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"ADVANCES IN DNA TECHNOLOGY AND AREAS OF POTENTIAL IMPACT ON THE LAW"

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ADVANCES IN DNA TECHNOLOGY AND AREAS OF POTENTIAL IMPACT ON THE LAW

I PREAMBLE

The overall theme of this year's meeting of the Canadian Institute of Judicial Administrators explores the legal consequences of scientific advances in biotechnology. This is such a wide ranging topic that in order to use the time allotted to me effectively, I have chosen to focus specifically on advances in DNA technology. I am not going to touch on such fascinating things as in vitro fertilization, the therapy of the fetus, etc. Even omitting other areas to focus on DNA developments, I will only have time to touch on some highlights in this field.

II SCIENTIFIC BACKGROUND

In order to understand the issues raised by DNA technology, it is essential to have some knowledge of what DNA is and what it does. I therefore will begin by outlining the basic background information about DNA you need.

What is DNA?

DNA stands for deoxyribonucleic acid. This is a long chemical molecule which contains the genetic information to specify the production of the proteins and enzymes that build our cells and perform all life functions. DNA contains genetic information in a manner which is analogous to the way in which a written text contains information - a small number of letters (or spaces) are arranged in a linear sequence. In a written text, the letters of the alphabet convey information because they are arranged one after another to form words and sentences. In DNA, four chemicals (known as bases) are arranged one after another to form codons. A codon is a triplet of bases which specifies an amino acid. A particular string of amino acids makes up a particular protein. The gene for that protein is the string of codons that specifies the amino acid sequence for it. Genes are the functional units of DNA.

In the human genome, less than 10% of the length of our DNA is taken up by genes. It has been estimated that humans probably have about 100,000 genes, since we make about that number of different proteins. What exactly the rest of the DNA does is not well worked out yet, but it is probably important in controlling the genes. A gene may be actively making its product or it may be turned off. For example, a bone marrow cell makes hemoglobin, but a hair follicle cell doesn't. Some genes are active in all cells, whereas other genes may only make their product in certain cells, or at certain times in the life cycle.

The DNA molecule consists of a double helix with connecting rungs. Each rung is made up of two of the four bases that I mentioned - adenine, thiamine, guanine, and cytosine. The first two always pair together in a rung, as do the second two. This provides the mechanism for the molecule to replicate itself. As you can see, when the DNA molecule separates during cell division, an exposed T half rung will always attract an A (adenine) floating in the cell; an exposed A half rung will always attract T, and so on until you get two double helices again, each identical to the original. It is this "complementary" structure that allows replication.

The human genome has 3 billion bases in its sequence - long enough that it would fill well over half a million pages if it were made into a book. Most genes consist of between 10,000 and 150,000 code letters. This means as I said that most of our DNA consists of sequence that does not make protein, and is not "genes" in the usual sense. At intervals along the DNA sequence there are variations between individuals which have no functional significance but which are inherited. Just as our fingerprints will identify us uniquely, testing for these frequent and harmless variations or markers along the sequence, will also identify each one of us uniquely (except for identical twins).

Some individuals have changes in the part of the sequence making up a functional gene. If that gene is a necessary one, this will cause disease and these diseases will be inherited in Mendelian patterns in families.

How is DNA Tested?

The "complementary" structure of the DNA molecule is taken advantage of to test DNA. A short sequence of bases can be tagged with a label that is detectable, e.g. radioactivity. This tagged sequence is then known as a probe. If this probe is exposed to a person's DNA that has been broken up in a test tube and treated so that the double helix has come apart, the probe will always join with a corresponding complementary sequence of bases in the DNA. If the complementary segment is not present, it will not join to the DNA. This means if the test probe joins with the person's DNA, the sequence must be present.

At present there are three main ways DNA probes are used.

1. A probe may consist of a piece of sequence that directly detects an abnormality in a gene.

2. A probe may be complementary to a piece of DNA which has variations between individuals and which is known to be physically next to a disease gene. This nearby stretch of sequence to the disease gene is known as a "linked DNA marker" because it will usually be inherited along with the gene as it is so close to it. Thus a probe can be used to see if a marker that reveals the presence of a particular gene is there or not.

