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**COLLATERAL ANALYSIS
AND VERIFICATION OF
BIOLOGICAL AND TOXIN RESEARCH:
A SECOND CASE STUDY**



NOVEMBER 1992

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- Annex E: Plant Pest and Disease Research Laboratory, Tehran
- Annex F: Department of Medicine, Shiraz University, Shiraz
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PREFACE

The Gulf War brought to the surface the serious concerns about the potential for developing, producing and stockpiling biological and toxin weapons. In regard to Iraq, this matter has been the subject of investigation under United Nations Security Council Resolution 687. But concern about such matters neither began, nor ended, with the Gulf War. For example, prior to that conflict, the Iraq-Iran war also prompted various media speculation about what might have been going on behind closed laboratory doors in each of the countries.

An uncertain political and security environment can become fertile ground for such speculation. Even legitimate programs, in such a climate, can fuel concerns and lead to responses in of terms secrecy or actions that, in turn, become further destabilizing. This was clearly recognized at the Third Review Conference of State Parties to the Biological and Toxin Weapons Convention (BTWC), held in September 1991, when a refined and expanded set of confidence-building measures (CBMs) was agreed by the Parties to the Convention. Designed to enhance transparency, these CBMs not only implicitly recognize the dual-use nature of various technologies and activities, but also explicitly recognize the value to be gained at the international level through the exchange of information.

It must be absolutely clear from the outset that this paper does not address the question of biological and toxin warfare. It is about technology, research and the free flow of information. Iran has been chosen as a case study because it has been the subject of media speculation, undoubtedly much to its chagrin. Clearly, the sooner one might be able to set such speculation to rest, the better off we all will be. This paper examines the utility of "collateral analysis" as a tool to help clarify such situations and to enhance transparency.

This case study uses "collateral analysis" to identify from the public literature the types of biological research that have been conducted in Iran and published. This can accomplish the following:

- identify specific areas of published research activity;
- identify institutions and scientists associated with such published research activity;
- identify the absence of published research activity in specific areas of endeavour.

Such collateral analysis can give indications of a country's technological base. It bears repeating that this report does not suggest that the work of the institutes and authors cited is in any way associated with biological warfare programs. This paper simply collates publicly-available documentation as published by the institutes and authors concerned, and it draws no conclusions on the basis of that information.

Clearly, collateral analysis cannot be expected to reveal activities that anyone might choose deliberately to conceal, nor is that the subject of this study. It can, however, assist in the formulation of questions about the capabilities and activities of various facilities, in conjunction with other sources of information, with a view to enhancing transparency and confidence.

Such is the purpose of this document: to promote discussion with regard to transparency, confidence-building measures and the utility of collateral analysis. One also wonders whether this and other case studies like it might be useful in the context of the work of the Ad Hoc Group of Experts examining potential verification measures in relation to the BTWC.

This is a report of a research project. The views expressed herein do not necessarily reflect those of the Canadian Government.

ACKNOWLEDGEMENT

External Affairs and International Trade Canada wishes to acknowledge the work performed under contract by Brac Scientific Consulting, in collaboration with the Verification Research Unit of this Department.

PRINCIPAL FINDINGS AND CONCLUSIONS

- Various computerized databases, containing over 32 million records of scientific research from over 130 countries during the period 1966-1992, were accessed using key words related to biological and toxin research.
- Publication titles thus found were reviewed to avoid duplication and ensure relevance.
- The records of the published research were analyzed in terms of:
 - sites of research;
 - patterns of the publications over time;
 - authors; and
 - apparent nature of the research.
- For the period 1970-1992, there were 9,834 publications identified from Iran in the various databases (including duplicate reporting).
- A unique set of 672 Iranian publications was established using key words, and this formed the basis of the subsequent analysis. These publication titles appear in the Annexes to this paper.

