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1 **Chapter 2**

2 **Research Use of Human Biological Materials**

3

4

5 **INTRODUCTION**

6

7 Historically, the science of pathology has led the way in the investigation of the mechanisms of
8 disease causation by proceeding progressively from whole organs and tissues to cells, and then
9 from the subcellular to the supramolecular and molecular manifestations of disease expression
10 (Rosai, 1997).

11

12 The range of medical benefits already obtained through the use of stored biological
13 samples is impressive.¹ For example,

14

15 In 1953 autopsies of young American soldiers killed in the Korean conflict revealed that
16 atherosclerosis begins at a much earlier age than was previously thought and that blockage
17 of arteries can be far advanced in the absence of symptoms; this research contributed to
18 findings concerning diet and exercise which have had a major public health impact in this
19 country, evidenced by a significant reduction in coronary artery disease (Enos, 1953;1955;

¹ For a survey of such benefits, see David Korn, "Contribution of the Human Tissue Archive to the Advancement of Medical Knowledge and the Public Health" (A report to the National Bioethics Advisory Commission), January 1, 1998.

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1 Solberg,1983; Strong, 1986).

2

3 In the late 1960s the study of samples of tissue from an unusual tumor of the vagina led to
4 the discovery that a non-steroidal estrogen hormone diethylstilbestrol (DES), then
5 commonly given to women during pregnancy, is carcinogenic (Herbst
6 1970;1971;1974;1981)

7

8 Thirty years ago a series of studies on tissue samples of precancerous lesions of the uterine
9 cervix led to the routine use of Pap smears, which have played an important role in the
10 early diagnosis and more successful treatment of cervical cancer. (Herbst
11 1970;1971;1974;1981; Younge, 1949).

12

13 Analysis of tissue from autopsies of persons in certain occupations, such as chemical
14 manufacturing and uranium mining, have established causal links between exposure to
15 environmental substances and certain diseases, including a cancer of the liver known as
16 hepatic angiosarcoma and cancer of the bronchial epithelium (Creech, 1974; Falk, 1981;
17 Dannaher, 1981; Popper, 1978; Regelson, 1968; Roth, 1957).

18

19 The analysis of autopsied lung tissue from smokers played a major role in establishing that
20 smoking causes lung cancer, that the risk of cancer increases with the duration of
21 exposure to the chemicals contained in cigarette smoke, and that precancerous changes in

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1 the bronchial epithelium can be reversed by cessation of smoking (Auerbach, 1962; 1979;
2 Flehinger, 1984; Frost, 1984).

3
4 As the science and knowledge of human disease have progressed, students of disease have
5 developed or co-opted in steady succession, the newest in scientific tools and methodologies.
6 Novel insights and expanded knowledge of agents and mechanisms of disease causation have
7 attracted a broader representation of the biomedical research community, including
8 immunologists, virologists, and geneticists, to the vast and valuable resource of human biological
9 materials for investigating human disease.

10
11 The tools used to analyze biological specimens have evolved from studies of morphology,
12 to light and electron microscopy, to sophisticated histochemical approaches to probe the chemical
13 composition of tissues, to the development of antibodies and gene probes. These tools have
14 revolutionized diagnostic and experimental pathology, as well as biomedical research. For
15 example, with appropriately tagged antibodies, it is possible to identify with great precision the
16 presence, location, or absence of specific protein molecules, and thereby begin to understand the
17 differences between normal tissues and pathological lesions.

18
19 Within the past 30 years, that we have entered the era of molecular and genetic medicine.
20 To understand the chemistry and genetics of normal biological functions and their pathological
21 arrangements, molecular biologists and pathologists increasingly collaborate to define disease

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1 entities and their patterns of expression on the basis of pathologic criteria. All new methods for
2 the study of disease, whether they be monoclonal antibodies, new molecular genetic technologies,
3 or others yet to come, ultimately must be interpreted and validated with reference to known
4 disease entities and appropriate controls. That process frequently requires that the methods be
5 developed and evaluated with authenticated pathologic materials.

6

7 **IDENTIFIABILITY OF SAMPLE SOURCES**

8

9 Before examples of research uses of human biological material are presented, several
10 terms and concepts used in this report need further clarification. This section explains the
11 terminology the Commission used to describe the identifiability of sample sources, and provides
12 definitions for human biological material and research samples.

