Perspective

Medical Research in Israel and the Israel Biomedical Database

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In 1991 the Chief Scientist of the Ministry of Health recognized the need to collect reliable data on the specifics of biomedical research in Israel. The rationale for this effort was the recognition that medical research is an activity that is poorly understood and inadequately characterized by many individuals and institutions responsible for the support and the maintenance of this essential element of the health care system. It is well established that the highest levels of medical care exist in countries in which vast funds are contributed to medical research. By sad comparison, in Israel the per capita government spending via the Chief Scientist's Office of the Ministry of Health for medical research is the lowest among developed countries, a dismal $0.40 [Figure 1] [1].

The medical research establishment is complex. It should not be characterized as simply the disjointed efforts of physicians in hospitals engaged in clinical trials of the latest medications and clinical techniques. Rather, a very intricate relationship of activities exists, which include basic medical studies in disease-related processes, social and psychological analyses of medically related situations, the application of basic findings on disease pathology, new clinical modalities, and clarification of methodologies for better delivery of primary, secondary and tertiary health care. To best understand how to support these activities requires specific information about the dimensions of activities of individuals and institutions. It is essential also that this information cover a reasonable period so that areas of strengths and deficiencies can be identified. Only then can informed decisions be made about financing medical research, and pertinent research activities chosen by potentially interested international partners.

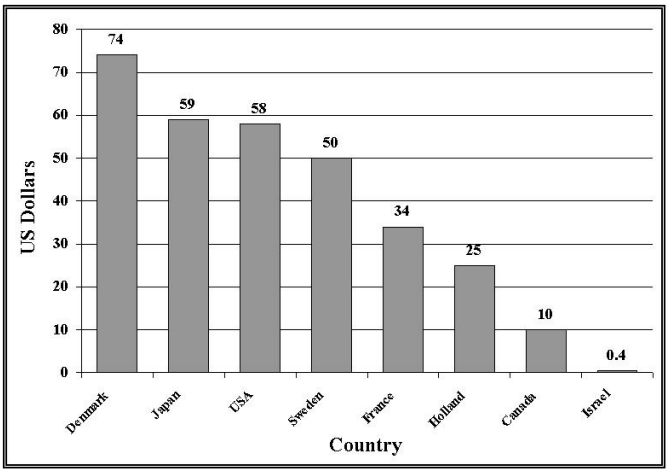

Figure 1. Government spending per capita (1995). Public funding for health research and medical research per capita in developed countries and in Israel [1]

The effort began with the formulation of the Israel Biomedical Database. The Database was to be constructed to contain specific information about every possible investigator. The following information was to be solicited:

- Academic affiliation, and rank if any
- Hospital affiliation if any
- Keywords describing research activities
- Discipline of training of the investigator
- Research interests of the investigator
- Titles of current research projects (last 3 years)
- Categories describing research area according to: a) organ-specific diseases, b) clinical categories, and c) scientific, medical and methodological approach
- Funding sources of the investigator outside of in-house (last 3 years)
- Scientific collaborators
- Patents of investigators (last 3 years)
- Publications in peer-reviewed journals with co-authors and keywords (last 3 years)
- Telephone, fax, and email address

All of the above information was to be entered into a relational database and linked to an investigator number assigned to each research investigator. In the initial effort the names of investigators were obtained from institutions, universities and hospitals and questionnaires were sent to each individual. All information was carefully scrutinized to include only individuals with identifiable research activities in the biomedical area. Even if an investigator was employed at a hospital or medical school and the research activity could not be identified as somehow disease oriented it was not included. Conversely, non-medical facility-employed individuals with identifiable medical research activities were included. The initial response was supplemented by using

information available in the university databases. A total of 1,585 individual investigators were included in the initial database (1990–93) and one-third of these were taken from the information available from the university sources. In a second survey (1994–97), only individual responses (1,450) were used in the database since it was determined that much of the institutional database information was out of date. Only forms returned with complete information were used minimum research project titles and/or publications), and only investigators with some established activities were included (post-doctoral were excluded and younger investigators were sought out and included). The Paradox Relational Database was used to collect the information.