- The main laboratories and institutes publishing on biological and toxin matters were identified as:
 - the Faculty of Medicine, University of Tehran, Tehran;
 - the School of Public Health, Tehran University of Medical Sciences, Tehran;
 - the Razi State Vaccine and Serum Institute, Tehran;
 - the Plant Pest and Disease Research Laboratory, Tehran;
 - the Department of Medicine, Shiraz University, Shiraz;
 - the Faculty of Veterinary Medicine, University of Tehran, Tehran;
 - the Pasteur Institute, Tehran;
 - the Institute of Biochemistry and Biophysics, University of Tehran, Tehran;
 - the School of Medicine, Isfahan University, Isfahan;
 - the Faculty of Agriculture, University of Tehran, Tehran;
 - the Iranian National Blood Transfusion Service, Tehran;
 - the College of Agriculture, Isfahan University, Isfahan;
 - the Department of Plant Protection, College of Agriculture, Shiraz University, Shiraz;
 - the Department of Microbiology, Shiraz University, Shiraz;
 - the Department of Biology, Faculty of Science, University of Tehran;
 - the Mashad Medical Sciences University, Mashad; and,
 - the Pharmaceutical Research Center, Darou-Pakhsh Company, Tehran.

- In some cases, the government laboratories appear to be superior to the university laboratories.
- It appears that the most important sites of research were the Razi State Vaccine and Serum Institute; the Pasteur Institute; and the Institute of Biochemistry and Biophysics, University of Tehran; all in Tehran. This conclusion is based on the nature of the published research, and on the inference of the types of equipment needed to conduct that research.
- Also notable for the advanced level of research was the Pharmaceutical Research Centre, Darou-Pakhsh Company, in Tehran. However, this Institute has had a much smaller output of published papers, with only 10 publications published during the years 1985 to 1990.
- The time distribution found in this study of Iranian biological and toxin research differs somewhat from that found by other studies of Iran's neighbour, Iraq.
- The Razi Institute reported the capability to make 20 million doses of *Clostridium perfringens* vaccine for veterinary purposes on an annual basis in Iran. This is clearly a very large-scale effort in vaccine production.

- *Bacillus anthracis* (the bacterium which causes anthrax) was the subject of ten publications.
- *Clostridium botulinum* (the source of botulinum neurotoxin which causes botulism) was not the subject of any publications over the period 1970-92. Only a single paper on botulism was found from Iran in the research publications from 1970 to 1992. This paper dealt with a large outbreak of botulism type E poisoning. There was none on botulinum toxin itself.
- During the period 1970-1992, 3 publications dealt with tetanus toxin. There is an apparent lack of publications in the area of neurotoxins in general.
- Fungal toxins appear to pose a health problem in stored foods in Iran. Of the 25 publications from Iran dealing with mycotoxins and aflatoxins, 22 were published between 1975 and 1982. In the past 10 years, there have been only 3 publications on fungal toxins. Iran has not published any research on mycotoxins since 1989.

1.0 INTRODUCTION

In the aftermath of the Gulf War, there has been heightened concern about the potential for proliferation of biological and toxin weapons. This paper does not directly address the issue of biological and toxin weapons per se.

During the Iraq-Iran war from 1980-1988, there were confirmed reports that Iran had been attacked with chemical weapons by Iraq. During that war, there was unconfirmed speculation about novel toxin agents and biological agents as well.

Security Council Resolution 687, dated 3 April 1991, requires that Iraq accept destruction, removal or rendering harmless, under international supervision, of all chemical and biological weapons and all stocks of agents and all related subsystems and components.

The Biological and Toxin Weapons Convention (BTWC) forbids the development, production and stockpiling of such weapons, as is indicated from the enclosed box (see page 2). The Third Review Conference of the BTWC, held in September 1991, sought to address certain concerns through agreement on a refined and expanded set of confidence-building measures (CBMs) designed to provide greater transparency among States.

This is the recent background against which this case study was conducted of Iranian publications on the subject of biological and toxin research. The term "collateral analysis" has been used to describe a method of information gathering that involves the collection and systematic examination of publicly-available scientific, technical and other information. It makes no judgement as to the purpose of the research. This analysis may provide an initial

picture of a country's technological base and of its capacity to move in a variety of directions, some of which may be of concern and, therefore, a potential area for directing CBMs to enhance transparency. Similarly, a lack of publication in certain areas of endeavour, when coupled with other sources of information, could raise certain questions. It must be added, however, that collateral analysis cannot be

expected to reveal activities that are deliberately concealed.