13

14 In the debate about research use of human biological materials, the language used to
15 describe the identifiability of research samples varies (see chapter 6 for further discussion).
16 Previous guidelines and reports have categorized samples by the conditions under which they are
17 stored (with or without identifiers), although current federal regulations permit investigators to
18 take stored samples without seeking consent, make them anonymous by removing identifiers, and
19 then use them in research (see chapter 6 for further discussion).

20

21 Part of the confusion arises from the fact that people sometimes refer to the state of the

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1 information attached to the biological material in the repository and sometimes refer to the
2 information that is sent forward to the researcher. For example, the material might be identified in
3 the repository but no identifying information is forwarded with the research sample sent to the
4 scientist. This is an important distinction and of considerable importance because the potential for
5 benefit or harm is greater when the sample is directly or easily linked to the donor, placing the
6 burden of protection in different places, depending on who has access to the information (e.g., the
7 researcher or the pathologist, or both).

8

9 In a simple way, research samples fall into two categories: 1) those for which the source
10 can be identified (more or less), which means the sample can be connected, or linked, to the
11 person from whom it came; and 2) those samples for which the source cannot be identified at all.
12 The reason one refers to the former as “more or less” identifiable, is because the information
13 content of the research sample varies, from a very few data points that, nevertheless could allow
14 you, perhaps with some difficulty, to identify the sample with the person, to a sample that contains
15 an exhaustive number of data points allowing very easy identification with the person from whom
16 the sample was obtained.

17

18 For purposes of clarity and to facilitate discussion, NBAC adopted the following
19 definitions of the diverse status of human biological materials, depending on whether they are
20 sitting in storage, or selected for research purposes.

21

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1 In this report, **human biological material** is defined to encompass a full range of
2 specimens, from subcellular structures like DNA, to cells, tissues (blood, bone, muscle,
3 connective tissue and skin), organs (e.g., liver, bladder, heart, kidney, placenta), gametes (sperm
4 and ova), embryos, fetal tissues, and waste (hair and nail clippings, and urine, feces, sweat, and
5 shed skin cells). Such materials are of two types:

6

7 *Unidentified materials* are those for which identifiable personal information was not
8 collected or, if once collected, is not maintained and cannot be retrieved by the repository.

9

10 *Identified materials* are those linked to personal information, such that the person from
11 whom the material was obtained could be identified by name, patient numbers, or clear
12 pedigree location.

13

14 **Research samples** are the portions of human biological materials provided to investigators by
15 repositories. Such materials are of at least four types, which are differentiated by the amount
16 of information that is conveyed to the investigator about the person from whom the sample
17 comes:

18

19 *Unidentified samples*—sometimes termed “anonymous”—are those supplied by
20 repositories from unidentified materials.

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Unlinked samples—sometimes termed “anonymized”—are those supplied by repositories from identified materials without identifiers or codes such that the ability to identify particular individuals via clinical or demographic information supplied with the sample, or biological information derived from the research would be very difficult if not impossible for the investigator, the repository, or a third party.

Coded samples—sometimes termed “identifiable” —are those supplied by repositories from identified materials with a code rather than a name or any other personal identifier such as a patient number, where the repository (or its agent) retains information linking the code to particular human materials or where the extent of the clinical or demographic information provided with the sample is sufficient that the investigator, the repository, or a third party could link the biological information derived from the research with material from a particular person or a very small group of identifiable persons.

Identified samples are those supplied by repositories from identified materials with a personal identifier (such as a name or patient number) sufficient to allow the biological information derived from the research to be linked directly with the particular person from whom the material was obtained.

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1 In each of the examples described below, there was tremendous variability in the
2 identifiability
3 of the samples used depending on the research purpose. In some cases, such as the study
4 of the Hantavirus, it was not necessary to identify the individuals who served as the sources of the
5 stored samples. For other types of research, such as the studies of families with a high prevalence
6 of mental illness where extensive information on demographics, diagnosis, and family history was
7 crucial, the ability to identify the source of the sample may be necessary.

