

The Ethical Dimensions of Nanomedicine

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Medical practice is about to enter a new era focused on the nanoscale and the practice of “nanomedicine.” Nanomedicine may be defined as the monitoring, repair, construction, and control of human biological systems at the molecular level, using engineered nanodevices and nanostructures [1]. Nanomedicine is, in a broad sense, the application of nanoscale technologies to the practice of medicine, namely, for diagnosis, prevention, and treatment of disease and to gain an increased understanding of complex underlying disease mechanisms. The creation of nanodevices, such as nanobots capable of performing real-time therapeutic functions *in vivo*, is one long-term goal. Advances in delivering nanotherapies, miniaturization of analytic tools, improved computational and memory capabilities, and developments in remote communications will eventually be integrated [2,3]. These efforts will cross new frontiers in the understanding and practice of medicine. The ultimate goal is comprehensive monitoring, repair, and improvement of all human biologic systems—basically, an enhanced quality of life.

The potential impact of nanomedicine on society could be huge [4]. Nanomedicine could drastically improve a patient’s quality of life, reduce societal and economic costs associated with health care, offer early detection of pathologic conditions, reduce the severity of therapy, and result in improved clinical outcome for the patient. Numerous companies are actively involved in nanomedicine research and development, with many nanomedicine-related products already on the market or under development [5]. The nanopharma

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market is expected to grow significantly in the coming years. Analysts project that by next year, the market for nanobiotechnology will exceed \$3 billion, reflecting an annual growth rate of 28% [6]. According to another recent report, the United States demand for nanotechnology-related medical products (nanomedicines, nanodiagnostics, nanodevices, and nanotech-based medical supplies) will increase more than 17% per year to \$53 billion in 2011 and \$110 billion in 2016 [7]. This report predicts that the greatest short-term impact of nanomedicine will be in therapies and diagnostics for cancer and central nervous system disorders. Yet, despite all of this research and development in nanomedicine, federal funding related to the research and educational programs on ethical issues have clearly lagged behind. It is critical that ethical, social, and regulatory aspects of nanomedicine be proactively addressed to minimize public backlash similar to that seen with other promising technologies, most notably, genetically-modified foods in Europe. The public should be properly educated regarding the benefits and risks of nanomedicine. Such an approach is essential for greater public acceptance and support for nanomedicine. In fact, it is critical for commercial viability of nanotechnology in general.

Given this backdrop, it is possible that nanomedicine is poised to add a profound and complex set of ethical questions for health care professionals. Once nanobased interventions are tested in clinical trials and given Food and Drug Administration (FDA) approval, it becomes the domain of health care practitioners to use nanotechnology for the improvement of human health and populations. But for many physicians, nanomedicine is an entirely new area for preventive and diagnostic interventions and curative therapies that will require continuing education, patient education, and a heightened awareness of the risks for and benefits of nanotechnologies as applied to medicine. We will focus primarily on issues that are likely to emerge once nanomedicine moves out of the preclinical and clinical stages of research and development. In other words, our discussions will be limited to nanomedicine products as they enter the market and find medical applications in diagnosis, prevention, and treatment of disease.

Nanomedicine raises fundamental questions, such as what it is to be human, how human disease is defined, and how treating disease is approached. Just as with the era of genetics and molecular biology, physicians will have to reconceptualize how they think about the diseases they treat, the means they have to treat them, and the meaning of the phrase, "do no harm."

Yet, nanomedicine is not a single class of medical interventions that can easily be analyzed from an ethical perspective. Nanomedicine includes a wide range of technologies that can be applied to medical devices, materials, procedures, and treatment modalities. The simplest way to distinguish categories of nanomedical interventions is to differentiate diagnostic nanomedicine from therapeutic nanomedicine. Diagnostic nanomedicine can include a wide range of interventions, from the use of nanoparticles for detecting tumors or cells with imaging technologies to chips or other

implantable devices that can be created using nanoparticles and nanotechnology techniques that can be used to monitor or detect changes in blood chemistry, DNA, or other materials [2,3]. It has been postulated that by 2016, clinicians or health care workers will be capable of scanning an entire genome within a few minutes [8]. Therapeutic nanomedicine includes a wide range of interventions—from nanopharmacology to nanobased medical devices, such as surgical nanobots or drug-delivery devices [5,9] to nanomaterials used for bone grafts or other body implants [2,3].