This study had three objectives:

- 1) to identify specific areas of published research activity;
- 2) to identify institutions and scientists associated with such published research activity; and
- 3) to identify the absence of published research activity in specific areas of endeavour.

Article I

Each State Party to this Convention undertakes never in any circumstances to develop, produce, stockpile or otherwise acquire or retain:

(1) Microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes;

(2) Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.

2.0 STUDY METHODOLOGY

A major part of this study depended upon the gathering of information available in the open scientific literature, specifically computerized databases. Therefore, the sources and quality of the information played an important role in determining the usefulness of collateral analysis. The contractor has direct access to relevant databases to make literature searches and can load the results directly to his computer for analysis. Table 1 lists five databases that have been found to provide particularly useful coverage of biological, biochemical and medical research. Together, these databases contain over 32 million records of scientific research from over 130 countries. Accordingly, they were the primary sources of information used in this study of Iranian research. The databases provide consistent coverage during the time period 1970-1992. The following sections will describe the databases and their breadth of coverage.

Table 1. Major Scientific Databases

DATABASE	COVERAGE	RECORDS
BIOSIS Previews	1969-present	7,713,784
Embase	1974-present	4,714,889
Medline	1966-present	6,856,539
CAB Abstracts	1972-present	2,878,913
CS Search	1969-present	10,570,791

2.1 BIOSIS Previews

BIOSIS Previews contains citations from Biological Abstracts (BA); Biological Abstracts/RRM (Reports, Reviews, Meetings [BA/RRM]); and BioResearch Index (BioI), which are the major publications of BIOSIS. Together, these publications constitute the major English-language service providing comprehensive worldwide coverage of research in the biological and biomedical sciences. Biological Abstracts includes approximately 280,000 accounts of original research yearly from nearly 9,000 primary journal and monograph titles. Biological Abstracts/RRM includes an additional 260,000 citations a year drawn from meeting abstracts, reviews, books, notes, letters, selected institutional and government reports, and research communications. U.S. patents are included from 1986 through 1989. The time period covered by BIOSIS Previews is 1969 to the present. The subject coverage in this database includes all life science subjects, including but not limited to the following: Agriculture, Anatomy, Bacteriology, Behavioral Sciences, Biochemistry, Bioengineering, Biophysics, Biotechnology, Botany, Cell Biology, Clinical Medicine, Environmental Biology, Experimental Medicine, Genetics, Immunology, Microbiology, Occupational Health, Parasitology, Pathology, Pharmacology, Physiology, Public Health, Radiation Biology, Systematic Biology, Toxicology, Toxin Research, Veterinary Science, Virology, Zoology. The material scanned for BIOSIS Previews includes the following: approximately 9,000 primary journal and monograph titles, books, reviews, technical reports, meetings and meeting abstracts, notes, letters, annual reviews, U.S. patents from 1986 through 1989, bibliographies, guides, and research communications.

2.2 Embase

Embase (Excerpta Medica) is a comprehensive index of the world's literature on human medicine and related disciplines. About 350,000 records are added annually, over 60% of which contain abstracts. All journal articles are added to the database within 30 days after receipt of the journal, and all records appear on-line with complete indexing.

Subject coverage includes Adverse Drug Reactions, Anaesthesiology, Bacteriology, Biochemistry, Bioengineering, Cancer, Cardiovascular Disease, Endocrinology, Environmental Health, Forensic Science, Genetics, Gene Technology, Health Economics, Hematology, Immunology, Industrial Medicine, Infectious Diseases, Internal Medicine, Microbiology, Neurology, Nuclear Medicine, Occupational Health, Parasitology, Pathology, Pharmacology, Physiology, Physiotherapy, Pollution Control, Psychiatry, Public Health, Radiology, Toxicology, Virology.

Embase provides access to periodical articles from more than 2,900 primary journals from over 110 countries. An additional 600 journals are screened for drug articles. This database provides coverage of research from 1974 to the present.

2.3 CA Search

The CA Search database includes citations to the literature of chemistry and its applications. A significant part of its coverage includes biological chemistry, biotechnology, peptides, toxins and genetic engineering. CA Search is an expanded database which contains

the basic bibliographic information appearing in the printed Chemical Abstracts. The subject coverage includes Applied Chemistry, Biochemistry and Biology, Chemical Engineering, Classes of Substances, Macromolecular Chemistry, Organic and Inorganic Chemistry, Physical and Analytical Chemistry, Properties and Reactions.

