Injury, Int. J. Care Injured (2008) **39**, 643—650

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INJURY
INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED

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Translational research: From benchside to bedside

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Accepted 23 January 2008

This study is dedicated to Mary Woodward Lasker, philanthropist and health activist, who founded the Lasker Foundation which has presented the prestigious US Lasker Awards for clinical and basic biomedical research since 1946.

KEYWORDS
Translational research;
Basic science;
Clinical practice;
Clinical research

Summary Translation of the achievements of basic science into everyday clinical practice remains a major issue in contemporary medicine, and is addressed through a new discipline, translational research, which aims to bridge the gap between basic and clinical research. Translational research encompasses laboratory studies, clinical demands, public health and health management, policies and economics; it is crucial in the evolution of contemporary biomedical science; and its interventions follow the political—economic, ethical—social and educational—scientific approaches. Translational research can progress through reorganisation of academic teams in a translational way. New academic posts translationally orientated are urgently needed, particularly in the field of trauma medicine, where lack of awareness of this new evolution is evident.

'If you think research is expensive, try disease.' Mary Woodward Lasker (1901—1994).[18]

Introduction

Throughout human evolution, scientific discoveries have been considered complete and fruitful when they have been put into practice. Medical science typically follows this rule, beginning at the bench of a basic science laboratory with an observation at a molecular or cellular level, and gradually progressing through different levels and obstacles until used in the clinical setting of the bedside, or vice versa.

The translation of theoretical knowledge and experimental breakthroughs into the clinical practice of medicine has always been difficult. During the past few decades, growing barriers between clinical and basic research, the size of the acquired scientific data and the ever-increasing complexities of conducting clinical research according to

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0020-1383/$ — see front matter
doi:10.1016/j.injury.2008.01.051

government regulations and financial constraints, have made this translation even more problematic.[23] These challenges have affected clinical research enterprise at a time when it should be expanding, and have often discouraged the active involvement of contemporary medical personnel from basic sciences.[2]

Translational research has emerged as a scientific discipline rather recently, in order to bridge the gap between basic and clinical research. The translational researcher functions as the link or translator between the two branches having experience of both fields and translating the messages of one branch into the language of the other. The translational researcher can identify the underlying clinical consequences of the new discoveries of basic research, and can relate them to the confirmed needs of the clinician. Thus, translational research is currently defined as the process of transforming research innovations into new health products and diagnostic and therapeutic methods, and is usually carried out in academic institutions.[21] Like basic science, it is usually performed in a laboratory environment, but its endpoints and progress are realised in the clinical setting of medical practice.

The process of translational medicine has increased significantly the number of people who participate in clinical trials, both in the discovery stages and in the clinical testing. Translational medicine has also offered to patients the opportunity to become actively involved in breakthrough science, as it demands a willingness on the part of patients to participate in all aspects of research through clinical care. The patient-centred nature of the translational process has become the new basis of clinical evolution. This new basis aims to accelerate the advance of scientific innovations to the clinical level in a timely and efficient manner, comparable with the manner in which researchers are making basic science discoveries in the laboratory.[13,16,27]

The patient-centred nature of translational research not only influences the structure and management of research procedures, but also the very essence of research strategies. The needs and aspirations of patients, and consequently of society as a whole (the public, industry, insurance organisations, health systems), become the fulcrum of the new and integrated research strategy, which creates a fresh, dynamic link between clinical practice and basic science. Basic scientists provide the clinicians with novel diagnostic and therapeutic tools, and at the same time clinical research and applied knowledge stimulate further basic scientific investigations by their observations. The concepts of patient-driven research and research-driven medical practice have essentially powered the evolution of translational medicine as a relatively new member of health sciences.