Just as different ethical issues exist for preventive medicine versus curative or therapeutic medicine, there exist very different kinds of ethical issues that arise out of diagnostic nanomedicine versus therapeutic nanomedicine. Interventions based on nanotechnologies likely will resurrect old questions about human enhancement, human dignity, and justice that have been asked many times before in the context of pharmaceutical research, stem cell research, and gene therapy.

Much of what is discussed or “hyped” as the future of nanomedicine, however, has yet to occur. Therefore, it is difficult for ethicists to predict in advance of the arrival of actual technologies what kinds of issues might arise out of nanomedicine. Yet, on the basis of other kinds of biomedical technologies that have affected health care, it is possible to conjecture what some of the perennial ethical issues and novel ethical problems for nanomedicine will be. Therefore, this article outlines a range of potential ethical issues for preventive and therapeutic nanomedicine that may occur as these technologies move from the laboratory to the clinic. Specific focus is on the ethical question of enhancement versus therapy, the risk for and benefits of nanotechnologies in health care, changing understanding of human disease, and privacy and confidentiality.

Understanding human disease

Diagnostic nanotechnologies eventually will provide the ability to detect and characterize individual cells, subtle molecular changes in DNA, or even minor changes in blood chemistry—scenarios that will likely cause pause and reconsideration of what it means to be a “healthy person” versus a “person who has a disease.” In a “nanoworld,” we might have to reconsider how to diagnose someone who has, say, cancer. Is the presence of a genetic mutation known to have a predisposition for causing cancer in a single cell a diagnosis? Or is it simply a risk factor? How many cells from the body must be of a cancerous nature for it to be defined as cancer? 1? 50? 1000? The answers to these questions are difficult because at this point no one knows exactly how to define, diagnose, or detect disease with this level of sensitivity. Eventually, disease may be able to be detected in this way, but it is important to remember that the development of such diagnostic technologies will require reconceptualizing understanding of disease. This will have a significant impact on health care professionals and patients.

The key is that if the slightest abnormality *can* be discovered, one must ask whether or not such information will have clinical relevance. If such knowledge does have clinical relevance, then it seems reasonable to develop technologies that could detect diseases at their earliest stages with the hope that this early detection would result in fewer side effects, less aggressive treatments, and better survival rates.

There may be some cases, however, where more information is simply too much information [10]. Such heightened awareness simply could result in anxious patients, worried family members, or an entire group of the “worried well.” One must, therefore, think carefully about which diseases and conditions it would be appropriate to apply such nanotechnologies to so that those interventions are helpful in understanding those diseases, rather than creating a burden or risk for patients and others. Therefore, the balance of information processed and disseminated versus benefit to society and individual health is a significant consideration for the ethics of nanotech-based diagnostic technologies [10].

Enhancement versus therapy

A related distinction for judging the morality of a medical procedure or treatment is whether or not it is regarded as therapeutic or enhancing—a subjective determination that is coupled with the determination of whether or not the procedure or treatment results in a normal or abnormal individual. A little analysis, however, reveals these distinctions to be unavailing because both enhancement and therapy are based on the relative concept of “normal” [11]. Most novel medical technologies that are employed for diagnosis, prevention, or treatment of diseases can also be used to enhance the function of the human body or mind. The traditional distinction between therapy and enhancement lies in the fact that therapy is concerned with maintaining, repairing, or restoring bodily parts or functions that a patient previously had or used. Enhancement, however, is concerned with the creation or improvement of bodily parts or functions that were absent, undamaged, or previously malfunctioning. Using this distinction, the implantation of a nanoscale device that emulates the function of a congenitally absent organ paradoxically would be enhancing rather than therapeutic.

As to this question, a frank prohibition pragmatically is unworkable. There are simply too many potential benefits that implantable nanoscale medical devices offer, and policing their use will only be effective when society has reliable methods to detect violations.

Rather, at the level of the profession, the practice of nanomedicine must be governed by a nanomedical ethic that maps the classical principles onto a transhuman and posthuman reality. Of these, the principle of “justice” in access to nanomedical procedures and entitlement to nanomedical treatment likely will be the most contentious. In this context, issues relating to unfair competition, socio-economic inequality, discrimination, and bias will arise

and need to be addressed. At the level of civilization, a morality must be crafted that honors an unprecedented expansion in the meaning of human being and militates against any eugenics agenda.

