aging and how that relates to cancer.
- **The National Cancer Statistics Clearing House** enables the development and communication of national cancer statistics. It publicises statistics, allows tracking of people with cancer, and enables exchange of technical information and the standardisation of this data.

Studies of People Currently Being Treated

- The number of cancer patients participating in clinical trials and population studies has grown from three percent to five over the last ten years, with some more high profile studies even approaching ten percent.
- **Long term follow up** for detection of recurrence of metastatic tumours and to monitor side effects of treatment.
- Use of **complementary medicines**. NBCF has funded a study into Qigong a Chinese therapy that involves physical activity and meditation.
- A two year investigation into the **patenting of genetic material**. The investigation culminated in support of a bill which would ban gene patents and allow doctors free access to any naturally occurring biological material.
- **Australian National Endometrial Cancer Study** is a study of 2000 women with endometrial cancer. Researchers will be collecting information on lifestyle, family history of cancer, medical information and biological specimens.
- An international research project evaluating the effectiveness of combined **radiotherapy and chemotherapy on melanoma** in 100 volunteers.
- Study of biological samples from people being treated for cancer to counteract the ill effects of chemotherapy.
- Collection and analysis of information from people suffering from **lung cancer** to identify discrepancies in treatment and provide a more uniform approach to treatment.

Family and Twin Studies

- **Twin studies** to unravel the secrets of **cervical cancer.**
- **Study of families** with multiple cases of blood cancers to understand the genetic factors involved in cancer development.
- A study looking at a link between **inherited genetic faults and mammographic density**.

Tissue Studies

- **Tissue banks** and the development of microarray technology have allowed researchers to scan thousands of tissue samples. Efficient cataloguing of these results is needed so that researchers can locate the information they require.

Prevention

- Focus on prevention. The **National Action Plan** is a 30 year timeline describing the prevention of mortality and morbidity and the disease itself.
- **Colon Cancer Family Research Database** with health and behavioural information on over 300 families. It helps to identify environmental factors such as use of hormones and ways other than surgery to reduce the risks of a hereditary cancer known as HNPCC.
- **Investigation of behavioural factors** such as poor nutrition and obesity, to better understand what contributes to the development of cancer, and exploration of ways to reduce high risk behaviour.

Early Detection

- The World Health Organization advises that early detection of cancer creates greatly improved chances for survival. There are two facets of early detection; the first is for individuals, physicians, nurses and other health care providers to recognise early warning signs and act on them. The other is the use of screening devices. In Australia, for example, women are encouraged to have mammograms to screen for breast cancer, and to have regular pap smears to detect cervical cancer. Men can have regular prostate checks, and a bowel cancer screening tool has also been launched.

All of these research avenues are providing relevant information about the biology and background of cancer and the efficacy of treatment. There is no shortage of data, and combined with the growing number of efficient in-vitro (non animal) testing alternatives, it seems as if the days of animal testing must surely be numbered. Even the Therapeutic Goods Administration which is the body regulating drugs in Australia states that consideration should be given to replacing animal studies with in vitro models.

In summary:

- Cure rates for cancer are increasing but also the rate of diagnosis is on the rise.
- Cancer is more prevalent in developed countries.
- While a third of cancers are preventable, many Australians are opting to take a passive approach to their health.
- Treatments being used are still based on old drug regimes.
- Research still favours animal models even though they are unreliable and many alternatives exist, but researchers are turning to epidemiology, pathology and the establishment of tissue banks and data bases to provide them with information regarding the cause and progression of cancer and efficacy of treatment.

Unfortunately, this isn't a 'happy ever after' story because as we speak there are millions of animals living solitary and unnatural existences. They are enduring pain that has been inflicted on them, all in the name of finding a cure for a disease in another species.

With the growth in imaging and communication technology, and the availability and storage of specimens, there should be no shortage of research alternatives for cancer prevention and treatment, both of which will be better tailored to the human animal.

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