The following sources are included in CA Search: journal articles, patents, reviews, technical reports, monographs, conference and symposium proceedings, dissertations, and books. Over 10,000 primary journals are abstracted. This includes coverage from over 120 countries. The database is updated two times a week with approximately 17,000 records per update. CA Search covers the time period 1967 to the present.

2.4 CAB Abstracts

CAB Abstracts is a comprehensive file of agricultural and biological information containing all records in the 26 main abstract journals published by Commonwealth Agricultural Bureaux. Over 8,500 journals in 37 different languages are scanned for inclusion, as well as books, reports, theses, conference proceedings, patents, annual reports, and guides. In some instances less accessible literature is abstracted by scientists working in other countries. About 130,000 items are indexed each year. Significant papers are abstracted, while less important works are reported with bibliographic details only. The journals included in CAB Abstracts cover the following subjects: agricultural engineering, animal disease, biotechnology, horticulture, nutrition, veterinary science, entomology, plant pathology, pesticides, fertilizers, weeds, and world agricultural economics.

The material scanned for CAB Abstracts includes the following: scientific journals, books, monographs in series, textbooks, technical reports, published theses, symposia, conference proceedings, review journals, patents, annual reports, bibliographies and guides, and translated journals. The dates covered are 1972 to the present. The database is updated monthly.

2.5 Medline

Medline (Medlars on-line), produced by the U.S. National Library of Medicine, is one of the major sources for biomedical literature materials. Additional materials not published in Index Medicus are included in the Medline database in the areas of population and reproductive biology. Abstracts, which are taken directly from the published articles, are included for over 47% of the records added from 1975 forward. Records added before 1975 do not contain abstracts; records added from 1984 to the present have abstracts for about 59% of the records. Approximately 300,000 records are added per year, of which over 75% represent publications written in the English language.

Subject coverage includes Clinical Medicine, Experimental Medicine, Hospital Literature, Population and Reproductive Biology, Pharmacology, Psychiatry, Environment and Public Health, Veterinary Medicine, Pathology, Anatomy and Physiology, Microbiology and Parasitology, Toxicology. Medline indexes articles from approximately 3,300 journals published in over 70 countries. Dates covered include 1966 to the present.

2.6 Selection Criteria for Iranian Publications

After Iranian publications were identified in the major databases, the next step was to use key words to identify certain types of research. These key words are some of the indicators sometimes suggested to have a potential relationship to biological warfare research. It should be clearly noted that the presence of these key words described below does not imply any direct connection between the research and biological weapons programs. Key words are tools with which to identify particular types of research. Only after the patterns, concentrations and possible gaps in the published research are identified can any attempts be made to draw any firm connections between the published research and any potential diversion of biological materials.

Search strategies were used to identify Iranian research associated with the following topics. The following are key words:

- 1) Microbiology, virology, bacteriology, infectious diseases;
- 2) toxins, neurotoxins, (see Box 1 for specific key words);
- 3) recombinant DNA, gene-cloning, biotechnology;
- 4) large-scale production, fermentation, bioreactors;
- 5) vaccine technology, immunology, immunization;
- 6) aerosol, lyophilization;

abrin
apamin
brevetoxin
batrachotoxin
botulinum toxin
bungarotoxin
conotoxin
curare
diamphotoxin
latrotoxin
mycotoxin
palytoxin
phospholipase
ricin
sarafotoxin
saxitoxin
tetanus toxin
tetrodotoxin
tubocurare

1. Toxin Key Words

tulare?
anthrax
anthracis
brucell?
glanders
pseudomonas
cholera
salmonella
plague
typhoid
typhi
q-fever
influenza
ebola
marburg
lassa
west-nile
congo-crimean
dengue
yellow fever
smallpox

2. Key Words for Biological Agents

- 7) specific biological agents, such as bacteria, viruses, rickettsia (see Box 2 for specific key words); and,
- 8) bioregulators (see Box 3 for specific key words).