It is very useful to understand research as a continuum between basic and clinical research through the intermediary of translational research. This interactive relationship between the three branches of medical research is depicted in Fig. 1. The graph highlights the great importance of integration in medical enquiry. The identification of the clinical needs is the subject of the clinical researcher; the translational researcher formulates the research hypothesis aided by the clinical researcher (concerning the characteristics of the clinical problem) and by the basic researcher (concerning the basic science underpinning the problem). Then the three collaborate in order to produce a detailed research strategy, which is coordinated by the translational researcher. The basic scientist sets up the *in vitro* or/and *in vivo* preclinical stages of the research, and the clinician develops the clinical stages of the project (randomised clinical trials) and implementation in clinical practice. The translational researcher has a further duty: to audit the whole procedure in order to clarify possible pitfalls in coordination, hypothesis, research strategy planning and execution.

Translation goes far beyond coordination of research; it has to deal with public health, health policies and health economics—management. The translational researcher must have a holistic approach which includes epidemiology, public health, medical science and market-driven priorities in health research, as a combined clinician, scientist and manager. The role is complex, but also the necessity is pressing and for the scientific society is invaluable.

Our research aimed to identify the scientific and systemic importance of translational medicine and research, to clarify the impact that translation can have on trauma management, and finally to generate some proposals concerning the implementation of this innovative strategy in contemporary medicine.

Methods

A standard PubMed research, using the terms 'translational research' or 'translational medicine' in the titles of manuscripts, resulted in 402 hits starting from the early 1990s. During this period of almost 20 years, the annual number of published reports increased from just 5 in 1994 to 110 in 2007 (Fig. 2).

We also performed a search of selected websites concerning the changing perceptions on biomedical research of various decision-making bodies such as