8

9 **NEED TO IDENTIFY SOURCE FOR RESEARCH OR CLINICAL PURPOSES**

10

11 For samples that are identified or coded, there are several possible reasons for an
12 investigator wanting to go back to the source either to gather additional clinical or phenotypic
13 information or to provide potentially therapeutic information.

14

15 Increasingly genetic research requires that there be sufficient phenotypic information
16 accompanying the genotypic information extractable from the biological material. Thus,
17 investigators stratify populations and then intensively investigate a smaller subset. As smaller
18 subpopulations of interest are identified, clinical investigators are likely to need more clinical
19 information about the population being studied. This will require some mechanism for
20 information retrieval. With coded samples, the “trustee” of the sample has the ability to gather
21 more data for the investigator. With identified samples, the investigator can go back directly and

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1 request additional information. The possibility that the investigator, or an agent of the
2 investigator, will contact the source (or the source's physician) for additional information should
3 be discussed in the consent process (see chapters 4, 5, and 6).

4
5 There might also be circumstances for which an investigator may want to provide
6 information to the source, whether directly or indirectly. An example is an investigator who
7 discovers new information that leads to a better diagnosis of a clinical condition, an effect of a
8 previously administered therapy, or a misdiagnosis that might have important implications for the
9 health of an individual source. Another example is the discovery of an infectious agent with
10 public health implications. In both of these examples, there have been compelling arguments
11 made for the duty of the investigator to contact the source. In cases where the implications of a
12 finding are not as clear, that is, findings are preliminary or for which there is no effective
13 intervention available, contact is less desirable because of the possibility that people could act on
14 the findings in a way that may result in harm

15
16 **EXAMPLES OF RESEARCH USES OF HUMAN BIOLOGICAL MATERIALS**

17
18 **The Value of Human Biological Materials to Cancer Research**

19
20 Clearly, pathology specimens have been invaluable resources for much cancer research.
21 The availability of large archives of carefully documented and clinically correlated specimens

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1 permits the direct, much more rapid and less expensive approach of applying new detection
2 technologies for candidate genotypic and phenotypic markers directly to existing specimens.
3 To try to initiate prospective studies *de novo* for each new promising candidate marker for each of
4 the many varieties of human cancer would not only be extraordinarily costly in dollars and human
5 effort, but would require study periods of many years, or even decades, before definitive
6 endpoints could be reached. In contrast, being able to apply such new technologies to archival
7 materials, where clinical course, therapeutic response and outcome are already known, can save
8 time and money, to say nothing of human suffering.

9
10 Recent progress in elucidating the initiation and progression of cancer has been most
11 dramatic and gratifying in the area of colorectal cancer (Lenauer, 1997). During the past decade
12 at least five specific genetic changes have been found that seem to constitute an evolutionary
13 pathway from normal to neoplastic colon tissues. Some of these revelations have been derived in
14 subsets of patients with known hereditary forms of colorectal cancer, while others appear more
15 generally to be present in those without known patterns of familial inheritance. At least one of
16 these genetic changes, the inactivation of the p53 gene, is known to occur, at least at times, in the
17 germline, while the others appear to be exclusively of somatic origin (Kinzler, 1991a; 1991b;
18 1996).

19
20 Research on the role of the p53 gene was enabled by the availability of a large human
21 tissue repository containing various forms and stages of colorectal cancers, as well as blood

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1 specimens from the same patients. The tissue archive consisted largely of typically fixed and
2 embedded specimens, but in addition the scientists benefited immensely from a large collection of
3 frozen samples (Fearon, 1987; 1990; Goelz, 1985; Vogelstein, 1988; 1989).

4
5 There are countless examples in which investigators have used archival collections of
6 human tissues to search for specific chromosomal and genetic abnormalities of pathogenetic
7 interest. For example, a recent effort is attempting to decipher the genetics of prostate cancers,
8 the most common cancer in American men and a significant cause of cancer morbidity and
9 mortality (Smith, 1996). The goal of this new multi-institutional project is to differentiate the
10 various forms of prostate cancer, determine the most effective methods of treatment for each, and
11 eventually find a cure. The research is dependent on the availability of carefully characterized
12 tissue samples of prostate cancers and close correlation with clinical data to establish the natural
13 history of the tumors and their responses to different therapeutic strategies.