3. The third way in which DNA probes are used is for DNA fingerprinting. There are some short sequences of DNA that are repeated many times at random through the DNA. The pattern of these repeats is unique to an individual. Probe molecules will anneal in a unique pattern to a person's DNA. This pattern can be recognized by what is called DNA fingerprinting. This technique allows distinction between individuals with close to certain probability (except for identical twins). These patterns are inherited so familial relationships can be confirmed or disproved. The DNA tests can be done on very small amounts of material - even a hair follicle.

What can these new DNA tests tell us?

Depending on which test is done, we can:

- identify a particular individual
- identify a relationship
- detect if a disease gene is present or not
- detect by the presence of a DNA marker the likelihood of a disease gene also being present

III WHAT ISSUES OF LEGAL AND SOCIAL CONSEQUENCE WILL BE RAISED BY THIS NEW ABILITY?

The impact of these new tools will be very wide-ranging on society. We need to think through some of the questions and issues the new technology will raise. Many of them will impact on our courts and our justice system since there are wide ranging social, ethical, and legal ramifications. I would like to discuss this topic under seven headings.

1. Paternity

The paternity tests that were previously available could disprove paternity when a child had a genetic factor that wasn't present either in the mother or in the putative father. It could not usually prove that a particular man was the father. The new DNA testing achieves levels of probability that establish beyond any reasonable doubt who the real father is - if they are performed in high quality labs. This has been accepted as evidence in a number of courts and will change this area.

2. Immigration

In Britain, as in a number of other countries, resident immigrants can ask for resident status for certain relatives. DNA fingerprinting has been used for purposes of immigration to test if a claimed relationship is true. The claimed relationships turn out to be accurate in about 95% of cases, whereas only 50% are approved by the usual method of interviewing. It may very well come to be used routinely in any disputed immigration case.

3. Forensic Identification

In 1986 DNA tests established the same male had sexually assaulted and murdered two teenage girls in Britain. The murder hunt was focussed on three villages which had 2,000 male residents. Conventional testing eliminated all but 200 of these men. DNA fingerprinting was then used on the remaining 200 to identify the murderer and he was convicted. A 17 year old suspect was also ruled out in the process. DNA fingerprinting therefore seems to provide evidence that is acceptable to British courts of law. In the United States, DNA data have been considered (Nature, May 11, 1989) as evidence in more than 80 criminal, rape and murder trials in 27 states. There have been at least 60 convictions. The power of the technique is such that the likelihood of a match between two unrelated individuals is less than one in 100 million. A note of caution is in order however. To reach this level of accuracy, the laboratory quality control must be excellent, and human error - e.g. mislabelling of samples - must be guarded against. However, given this, the technique is extremely powerful.

It also raises issues of individual rights. In what circumstances can someone be forced to take such a test? Because there is no possibility of mistake if done accurately and with good quality-control, perhaps a case could be made for coercion? It is important to remember that this test can identify whether an individual's DNA matches that from a sample of tissue with extreme accuracy. The meaning of where the sample was found and how reliable that finding is as evidence must also be unambiguous.

The California Attorney General's office is developing a DNA data base which will be used to identify and prosecute repeat offenders. The first entries into the data base will come from over 5,000 blood and saliva samples

collected from convicted sex offenders in California in the past five years. We can expect that the use of DNA testing for forensic purposes will increase markedly over the next decade.

4. Disease risk prediction

(a) Single gene diseases

As our knowledge about DNA evolves, it increasingly is allowing us to identify individuals who have a gene for any of the several thousand known single gene caused disorders - such things as Huntington's disease, familial hypercholesterolemia, Duchenne muscular dystrophy. Because the DNA of an individual can in theory be ested at any time from conception on, identification of an individual who has a particular disease gene can be done before the disease happens, or can even be done in utero before the organ or tissue that will be diseased is formed. Prenatal testing can be done now for a number of serious genetic diseases which cause much suffering, retardation, and death in early life. Most people in our society view this as a benefit and most, though not all, would choose to terminate in such circumstances rather than carry to term an infant who would be affected. However, the testing of individuals for diseases which have a later onset with many years of normal life preceding the disease, or the testing of individuals who are presently clinically well but will become ill, raises many issues.