The initial results of the survey permitted publication in 1996 of the *Directory of Medical Research in Israel: Institutions and Scientists* [2]. This included a profile of each investigator grouped by Research Interest and cross-indexed according to Organ-Specific Diseases, Clinical Category, and Methodological Approach. It was also possible to extract aggregate data on publications funding and patents according to hospital and university affiliations. The aggregate data analysis was also published separately [3]. Included in the Directory was also an overview of research activities in over 40 different areas (cancer, infectious diseases, cardiology, etc.). The Directory was distributed to medical libraries in Israel, the USA, Europe and Asia. The first effort was extremely well received and identified as a valuable resource. The database was useful for the identification of research partner, experts for review, concentrations of research activities, and documentation of specific deficiencies in research activities.

The second survey was completed at the end of 1998. It is an even more valuable resource since it confirms much of the data collected in the first survey and also identifies some important trends. A second edition of the *Directory of Medical Research* was published in late 1998 and, like the first edition, was distributed internationally [4]. A request for 50 copies was received also from the European Union for the purpose of seeking potential research partners in Israel.

The database

The first concern is how inclusive is the database. What percentage of medical researchers has been listed in the database? In an effort to quantify and answer this question a logical comparison test was conducted. The Tel Aviv University Sackler Faculty of Medicine was selected for this analysis. This medical school presents the most challenging situation for locating investigators since members of the pre-clinical faculty may be resident on the Tel Aviv University campus or at any of at least seven major hospitals in the Tel Aviv area. The clinical staff is also distributed among at least seven major hospitals. The Tel Aviv University web site contains a listing of all faculty members of pre-clinical and clinical departments. All the names of faculty members who are senior lecturers and above in several departments were compared to entries in the database collected in 1993–96 and 1996–98. Three pre-clinical departments and three clinical departments were examined (Biochemistry, Epidemiology, and Human Genetics in the pre-clinical area, and Dermatology, Hematology and Internal Medicine in the clinical area). In the pre-clinical area 47 of 51 faculty members (92%) had database entries, compared to 103 of 121 (85%) in the clinical area. A perusal of MEDLINE for publications of the last 2 years by the missing faculty members quite often indicated no publications, and the university data were very slowly revised for retirements and other departures from the faculty. This sampling certainly represents the lower limit of the percentage of medical investigators listed in the database. A decision was made not to include entries that were not current in the printed *Directory of Medical Research*. We are confident that the 1996 and 1998 editions of the Directory together contain more than 90% of active medical research investigators in Israel.

In the database one can link investigators by using keywords, discipline of training, research interests, keywords in publications, co-authors, journals, funding sources, keywords in research project titles, organ-specific diseases, etc. An idea of the dimensions of the database and the search capabilities may be obtained by listing the number of entries for specific categories. There are more than 10,000 keywords, 9,500 publications, 4,800 research projects, 2,300 funding sources entries, 6,200 listings for methodological approaches and so forth. One can list all the investigators working on reperfusion or limit it to investigators who have an MD, trained in anesthesiology, work in a hospital, collaborate with Dr. Whoever, are funded by GIF, and were published in the journal *Circulation* in 1996.

Personnel

The latest survey shows that 62% of the investigators are employed at hospitals and the remaining 38% at university departments and research institutes [Figure 2]. Gender distribution of all investigators is 74% male and 26% female. The majority of both male (63%) and female (58%) researchers work in hospitals. Among those employed in hospitals 79% have professional medical degrees and 21% have a PhD or DSc. This is a significant change, since in the 1996 survey only 14% of research staff in hospitals did not have a medical related degree. While the majority of male researchers (67%) possess medical degrees (MD, DDS, etc.), the female investigators are predominantly (67%) holders of a PhD or DSc.