Risk versus benefit

Another important concern for nanomedicine is the need to balance the potentially significant benefits of nanomedical interventions with their potential risks. In the area of therapeutic nanomedicine, for example, it is clear that nanotechnologies will allow active chemical compounds or drugs to be more bioavailable and targeted to specific cellular structures [9,12]. Therefore, these compounds will be needed at lower doses and have fewer side effects [9,12]. One likely risk of nanomedicine, however, is that these drugs will receive FDA approval and be on the market long before the long-term risks are conclusive. Because nanomedicines have the potential to cross the blood-brain barrier [13] or enter cells easily, it is a concern that the retention of these molecules in the body may cause long-term or unintentional harm to healthy tissues. Because long-term follow-up data regarding nanomedicines do not yet exist, it is important that patients be informed, that there may be long-term consequences for using these drugs. Although this is not altogether different from the long-term risks associated with exposure to chemotherapeutic or radiologic agents, it is an important risk factor that must be disclosed to patients taking nanomedicines or any kind of intervention involving nanoparticles or nanomaterials.

Privacy and confidentiality

Another important ethical issue relates to the protection and maintenance of health information in the era of nanomedicine. Nanotechnologies will make possible the collection of an enormous amount of individual cellular/subcellular level surveillance data of the human body. Nanomedical technology is expected to miniaturize implantable devices so that they function at the subcellular or synaptic level with the ability to monitor or collect data regarding cellular activities and biochemical events within organs, tissues, or individual cells. One application of this technology would be to include a means by which that information could be transmitted remotely. For example, the VeriChip Corporation has declared the availability of the world's first and only patented, FDA-cleared radiofrequency identification implantable microchip [14]. The VeriChip is inserted under the skin and can be easily scanned with a reader. A small amount of radiofrequency energy passes from the reader energizing the dormant microchip, which then emits a radiofrequency signal transmitting an individual's unique verification number. This number then can be used for various purposes, including accessing personal medical information from a database or assessing

whether or not somebody has authority to enter into a high-security area [14].

If and when such technologies are made possible via nanotechnology, a key ethical question arises: Can the health information infrastructure handle, collect, process, and analyze real-time on-going health data? With so few health care institutions adopting electronic medical record systems or health information systems designed to accommodate increasingly large medical files across institutions and time periods, it is of concern that ways are being created to generate massive amounts of health information without a system to use it. Moreover, ensuring privacy and confidentiality in such a system would be of utmost importance; a system without adequate safeguards presents serious ethical problems.

Summary

It is difficult to predict how ethical issues related to nanomedicine will evolve in the years to come. Nevertheless, ethical considerations will likely play a significant role in the development and use of nanotechnologic interventions in medical care. Initially, some of the important ethical concerns will continue to focus on risk assessment and environmental management. Later on, novel ethical issues and unforeseen dilemmas will arise as the field advances further and intercepts other areas of biomedical research, including genomics, personalized medicine, bioinformatics, and neurobiology. As with other biotechnologic advances before it, nanomedicine will face significant challenges as it moves from proof-of-concept to clinical trials to clinics. Along the way, ethical questions regarding social justice, privacy, confidentiality, long-term risks and benefits, and human enhancement are certain to arise. Health care providers must be ready to answer such ethical questions for themselves and be able to address those questions for their patients. Ultimately, it seems likely that nanomedicine will usher in a new area in health care where pharmaceuticals will be more effective and less toxic, where disease monitoring can be done on a highly sensitive and specific level, and where injections, surgical procedures, and a host of other interventions will be made, less painful, less toxic, and with fewer side effects than their current counterparts. It is important to ensure, however, that these advances in medical care do not come at the expense of fairness, safety, or basic understanding of what it means to be a healthy human being. Ultimately, public and political interest for regulations need to be carefully balanced with the interests of scientists and businesses for uninhibited science and technological efforts. Hype or excitement about nanomedicine should not obscure the important ethical and societal implications of these technologies. Nanomedicine's future appears brightest if it can be assured that it also will be a future where such ethical issues are addressed by the health care profession.

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