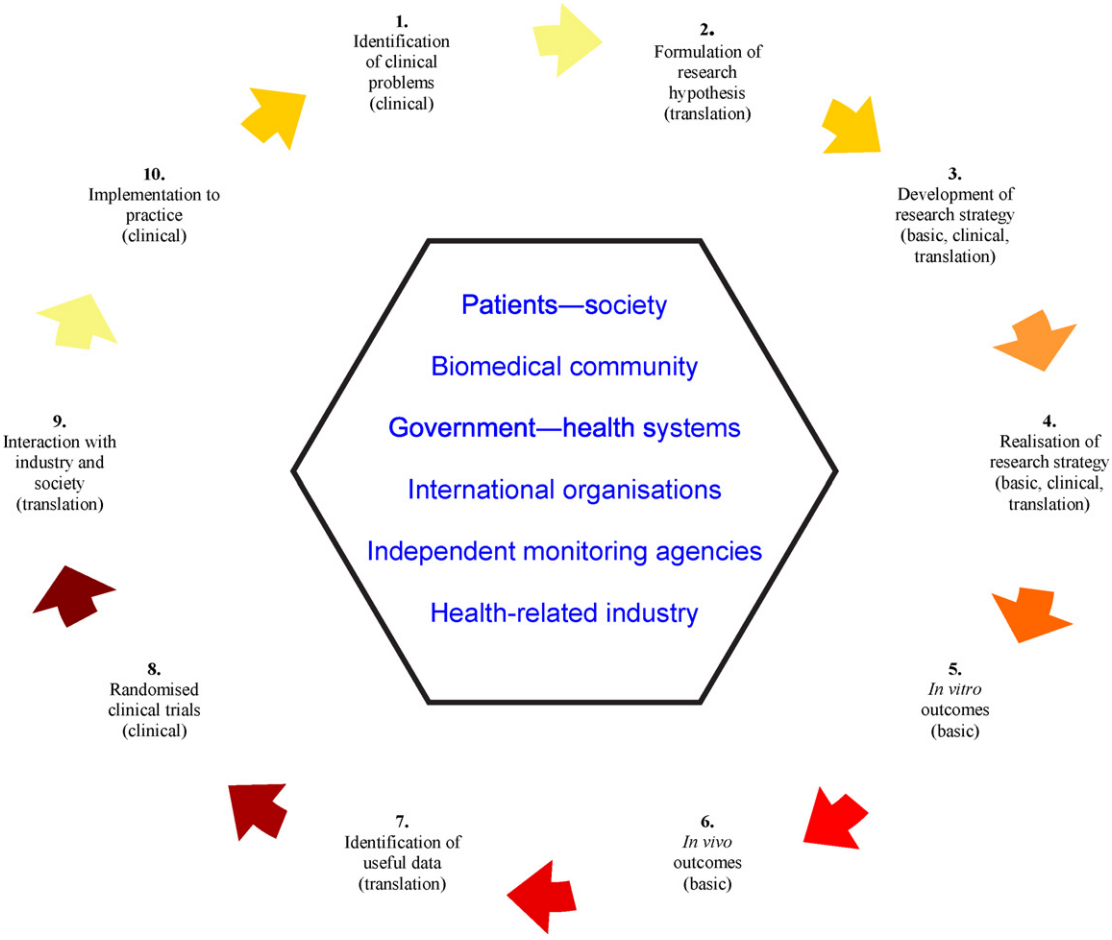

Figure 1 The circle of integrated medical research.

the Commission of the European Union,[10,11] the UK National Health Service[24,30] and the USA National Institution of Health.[20,25]

Results

Trauma and translational research

The exponential increase in publications, particularly during the past 5 years, reflects the great expansion of the novel concept of translational research in all fields of medicine. Interestingly, only 10 of the publications concerned with the multispecialty area of trauma management use these terms in their titles.[28,3,4,7,9,12,17,22,29,32] This indirectly reflects the large deficit of translational research programmes focused on the major, largely unrecognised, public health problem of trauma. According to the National Trauma Institute: "...urgent subject areas of trauma-related translational research include injury prevention, triage, haemorrhage control, resuscitation, orthopaedics, burn care, head injury, critical care, tissue engineering, rehabilitation and recovery, with categories devoted specifically to the extremes of age within each subject area".[19] Examples of translational research projects that have been published are mostly related to spinal[28,7,9] or brain[12,17] injury, and mainly represent efforts to connect basic neuroscience findings with the clinical quests of neurosurgery and trauma management.

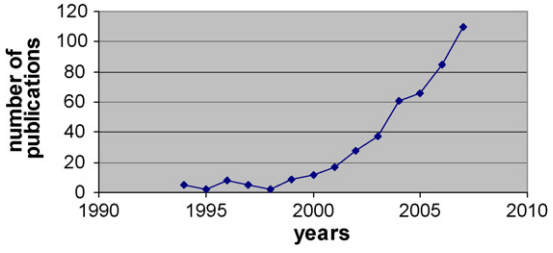

Figure 2 The exponential increase of publications on PubMed which include in their titles the term 'translational research' or 'translational medicine'.

The overall demands on trauma translational research and specific recommendations were summarised in the publications of the PULSE Trauma Work Group in 2002.[3,4] The comparison of the assets

invested in other fields of medical research with those invested in trauma management was distressing; a major cause of death among the active population[31] still attracts but a small portion of the overall funding for basic, clinical and translational research.

Systemic translational research

In modern societies, the issue of quality of life has replaced survival as the key aim. One of the most important pillars of quality of life is the promotion and maintenance of good health status. The increasing expenditure of health systems reflects the agonising effort of society to respond to the increasing demand for health-related services. Investment in health research is investment in the better delivery of health systems (e.g. new diagnostic tools and treatments, improvements in organisation of health services delivery).

A survey funded by the Mary Woodward Lasker Foundation and Charitable Trust showed that the benefit from the decreased cardiovascular and stroke mortality between 1972 and 1992 was US$ 1.5 trillion per year.[11] The same institution estimated that almost 50% of the gain in US living standards during the past 50 years could be attributed to medical innovations and the evolution of health care. With an even more conservative assumption that only one-third of this gain came from medical research, the return on investment in research (US$ 500 billion per year) was 20 times the annual spending on medical research.[11,8] These data underline the necessity of a large increase in medical research (mainly in the clinical and translational sectors) not only for humanitarian reasons, but also for purely financial reasons. There is hardly any kind of investment that could return the initial invested resources 20 times![11] This direct effect on every human being's life is the basis of the differentiation of medical research from any other research field and of the immediate importance of clinical and translational research, when compared with the less direct effect of basic medical and other research fields.