Institutions

The major institutions where most of the medical research is conducted in Israel are the several medical schools and affiliated hospitals, the university faculties and the Weizmann Institute. It is noteworthy that in two of the four medical schools more than 90% of the clinical staff are from one hospital. At Ben-Gurion University more than 90% of the clinical staff are from the Soroka Hospital and at the

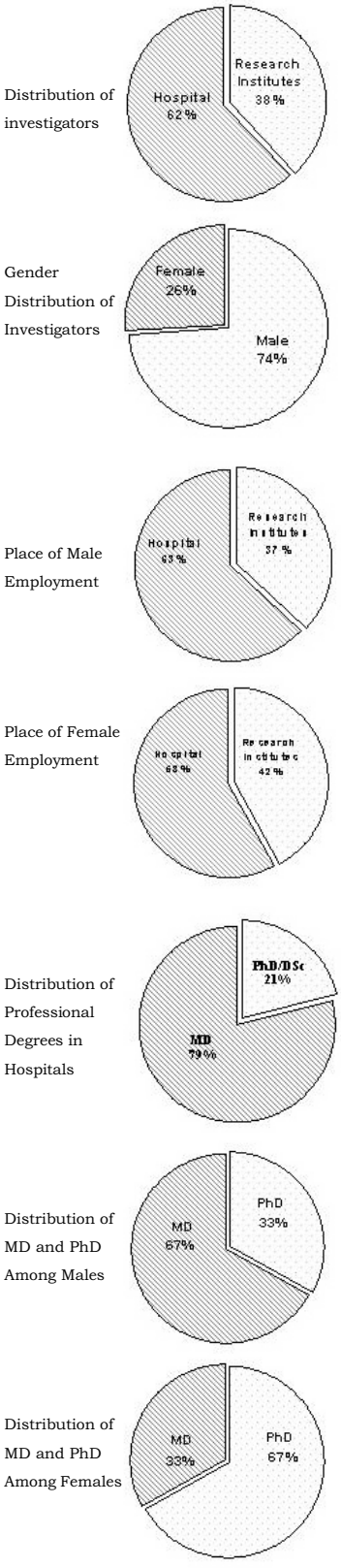

Figure 2. Profiles of biomedical and clinical investigators. Distribution of investigators, gender differences and differences between MDs and PhDs.