Doing testing on families with Huntington disease to identify which of the adult offspring have inherited the gene raises questions of ownership of information, and confidentiality. For example, in one specific case a young man who had recently married and wished to have children requested testing to see if he had the gene or not since this was going to alter his reproductive choice. To give him a result it was necessary to have a sample of his mother's blood who was in a chronic care institution suffering from Huntington disease. She refused to be tested, thus depriving her son of knowledge that some may interpret as his right. What if that mother had been tested previously but just refused to give consent for release of the information? Would a court be likely to override that refusal? In fact, who owns the information with regard to genetic makeup?. Perhaps it should no longer belong to an individual but to a family?

With regard to confidentiality, who should have access to genetic test results, for example in Huntington disease? Should a spouse, should an employer? There are situations where the public good may override the value of confidentiality. For example, an airline pilot responsible for the lives of hundreds of people may on testing be shown to have the gene for Huntington disease. Some of the first signs of this disorder are inattention lasting for short periods, and inappropriate emotional responses. What is the responsibility of the physician with regard to confidentiality here? Competing "goods" make decision making very difficult.

Identification of individuals who have a gene for a single-gene disorder such as Huntington disease, where all those with the gene will become affected, poses difficult enough questions. Single-gene conditions such as these are relatively infrequent in our population, but diseases in the next category are extremely common.

(b) Multifactorial Disease

Because of the frequency of multifactorial adult onset diseases, the new genetic tests will have an even greater impact here. We now know that many common diseases with adult onset, like atherosclerosis, manic depression, diabetes, Alzheimer's disease are multifactorial. That is, a gene or genes determine whether external influences are likely to cause that illness.

Increasingly it is becoming possible to identify by DNA tests which diseases a person is specifically at higher risk for. If you can identify individuals at risk, you may be able to offer some avoidance strategies. For example, if you identify those susceptible to atherosclerosis and they go on an appropriate medication and diet early in life, they have a very substantial decrease in the likelihood of having early heart disease. However, the impact of identifying by screening or at birth a "genetics profile" has major implications socially, medically, and probably legally.

As we become able to identify such individuals where the outcome is less clear because interaction with a particular environment is also a determinant along with the gene, how will we limit whether such programs should be offered or not? Would identification as having a genetic vulnerability cause damage by harming one's self concept? By becoming a self fulfilling prophecy? This is important because so much of illness is perception and attitude. Would it lead to discrimination against the individuals identified? How would such data be kept confidential? Should there be prohibition against using genetic testing prenatally since there may be societal pressure if abnormality is found for the parents to terminate such a pregnancy? Eventually it will be a matter of definition as to what is acceptable human genetic variability and what is a genetic disease. All of us are genetically unique and all of us have weaknesses and strengths.

5. Workplace Testing

All of us have inherited slightly different metabolic machinery for dealing with chemicals in our home and work environments. Some of us have genes that make us less able to handle particular pollutants so that we are more likely to develop lung disease or other problems after exposure. Should employers have the right to ask for genetic testing of these abilities? They may wish to do this so that their medical and life insurance plan costs will remain low because they only employ a workforce that remains healthy. This could mean that those individuals genetically vulnerable to particular pollutants are not employed and are thus discriminated against. Another danger is that a strategy of employing only "resistant" individuals may enable industry to avoid cleanups which they view as too expensive.