This does not imply that medical research cannot affect human society in other more conventional ways. Health research can also be translated into innovation, scientific and technological progress, economic development and growth, new jobs in the pharmaceutical sector and the biomedical equipment industry. Increased investment in medical research and development today is a *sine qua non* for reducing the healthcare costs of tomorrow.

There is great inequality in the fields of technology, research and innovation. It has been observed that the vicious cycle of poverty, underdevelopment and dependence cannot be adequately and definitively broken until the nations suffering from these problems can improve their research and technology capacities, as was also mentioned in a statement in 2004 by the UN Secretary General.[1] The sub-Saharan Africa and the Islamic—Arabic worlds hardly figure in research statistics. The educational, technological and research potentials of China and India are the solid ground on which the sustainable and exponential development of those two gigantic countries is based. Even in the so-called developed world (where statistical comparisons are easier), striking differences can be observed.

We can use translational research as a means of comparison between the UK, USA, Sweden and the European Union.[15] Table 1 shows some causes of the predominance of the USA in international biomedical research and of the European (and UK) deficit in implementing translation in biomedical research.

Discussion

Our propositions divide into three approaches: political—economic, ethical—social and educational—scientific.

The political—economic approach

This has to deal with the new institutions and frameworks that have to be founded or developed in order to restructure biomedical research. The task is not easy, because a new relationship based on confidence must be built between society (the public), industry, charitable funds, universities, basic researchers and health systems including clinicians. All these must be considered not only at national level, but also in a broader European context. The foundation of the European Research Council[26] and the functioning of the European Medical Research (EMRC)[11] are very positive steps in this direction. These regulatory boards can coordinate the procedure of reform more effectively. It is encouraging that neither council is composed of bureaucrats, but of scientists and researchers working in close collaboration with policy makers. This way both the flexibility of the system and social control can be safeguarded.

However, the situation will not improve without adequate increase and restructure of spending on medical research. The target of 3% of gross domestic product (GDP) is a very good (but probably optimistic) goal. The balance must change and more emphasis should be put on clinical and translational medicine; these were the recommendations of the

Table 1 Comparison of implementation of translational research in the UK, USA, Sweden and the EU

Research	Country			
	UK[6,24]	USA[6,11,15]	Sweden[6,14]	EU[6,10,11]
Structure	Biomedical basic science +++, clinical research +, translational research +	Biomedical basic science ++, clinical research +++, translational research +++	Biomedical basic science ++, clinical research ++, translational research ++	Biomedical basic science ++, clinical research +, translational research +
New strategies in translational research	Best research for best health (2006)[24]	NIH Roadmap (New Pathways to discovery Research teams of the future, Director's pioneer awards, Interdisciplinary research training initiative, Re-engineering the clinical research enterprise)[20]	European leaders in Lisbon strategy implementation[10]	Lisbon strategy 2000 (aim: 3% of European GDP directed to research)[10]
	A review of UK health research funding. Sir David Cooksey report (2006)[6]	Clinical translational science awards (CTSA) consortium NIH Rapid Access to Interventional Development (RAID) pilot programme[25]		European Research Council (ERC) 2007[11]
	Medically and dentally qualified academic staff: recommendations for training the researchers and educators of the future (2005)[30]			European Medical Research Council's (EMRC) activities[11]
Examples of excellence in translation	National Institute of Health Research (NIHR)[20,25]	Duke Translational Medicine Institute (Duke Clinical Research Institute, Duke Clinical Research Unit, Duke Community Clinical Research)[8]	Karolinska Institute[14]	European Research Council, European Medical Research Council[11]

GDP: gross domestic product.

Cooksey report also.[6] The main step forward would be the closer collaboration of scientists and clinicians, and therein lies a golden opportunity for translational research to provide added value to the effort. In the pharmaceutical industry new specialised 'translating' posts have already been appointed, and many more doctors with translational skills are urgently needed.