The approach was taken to use broad terms such as microorganism, virus, bacteria and toxin as well as specific key words. This was done to ensure coverage and not miss any significant area of Iranian research.

angiotensin
atrial natriuretic
peptide
bombesin
bradykinin
cholecystokinin
delta sleep-
inducing peptide
dynorphin
endorphin
endothelin
enkephalin
gastrin
gonadoliberin.
neurotensin
neuropeptide Y
somatostatin
substance P
thyroliberin
vasopressin

3. Bioregulator Key Words

Truncation was used so that minor differences in the ending of a key word would still allow its retrieval. For example, Box 2 gives *tulare?* as a key word. In this case, the question mark allows tularemia or *tularensis* to be selected. *Francisella tularensis* is the bacterium that causes the disease tularemia.

To avoid counting the same work twice, Iranian publications were selected on the basis of the presence of key words described above. When the publications from all five databases were selected containing these key words, duplicates were identified by comparing bibliographic information, and removed.

The unique set of references were stored in a Pro-Cite bibliographic database.

The records of the published research were analyzed in terms of:

- 1) sites of research;
- 2) patterns of publications over time;
- 3) authors of the publications; and
- 4) apparent nature of the research.

3.0 RESULTS OF THE STUDY

3.1 Iranian Publications

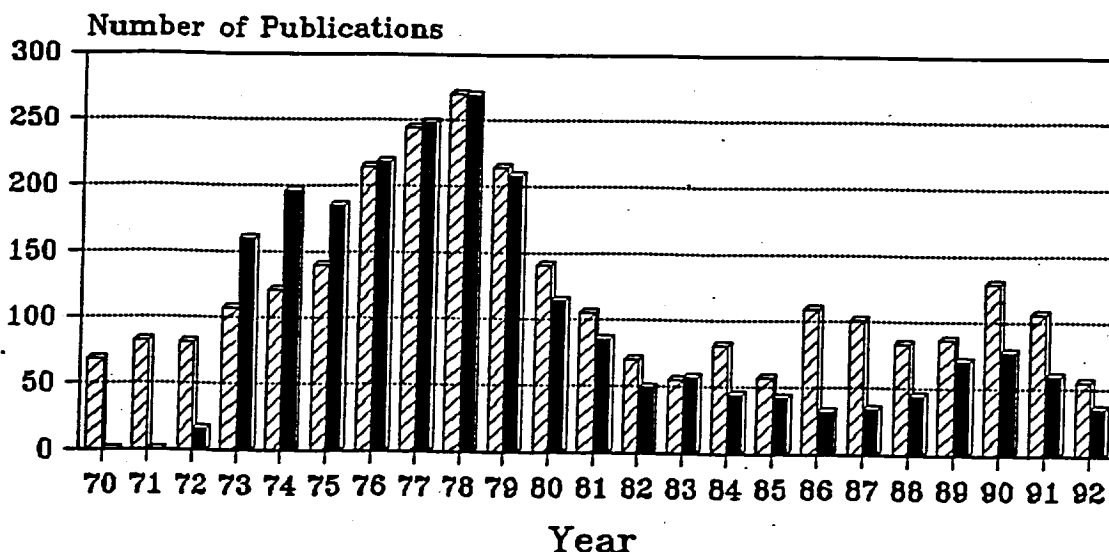
One of the prime objectives of this study was to develop a baseline of information in order to analyze the trends of published Iranian biological research. Once a baseline of research in Iran had been established, questions could be asked about the possible nature of the described research. This report uses the number of scientific publications as a measure of research done. Table 2 gives the total number of publications identified as having research carried out in Iran. In the time period under consideration, there were 9,834 publications from Iran. While thousands of publications would be indicative of a significant level of research, it is important to ask when and where this research was carried out. Of course, the nature of the research is of prime importance. As well, a unique set of publications must be selected on the pertinent topics as described in section 2.6, since the multiple databases may report the same item.