14 15 **Screening Human Biological Materials Archives to Track Viruses**

16
17 Stored biological samples can be valuable resources during public health emergencies,
18 when investigators are trying to identify or track an emerging virus. For example, in 1993 healthy
19 young people began dying in the Four Corners area of the American Southwest from a form of
20 pneumonia. Within months the Hantavirus was identified as the culprit. The solution of this
21 public health mystery can be attributed to many sources, including a suspicious clinician, an

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1 epidemiologist, observant Navajo elders, and two human tissue archives. One archive was that of
2 the Centers for Disease Control and Prevention (CDC), containing vast libraries of viruses, viral
3 proteins, and serum specimens from around the world. The second archive included pulmonary
4 tissues from the autopsied victims of this strange new disease. The CDC archive permitted initial
5 serological screening tests, from which arose the first suggestion that a Hantavirus might be
6 involved. The initial screens were followed by tests of autopsy tissue samples with specific
7 Hantavirus monoclonal antibodies, and ultimately, the tissue samples were exposed to Hantavirus
8 genetic probes that revealed the presence and tissue distribution of viral genetic material. These
9 molecular tools permitted identification of the local deer mouse as the host of the pathogenic
10 Hantavirus. Studies of older human autopsy tissue established that the virus was, in fact, not a
11 new variant but a fairly old virus with a well-established symbiotic relationship with the mice in
12 the region (Wrobel, 1995).

13

14

15

16 **Human Tissue as a Singular Research Resource in Brain Research**

17

18 Sometimes use of biological materials is the only way to study certain aspects of human
19 disease, for example, to study diseases of the brain and central nervous system. Currently there
20 are no accurate animal or tissue culture models for many common diseases of the human brain,

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1 including brain tumors and most of the primary neurodegenerative diseases (e.g., Alzheimer=s
2 disease, Parkinson=s disease, Amyotrophic Lateral Sclerosis, or Multiple Sclerosis). Neurological
3 samples, particularly of the brain, are often inaccessible.

4
5 Until relatively recently, most brain tumor research was conducted with animal models, or
6 with cultured immortalized glioma cell lines. Over the last five years, several studies have
7 correlated genetic alterations in human brain tumors with the degree of malignancy and prognosis.
8 These studies relied on frozen samples and specially fixed samples of human brain cancers to
9 assess gene amplification, gene deletions, gene mutations, and cell cycle parameters. Many
10 insights into the pathobiology of brain tumors are emerging from these studies (Blessed, 1968;
11 Masliah, 1991; Masters, 1989; Raine, 1997; Will, 1996).

12

13 **Longitudinal Studies**

14

15 Longitudinal studies, in which the same group of individuals is studied at intervals over a
16 period of time, often collect large numbers of specimens that can be used for both retrospective
17 and prospective research. Several well-known longitudinal studies have been conducted over the
18 years including the Physician's Health Study, the Nurses' Health Study, and the Framingham
19 Heart Study. Other large longitudinal studies include the Health Professionals Follow-up Study,
20 Mr. Fit, the Family Heart Study, and the National Health and Nutrition Examination Surveys

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1 (NHANES).

2

3 The National Institutes of Health Women's Health Initiative (WHI) is a 15- year research
4 program, concluding in the year 2005, which focuses on the major causes of death, disability and
5 impaired quality of life in postmenopausal women. The overall goal of WHI is to reduce coronary
6 heart disease, breast and colorectal cancer, and osteoporosis in postmenopausal women through
7 prevention, intervention, and risk factor identification. The study will involve over 164,500
8 women of all races and socioeconomic backgrounds ages 50 to 79. The women are enrolled in
9 either a clinical trial or an observational study and will be followed for 8 to 12 years, during which
10 they will provide multiple blood samples. Participants sign a consent form that states that the
11 collection of blood samples is for use in future research, which may include genetic research, and
12 participants will not be informed of any test results. Participants may opt out of having their
13 samples used for genetic research, if they so desire. Participants' charts contain identifying
14 information including name, Social Security number, address and telephone number, and are bar-
15 coded. Blood samples are labeled with matching barcodes to link them back to the charts. All
16 study records are kept indefinitely for analysis and follow-up.