The health systems (for example the NHS) have to absorb the new strategies that make clinical research (via translational research as intermediary) a cornerstone of the modernisation of health services delivery. Moreover, health systems should improve their effectiveness—efficiency relationship, as postulated by the great Archibald Cochrane in his famous book: *Effectiveness and efficiency: random reflections on health services*.[5] The heavy financial burden of the health systems could be alleviated through their active participation in clinical and translational research. Nevertheless, change of research culture in enormous health systems cannot happen easily; systematic and systemic educational interventions are required.

The ethical—social approach

Here strengthening of social control of biomedical research is dealt with. The acknowledgement that biomedical progress is not only about 'blue skies' and basic science, but that it also affects applied and translational medicine, confers a different perspective. Biomedical research can expressly affect society's well-being and, since the investor is society either directly in the form of public expenditure and charitable funds or indirectly in the form of industrial resources, their interaction becomes consistent.

Society as represented by policy makers interacts with the medical community and influences the big decisions about the priorities of biomedical research. This probably clarifies an underlying and underestimated aspect of translational research; the translational process is not only a dynamic two-way relationship between basic and clinical research, but also a dialogue between the trends and priorities of the scientific community and society, industry and health systems.

The educational—scientific approach

This is probably more important than the previous two aspects. In the long term, only education can modify mentalities and perceptions. Through educational interventions new strategies of clinical and translational research can be implemented at all levels, including collaboration between scientists, clinicians, researchers and stakeholders (industry, society, state, health systems). Via education, the hospital manager will cease to identify clinical research with low-priority and non-cost-effective expense. Society will understand the true benefits of medical research. Scientists and clinicians will accommodate to public control and transparency of priorities and fund expenses. Finally, industry will invest more, and those in medical fields will learn to recognise the necessities of private sector investment. Here again, as mentioned before, the roles of translational clinicians and researchers are central.

The great challenge for the medical community is to adapt to the new challenges and to reap all the benefits of the new policies concerning research. This calls for reorganisation of academic personnel, particularly in clinical specialties. Notably in the UK, there is a decline in the number of academic clinical positions (a decrease of 30% at lecturer level).[30] Translation demands that people cross the divide between research and clinical practice without forgetting the aforementioned managerial skills. The academic personnel of clinical specialties are in the best position to lead this new era of biomedical research.

Consequently, the requirement for differentiation inside academic clinical faculties is urgent. In most academic clinical faculties, there is need for excellence not only in clinical performance but also in education and research. We should always remember that humans cannot be perfect; so it is highly probable that inside every academic clinical team some will excel more in the clinical field and others in the education—research field. A possible solution is to make this distinction clear within teams; then established interaction between those devoted more to academics (without losing links with clinical work) and those devoted more to clinical work (without losing links with academics) would be invaluable.

Thus there is a pressing requirement for more academic clinical positions, with emphasis on candidates with research, educational and clinical skills. These new workers will cooperate more fluently with the basic sciences without losing their clinical background. However, the most important result will be the stimulation of undergraduates and junior postgraduate doctors regarding research, particularly applied research. More academic opportunities and more exposure to research are urgently needed for junior doctors, particularly in the field of trauma. The result could be more awareness concerning the applied and translational character of research in the clinical setting, from medical school to postgraduate medical education and onwards to continuous medical education.

This is clearer in multidisciplinary sectors of clinical medicine such as trauma. Academic staff should play a very useful and necessary part in coordinating the different disciplines (basic or clinical) dealing with trauma, as well as producing significant advances in this scientific field. We should not underestimate the fact that that trauma medicine is linked not only with basic and clinical research, but also with public health (in other words with the very core of society). The majority of trauma victims are young and active, and their loss or extended inability to work affects many financial and social aspects of community life, apart from the obvious and huge psychological effects on their social environment.

The need for re-orientation is far more imperative in trauma medicine, where the deficit in translational research has been previously shown to be quite alarming. The representative bodies of trauma medicine should make it their priority to create a new strategy for the re-engineering of trauma education and research, in order to establish fresh perspectives in the era ahead of us.

Conflict of interest

None.

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