Table 2. Iranian Publications in Major Scientific Databases

DATABASE	COVERAGE	PUBLICATIONS
Biosis Previews	1969-present	1,657
Embase	1974-present	2,325
Medline	1966-present	198
CAB Abstracts	1972-present	2,872
CA Search	1969-present	2,782

Iran

Biological and Chemical Publications



source: Publications from Embase, n=2233
and CA Search, n=2894 (1992 estimated)

Figure 1. Iranian Publications

This section also describes the time course of the total publications from Iran. Analysis of publications from Iran in scientific databases showed marked changes in the number of publications during the period January 1, 1970 to September 15, 1992. Figure 1 shows the pattern of publications in scientific databases *Embase* and *CA Search*. It should be noted that this figure gives the total annual Iranian publications in each respective database. Thus, in the major biological database *Embase*, there were no publications from Iran between 1969 and 1974. Starting in 1975, there was rapid increase in biological and chemical publications which peaked in 1978 at over 250 publications. After the peak, the number of publications

declined dramatically by 1983. After the low number of publications in 1983, there is a smaller increase in publications peaking in 1990. However, the number of publications is less than 50% of the total in 1978. This pattern is evident in both databases. Similar patterns of Iranian publications in the time period under study were found in the three other major databases used in this study: BIOSIS, Medline and CAB Abstracts.

These results give an overview of all Iranian publications in major scientific databases used in this study. Clearly, there will be research included in these databases that is not at all pertinent to questions that this study is examining. Therefore, it is important to select and survey publications that have been chosen by the key-words that establish more direct relevance to biological and toxin research programs.

3.2 Key Word Selected Iranian Publications

From all identified Iranian publications in all databases, research was selected on the basis of key-words described in section 2.6. The objective was to select research containing key words describing research in key subject areas dealing with recombinant DNA, viruses, bacteria, toxins, peptides, bioregulators and other key areas of biological research.

Figure 2 shows the time course of 672 publications from Iran that were selected on the basis of key-words. These publications formed a unique set of database records which were the basis for this study's analyses. The pattern of published research shows a low output on selected topics from 1970 to 1972. There were fewer than 10 publications per year. It was only in 1973 that the output from Iranian laboratories started to increase. In 1978 the number of publications peaked at 80. After that year, the number of publications declined

to a low of under 20 within 5 years. After this time, there was an increase to a new peak in 1989 when 48 papers were published. After 1989, there was a 50% decrease in publications to 1991. It should be noted that since this study is inclusive up to 15 September 1992, the total Iranian publications for 1992 was estimated on the basis of publication output in the first eight months.

These large changes in Iranian biological research raise many questions about the nature of the research. However, in order to provide more detailed analysis, the research contained in the 672 selected publications was further broken down to describe the major