17

18 The NIH-sponsored Bogalusa Heart Study², at the Louisiana State University, and
19 ongoing since 1972, is the longest and most detailed study of children in the world. The purpose
20 of the study is to understand the environmental and hereditary aspects of early coronary artery

² Bogalusa Heart Study, <http://www.mcl.tulane.edu/cardiohealth/bog.htm>

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1 disease, essential hypertension and cardiovascular risk factors in a African American and
2 Caucasian children in the semi-rural community of Bogalusa, Louisiana. In addition, over 160
3 substudies have been conducted including special studies on socioeconomic evaluations, blood
4 pressure, lipid levels, genetics, exercise, heart murmurs, and pathology. Knowledge gained in the
5 study has been applied to develop, test and evaluate methods for cardiovascular risk intervention.
6 The research involves longitudinal observations of more than 14,000 children and young adults,
7 some of whom will be followed until 38 years of age.

8
9 Since 1960, the National Center for Health Statistics (NCHS) of the Centers for Disease
10 Control and Prevention (CDC) has conducted 7 health examination surveys of the population of
11 the United States, the National Health Examination Surveys (NHES) Cycles 1, 2 and 3, the
12 National Health and Nutrition Examination Surveys (NHANES) I, II and III, and the Hispanic
13 Health and Nutrition Examination Survey (HHANES). The surveys are designed to periodically
14 assess the health and nutritional status of children and adults in the United States through
15 interviews and direct physical examinations. The surveys employ interviews to answer questions
16 about demographics, socioeconomic status, dietary habits and health-related issues, and physical
17 and dental examinations, which include physiologic assessments and laboratory tests. Blood
18 samples are collected as part of the physiologic assessments, and placed in storage banks after
19 laboratory tests are completed.

20

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1 Cumulatively, all of the health examination surveys have analyzed and banked samples
2 from more than 85,000 participants. The most recent survey, NHANES III³, conducted between
3 1988 and 1994, performed laboratory tests on approximately 29,314 people of all races aged 2
4 months and older from 81 counties in 26 states. Some of the 30 topics investigated in the
5 NHANES III included high blood pressure, high cholesterol, obesity, second-hand smoking, lung
6 disease, osteoporosis, HIV/AIDS, hepatitis, *helicobacter pylori*, immunization status, diabetes,
7 allergies, growth and development, anemia, dietary intake, antioxidants, and nutritional blood
8 measures. The NHANES I analyzed blood and urine samples from 23,808 study participants, and
9 NHANES II analyzed 20,322 samples. The HHANES was a one-time survey conducted from
10 1982 to 1984 that provided data on 11,653 people of Hispanic origin.

11

12 **Relying on Stored Samples for Locating Genes**

13

14 The human genome is the complete set of genetic instructions for an individual. Though
15 the DNA of any two people is roughly 99.9 percent identical, the variation in this tenth of a
16 percent is the source of human biological diversity. Inherited susceptibility to various diseases—
17 which occurs when a particular form of the gene fails to give correct instructions for a trait or
18 function—is one small part of this diversity.⁴ Researchers search for genes by constructing finer

³ National Health and Nutrition Examination Survey (NHANES),
<http://www.cdc.gov/nchswww/about/major/nhanes/nhanes.htm>

⁴ Some research aims specifically to document human genetic variation, such as the Human Genetic Diversity Project of the National Institutes of Health. This project relies on stored blood samples collected as part of the National

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1 and finer maps of known gene locations and functions or by comparing DNA of affected and
2 unaffected individuals.

3

4 The first phase of identifying a disease-related gene is the collection of diagnostic
5 information and blood samples from an appropriate set of affected individuals and their relatives.
6 Typically, blood samples are drawn from family members, and the blood cells are immortalized so
7 they can be grown continuously in the laboratory. These immortalized cells, called cell lines, can
8 then be used to make DNA in unlimited quantities, allowing many different researchers access to
9 this resource. The art of this collection phase is in identifying appropriate families. Those in which
10 affected individuals have very similar symptoms are preferable, since members of such a similar
11 group are more likely to carry the same form of the gene than a symptomatically diverse family.
12 At this stage, having valid and definitive criteria that accurately determine a particular diagnosis
13 may make the difference between success and failure. The actual research designs selected in
14 molecular genetics studies and the selected participants are closely allied.