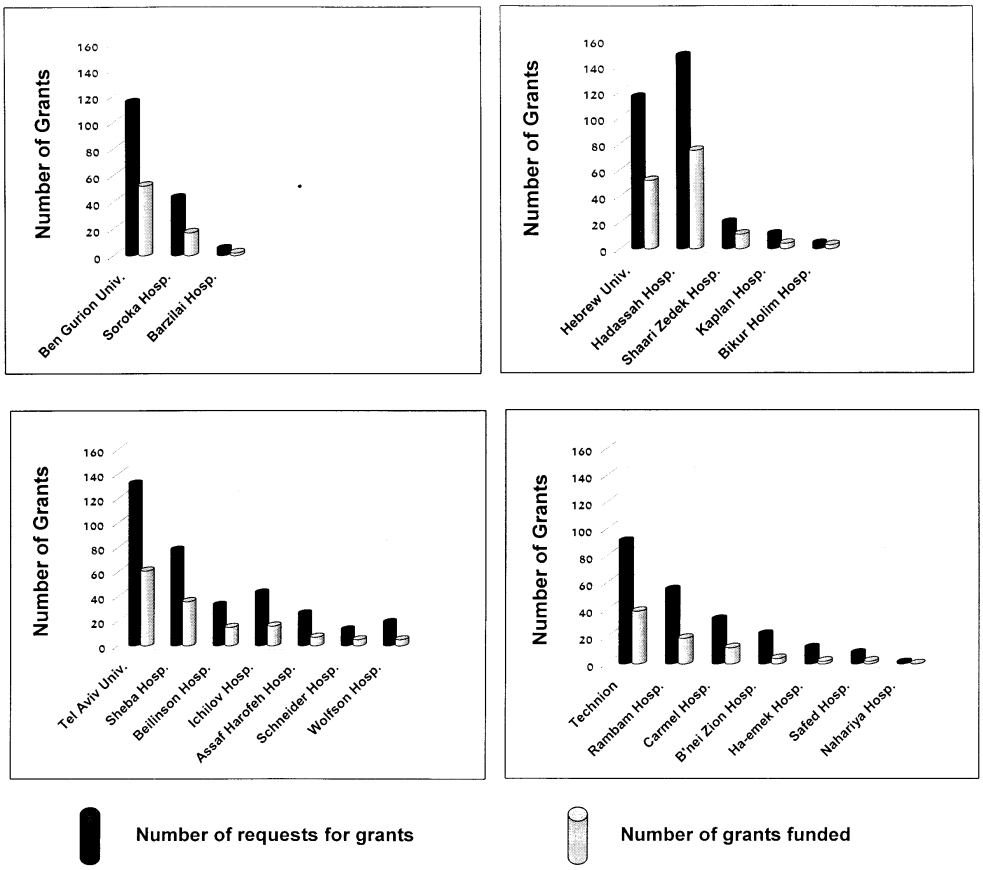

Figure 3. Distribution of biomedical and clinical investigators in medical school and affiliated hospitals (1997). The number of investigators who apply and receive grants depends on the size of the hospital and the affiliation with the university.

Hebrew University more than 90% are affiliated with Hadassah. One can see from Figure 3 the relative number of investigators at affiliated hospitals and several research institutions. For the most part the number of investigators at specific hospitals correlates with the relative size of the hospital and the strength of the affiliation.

Publications

The relative number of researchers who have published in peer review journals outside of Israel is extremely high. More than 94% of the hospital-based and non-hospital-based staff published during the 1994–97 period. In the latest survey the rate of publications (average number per investigator during a 3 year period) is comparable for hospital and non-hospital-based investigators (6.9 per investigator) [Table 1]. There has been a significant drop (10%) in the rate for non-hospital-based investigators (from 7.6 per investigator to 6.9) and a smaller (5%) decrease for hospital-affiliated researchers (7.2 to 6.9). A more complete analysis of these and other relevant data can be found in the Directory [4] and in a recent publication in *Public Health Reviews* [5]. It is unfortunate that the high relative number of

Table 1. Analysis of publication rates

	Year of survey	
	1996	1998
Institutions	**No. of publications***	**No. of publications***
Hospitals	7.2	6.9
Academic	7.6	6.9
All investigators	7.4	6.9

* Per investigator over a 3 year period [2,4]

publications does not represent a measure of the impact of publications internationally. The impact of Israeli publications (according to the Institute of Scientific Information) in the area of Computer Science is the highest in the world, ranking third in Chemistry, fifth in Molecular Biology, and tenth in Astronomy. The situation with the Medical Sciences is less impressive (publications in Psychiatry, Pharmacology, Immunology and Clinical Medicine rank from thirteenth to sixteenth in impact among the nations of the world) [G. Czapski, personal communication].

Funding

The current survey revealed some interesting information. The percentage of all medical researchers who are funded and employed at hospitals was 59% in the 1996 survey and 62% in the 1998 report. Further analysis indicates that among hospital-based investigators in the 1996 report 50% were funded, increasing to 65% in the 1998 survey. This growth could be explained by the fact that the hospital-affiliated PhD investigators receive funding, owing to a greater success rate among the non-academically affiliated investigators in hospitals nowadays (69% funded versus 61% of academically affiliated staff).

The observation of an apparent increase in funding of hospital-based investigators is tempered by the fact that the number of funding sources per investigator has decreased by almost 20% (from 2.4 per investigator in 1996 to 2.0 in 1998). This decrease reflects the paradox that while more investigators are being funded the actual amount of funding has decreased. Interestingly, the smaller percentage decrease is among hospital-based non-academic staff. The sources of funding remained essentially the same in both the 1996 and the 1998 surveys. The Chief Scientist's Office of the Health Ministry supports more than 40% of all funded investigators, which is more than double the percentage of the next highest source, the U.S.–Israel Binational Foundation, followed in decreasing order by the Israel Science Foundation, the Ministry of Science and Technology, the German–Israel Foundation, the Israel Cancer Association, the Israel Cancer Research Fund, and the National Institutes of Health [Figure 4].