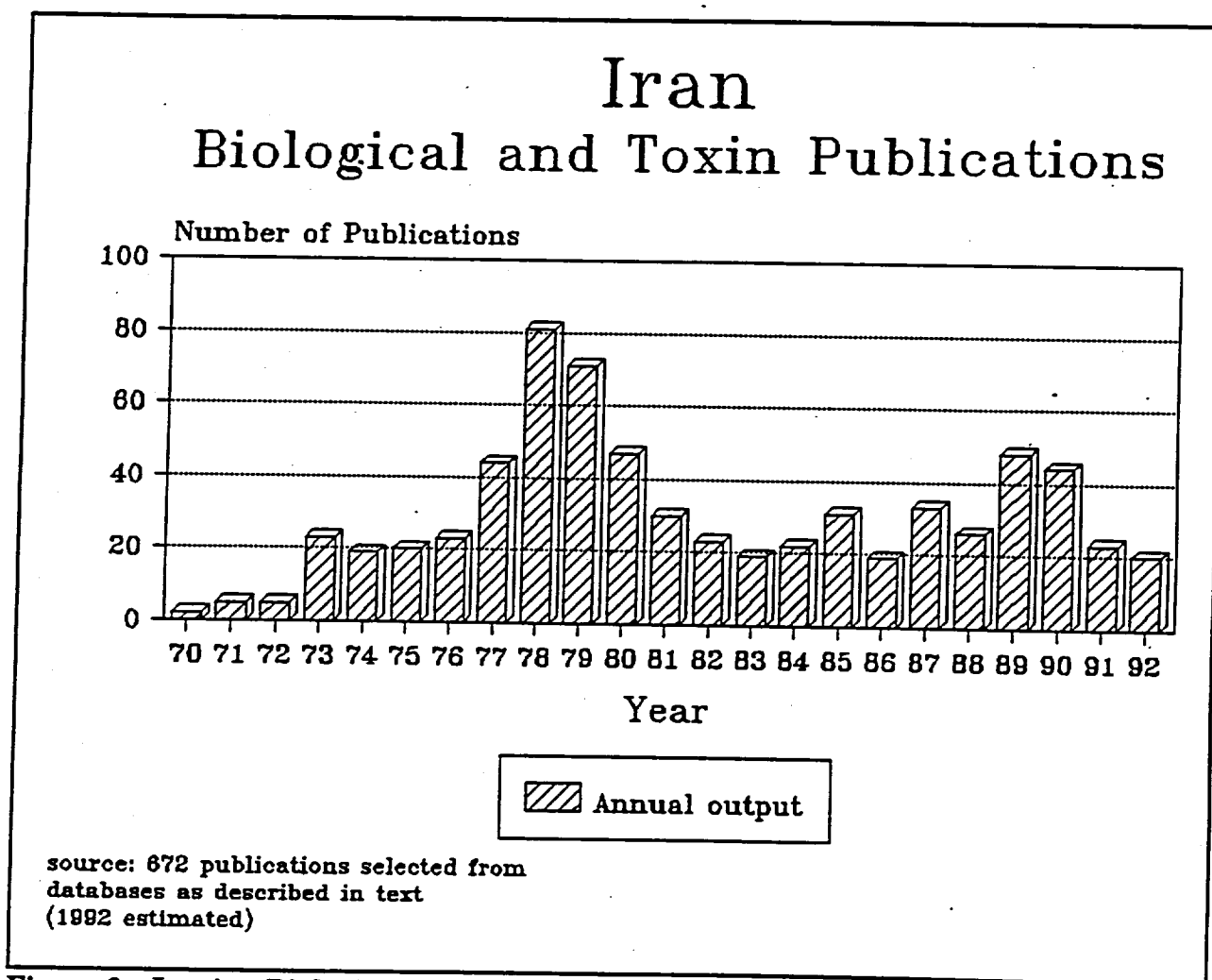


Figure 2. Iranian Biological Publications

laboratories publishing this research. Annex A lists these laboratories as determined by the institutional affiliation that the publications give. The following sections describe the main laboratories and institutes that publish in the scientific literature from Iran.

3.3 Faculty of Medicine, University of Tehran, Tehran

The Faculty of Medicine, located in Tehran, has published 85 publications during the study period on topics in biology. Annex B contains the bibliographic information of the publications from the Faculty of Medicine. As well, it contains a list of all 164 scientific personnel shown as authors in the publications. The main authors, who each have 5 or more publications are listed in box 4.

The Faculty of Medicine published research on a wide range of biological, biochemical and microbiological subjects. Box 5 lists some of the apparent research priorities including the microorganisms and toxins that the Faculty investigated.

Figure 3 shows the pattern of publications over time from the Faculty of Medicine. There were no publications from this Faculty before 1973. During 1973 to 1976 there was low but steady output of research, that was followed by a rapid increase in 1977 to 1979.

From 1980-88, there was low but steady output from the Faculty of Medicine, with a sharp increase in 1989-90 to 11 publications. After 1990, there was a decrease in publications from

Ala, F.
Khoyi, M. A.
Mahmoudian, M.
Shafiee, A.
Zarrindast, M. R.

4. Main Authors

Aflatoxins
Brucellosis
Pentagastrin
Pharmacology
Q-fever
Ricin
Tetrodotoxin
Vasopressin

5. Research Priorities

this Faculty. The research facilities at the Faculty of Medicine appear to be better than average in comparison to other Iranian laboratories identified in this study in terms of the required laboratory equipment and the level of sophistication of the reported research.