15

16 Linkage studies are widely used to detect and locate genes that determine susceptibility to
17 certain disorders. Such studies are often based on the identification of large, densely affected
18 families so that the inheritance patterns of known sections of DNA (called “markers”) can be
19 compared to the family’s transmission of the disorder. If a known marker can be correlated with
20 the presence or absence of the disorder, this finding narrows the location of the suspect gene.

Health and Nutrition Examination Survey (NHANES). No identifying information is stored with the blood samples used

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1 Great strides in linkage analysis, including laboratory and statistical methods, are increasing the
2 power of this method and decreasing its cost.

3

4 Linkage-disequilibrium studies in isolated populations capitalize upon the likelihood that
5 the susceptibility genes for a particular disorder probably came from one or a few founding
6 members. Whether the isolation is geographic or cultural, there are fewer individuals in the
7 community's genealogies and therefore fewer variations of the disease genes within the
8 population. This limited variation makes the search easier. In addition, the groups of markers that
9 surround each of these susceptibility genes are likely to have the same limited variation, which
10 further simplifies identification.

11

12 Association studies depend on the investigator hypothesizing that a specific gene or genes
13 may influence the disorder. In this type of study, the investigator examines whether those people
14 with the disorder have a different version of the gene than those without the disorder among
15 related or unrelated individuals.

16

17 Pinpointing the likely genetic anomaly in linkage and linkage-disequilibrium studies occurs
18 once an investigator narrows the search to a fairly small region in the genome. That "small"
19 region, however, may still be large enough to contain DNA that codes for dozens of traits, and
20 the investigator must now choose which parts of the region to study further. Because the Human

in the study.

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1 Genome Project is well on the way to identifying the location of all genes, this mapping of the
2 human genome will greatly simplify the identification of possible susceptibility genes. Once the
3 genes in a narrow DNA region are cataloged, they may each be tested and the susceptibility gene
4 identified.

5

6 An example of use of DNA repositories in linkage studies is the National Institute of
7 Mental Health's (NIMH) Genetics Initiative, begun in 1989.⁵ The goal of this special, large-scale
8 initiative in molecular genetics is to collect data from enough families to find the genes that
9 influence the onset of selected mental disorders. In addition, the Initiative enabled the
10 establishment of a national repository of demographic, clinical, diagnostic, and genetic data from
11 individuals with bipolar disorder, schizophrenia, or Alzheimer's disease to aid researchers in
12 identifying factors responsible for these disorders.

13

14 Diagnosis, family history, and DNA samples were collected using identical procedures
15 across multiple sites. The collecting researchers were given a 12-month proprietary period for
16 analyzing their data, at the end of which the data were made available to other qualified
17 investigators. The repository contains information on 862 individuals with Alzheimer's disease,
18 432 individuals with bipolar disorder, and 270 individuals with schizophrenia.

19

20 These researchers founded a resource that is in high demand. Requesting investigators

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1 receive a file of demographic and diagnostic variables necessary for genetic analysis, with
2 accompanying documentation, access to DNA samples, a code manual listing additional clinical
3 and demographic data, and pedigree drawings.

4
5 Although there are numerous investigator-initiated studies, some have not been able to
6 recruit the necessary number of participants. Determining the necessary number is problematic
7 since such estimates are specific to the underlying mode of genetic transmission, which is
8 unknown. The more complex the transmission pattern, the larger the study must be. Researchers
9 who began collecting 10 years ago would have thought that 100 to 200 affected individuals and
10 relatives would have been adequate. Now that multiple susceptibility genes are hypothesized,
11 much larger samples than previously expected are necessary.

12 13 **Research Requiring Unique Tissue Collections**

14
15 Most researchers using human biological materials have relied on specimens from
16 pathology laboratories or existing tissue banks. However, some research studies require
17 specialized samples, i.e., with a specific biological, clinical, or demographic characteristic, and
18 therefore must create a unique collection, which might have limited appeal to the broad research
19 community but high value to a small group of investigators.

20

⁵ See the National Institute of Mental Health at <http://www.nimh.nih.gov/>

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1 For example, the University of Southern California AIDS-Malignancy Clinical Trials
2 Consortium (AM-CTC) helps design, develop, and conduct clinical trials of novel agents to be
3 used against AIDS-related malignancies. In addition, the AM-CTC stores tumor tissue and other
4 relevant biologic materials that have been obtained from patients participating in their trials. As
5 another example, Stanford University is investigating the role of environmental toxicants and
6 genetic susceptibility factors in the etiology of Amyotrophic Lateral Sclerosis (ALS). It has a
7 specialize collection of samples from patients with ALS.