6. Insurance

We may very well need to evolve law to deal with how the new genetic knowledge should be limited in its application by the insurance industry as well as by employers. Should either medical or life insurance companies have the right to require genetic testing prior to coverage? Would they then charge higher premiums or refuse coverage to those at high risk because of their genotype? The principle of insurance is to spread risk over many individuals. It seems unjust to disadvantage individuals who through no fault of their own are likely to become ill. This is not as dramatic a problem in Canada with our universal health care system but it is

potentially a very important problem in the United States. If the insurance industry is not regulated in this regard in some way, it may be necessary for government to set aside funding for health care of such non-insurable individuals.

7. Gene Therapy

The new DNA technology raises the possibility of treating some severe genetic diseases by gene therapy. This approach involves insertion of new genetic material into an affected individual's body cells to perform the functions that their faulty inherited gene is unable to carry out. As usually proposed, it is analagous to other treatments in that it simply affects the body cells and not the sex glands. This means that if treated individuals go on to have children they will pass on the genes which they received from their parents. They will not pass on the inserted genes as only their body cells - not their germ cells - have been changed. This is a rapidly evolving area of investigation which has for the first time raised the hope of eventual treatment for some devastating human genetic disorders. However, it is breaking new ground and setting precedents and is an area that may in the future have legal implications. (e.g. If a treated individual no longer wishes to participate in follow-up but there is a risk of transmission of the gene to the cells of other people by the viral vehicle that is used to transfer the gene.)

If gene transfer is successful with these serious diseases, will it mean that genetic alteration is proposed for less devastating conditions? What should be the limits? Again, how much variation in difference from the norm in a fetus justifies testing and possible termination? Are we going to allocate societal resources to allow parents to use these techniques? If a severely abnormal fetus is detected that will use major amounts of health resources, even though the outcome is very poor, parents wishing to keep the pregnancy now do so. In the future, if it becomes more and more evident that resources are not infinite and that by doing this other normal infants may suffer, will it mean as a society we have to set some priorities and perhaps deprive parents of what we have always considered their rights? These techniques are going to force us to look at some very difficult issues much more explicitly.

It is worth making the point that many human characteristics such as intelligence, appearance, kindness, etc. are determined by the interactions of the effects of several genes with the environment. The possibilities of being able to modify characteristics such as these by changing the DNA of an individual are now so remote as not to merit anything more than distant speculations. The difficulties to be overcome even to correct the DNA of an individual with a well studied single gene determined disorder are formidable. We are much more likely to be able to influence desirable complex characteristics by environmental measures than by genetic manipulation for the foreseeable future.

IV SUMMARY AND CONCLUSIONS

It is evident that the new technology will affect many areas of our society and will pose often difficult choices. The new technology presents an opportunity and a useful tool if it is used wisely and humanely but also a danger if the implications for social justice of its use are not thought through. Screening programs in particular if applied prematurely may cause

harm and distress. If done well and with fully informed communication, they have the chance to decrease disease and better the human condition.

There is a need for discussion of many of these issues - a discussion involving the participation of the legal profession. The new DNA technology opens up so many questions which have wide ranging social, ethical, and legal ramifications. Our new abilities with the technology often highlight the difficulty of balancing the rights of the individual in contrast to the rights of the group. For example, should individuals, in some circumstances, not have the right to refuse to give samples for DNA testing or not to disclose information about their genetic makeup? Forensic medicine will change markedly.

Like any tool, depending on how it is used, this new DNA technology could bring benefit or cause harm to people. There are both opportunities and dangers in our new abilities. I hope as a society we will be able to take advantage of the new genetics and deal with the potential pitfalls and dangers in a wise way. We need to discuss how the new realities of genetic identification, both of particular individuals and of disease risk, can be incorporated into our evolving social ethic. I hope in this evolving discussion and in any law that is an outcome, that we can preserve the value of personal choice. Coercion exacts a considerable social and personal cost. Only when the availability of choice produces harms to others should legal limits be put on individual options. We cannot close Pandora's box. The new genetics is an irresistable development that cannot be wished away. The task is to channel our new abilities and knowledge into directions and policies that help justice, prevent disease and suffering, but preserve our heritage of individual choice and human genetic diversity.

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