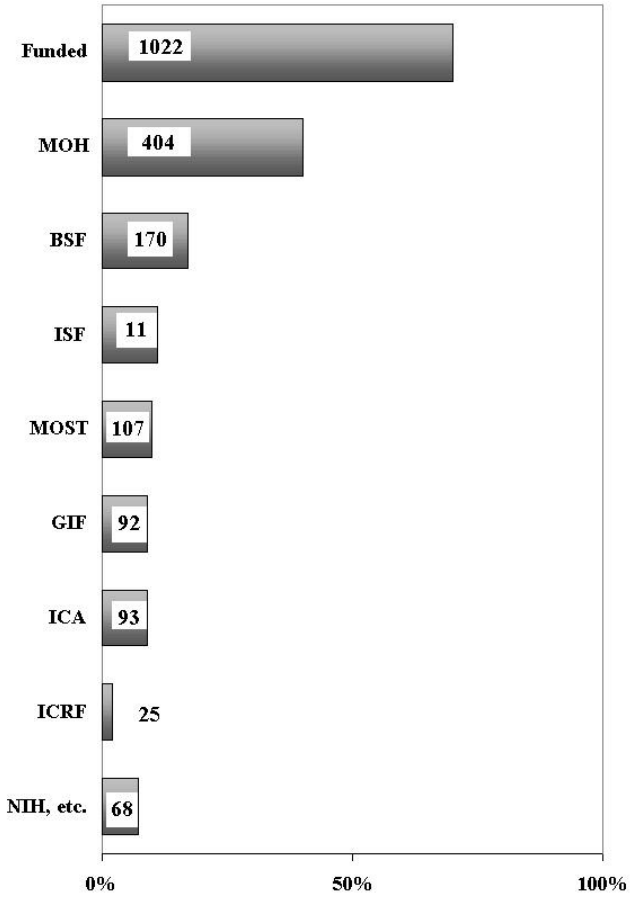

Figure 4. Number of funded biomedical and clinical investigators (1997). Percent and number of biomedical and medical Israeli investigators funded by the different agencies. MOH = Ministry of Health, BSF = U.S.–Israel Binational Science Foundation, ISF = Israel Science Foundation, MOST = Ministry of Science and Technology, GIF = German–Israel Foundation for Scientific Research and Development, ICA = Israel Cancer Association, ICRF = Israel Cancer Research Fund, NIH = National Institutes of Health, USA.

Summary

The data collected for the second edition of the *Directory of Medical Research in Israel* and the Israel Biomedical Database have yielded very relevant information concerning the distribution of investigators, publication activities and funding sources. The aggregate data confirm the findings of the first edition published in 1996 [2]. Those facts endorse the highly concentrated and extensive nature of medical research in the Jerusalem area, which is conducted at the Hebrew University and its affiliated hospitals. In contrast, Tel Aviv University, whose basic research staff is about two-thirds the size of the Hebrew University staff, has a more diffuse relationship with its clinical staff who are located at more than half a dozen hospitals. Ben-Gurion University in Beer Sheva and the Technion in Haifa are smaller in size, but have closer geographic contact between their clinical and basic research staff.

Nonetheless, all the medical schools and affiliated hospitals have good publication and funding records. It is important to note that while some aspects of the performance at basic research institutions seem to be somewhat better than at hospitals, the records are actually quite similar despite the greater burden of clinical services at the hospitals as compared to teaching responsibilities in the basic sciences. The survey also indicates the substantial number of young investigators in the latest survey who did not appear in the first survey. While this is certainly encouraging, it is also disturbing that the funding sources are apparently decreasing at a time when young investigators are attempting to become established and the increasing burden of health care costs precludes financial assistance from hospital sources.

The intensity and undoubtedly the quality of medical research in Israel remains at a level consistent with many of the more advanced western countries. This conclusion is somewhat mitigated by the fact that there is a decrease in available funding and a measurable decrease in scholarly activity at a time when a new, younger generation of investigators is just beginning to become productive.

In closing, we wish to stress that the collection of data for the Biomedical Database is a continuing project and we encourage all medical researches who may not have contributed relevant information to write to the Office of the Chief Scientist or contact the office by email.

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Capsule

Toxin and phage secretion

Cholera toxin is secreted from *Vibrio cholerae* bacteria harboring the filamentous bacteriophage CTX. Davis et al. examined the requirements for release of new phages from infected bacteria and discovered that a protein known to be involved in secretion of cholera toxin EpsD was also required for phage release. This finding is unexpected given the different size and nature of a protein toxin versus a protein-coated DNA molecule.

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