8

9 **Community-Based Studies to Determine Gene Frequency**

10

11 Certain diseases, particularly those with strong genetic components, are often found to be
12 more common in groups that share similar characteristics, whether they be genes, environmental
13 exposures, or lifestyles. For example, in the category of genetic disorders, Sickle Cell Anemia is
14 predominantly found in African Americans, Cystic Fibrosis in Caucasians, particularly of
15 European descent, Tay Sachs in individuals of Ashkenazi Jewish descent, and thalassemia in
16 Mediterranean populations. These are all autosomal recessive disorders, requiring two defective
17 genes for manifestation of the disorder, meaning otherwise healthy carriers (one defective gene,
18 one unaffected) can only pass the disorder to their children by mating with another carrier (and
19 even then the odds in each pregnancy are 1 in 4). The likelihood of two carriers producing
20 offspring is greater in populations that are geographically, politically, socially, or culturally

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1 isolated or segregated.

2

3 In the 1970s major Tay Sachs screening programs were begun in certain Jewish
4 communities in the United States. Because carrier status can be determined with a blood test,
5 some American Jewish community organizations urged persons of Ashkenazi descent to be tested
6 for carrier status. Tay Sachs is a lethal disease, severely affecting young children and resulting in
7 early and painful death. As a result of these large-scale screening programs, large quantities of
8 blood were stored after the carrier screening was completed. A collection of blood samples
9 stored at a Baltimore institution following a Tay-Sachs screening program in the 1970s became a
10 valuable resource to the investigators searching for clues to the genetic basis for *more to be*
11 *added here.*

12

13 In the 1980s there was growing evidence that there might be a genetic component to
14 breast cancer. In 1990, researchers had determined that mutations in a gene, labeled BRCA1, and
15 later another gene, BRCA2, cause inherited forms of breast and ovarian cancer. Knowing that
16 breast cancer runs in families, investigators collected data on women whose mothers,
17 grandmothers, or sisters had the disease (Easton, 1993; Tonin, 1995; add refs). Characteristic
18 mutations were found in Ashkenazi Jews. In one study, investigators aimed to estimate the risk of
19 breast and ovarian cancer in the Ashkenazi Jewish population through relatively simple assays to
20 determine the frequency of these mutations (Struewing, 1997). They enlisted the participation of
21 5,331 Jewish men and women over the age of 20 living in the Washington, D.C. area.

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1 Participants provided family histories and blood samples. Participants were told at the beginning
2 of the study that they would not be informed of the results of the test. The scientists found that
3 over 2 percent of Ashkenazi Jews in the study population carried mutations in the BRCA1 or
4 BRCA2 gene, conferring increased risks of breast, ovarian, and prostate cancer. In comparison,
5 less than one percent of the non-Jewish population carry a mutated BRCA1 and BRCA2 gene.

6

7 **CONCLUSIONS**

8

9 The previous chapter describes the large volume of pathology specimens that exist in the
10 United States at this time. In this chapter, examples are provided of how samples have been and
11 continue to be invaluable resources for a wide variety of studies aimed at understanding the
12 etiology and progression of disease, the effects of viral and environmental impacts on health, and
13 for finding genes that might be responsible for the underlying mechanisms of disease.

14

15 Many of the specimens sitting in repositories will never be used in research. Many
16 research studies will rely on large numbers of unidentified samples to investigate the basic
17 mechanisms of health and disease, or to screen samples for evidence of disease, environmental
18 insult, or responsiveness to potential therapeutic agents. Other studies will rely on samples that
19 are at least somewhat identifiable. That is, an investigator might initially request samples with no
20 linking data and later request additional clinical data linked to the sample. In still other cases, the
21 research might require that the investigator know who provided the sample, the sample source

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1 might even be a patient, as well as a research subject, of the scientist.

2

3 How human biological materials are used in research and the extent to which research
4 samples can be linked to their sources are critical considerations when trying to determine risks
5 and necessary protections.

6

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