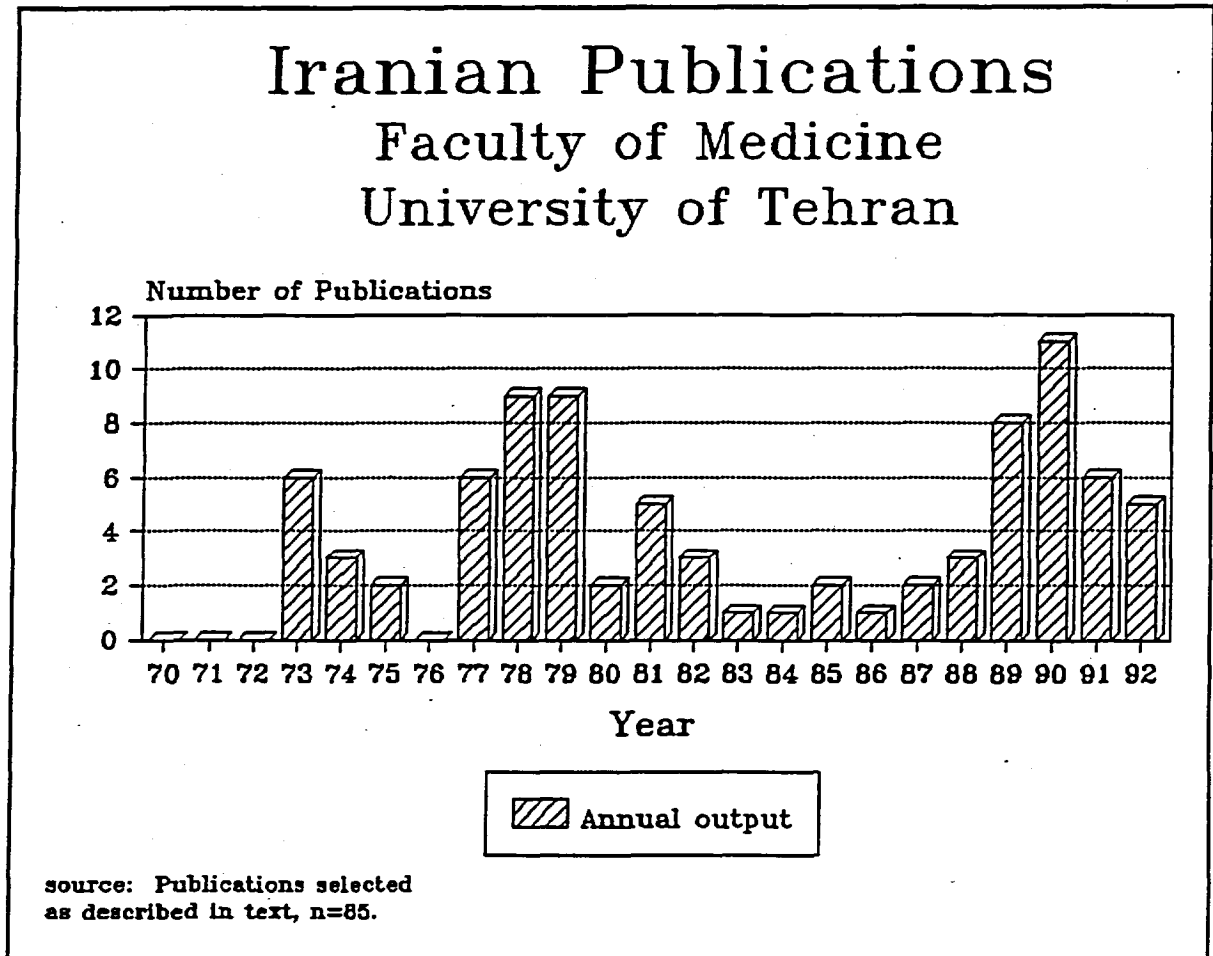


Figure 3. Faculty of Medicine

3.4 School of Public Health, Tehran University of Medical Sciences, Tehran

The School of Public Health, Tehran University of Medical Sciences, Tehran is a research facility publishing research related to the epidemiology of infectious diseases in

Iran. Figure 4 shows the time course of 64 publications from the School of Public Health. There have been many changes in the output of research publications from this Institute during the time period under investigation. For example, in 1972 there were no publications while in 1973, there were 8 publications. There is a cluster of publications from 1977 to 1979. In 1980-1986 there were fewer publications, including 1982 and 1986 when there were no publications. From 1987 to 1990, there were between 3 and 5 publications every year. In 1991 and 1992, there was a single publication each year.

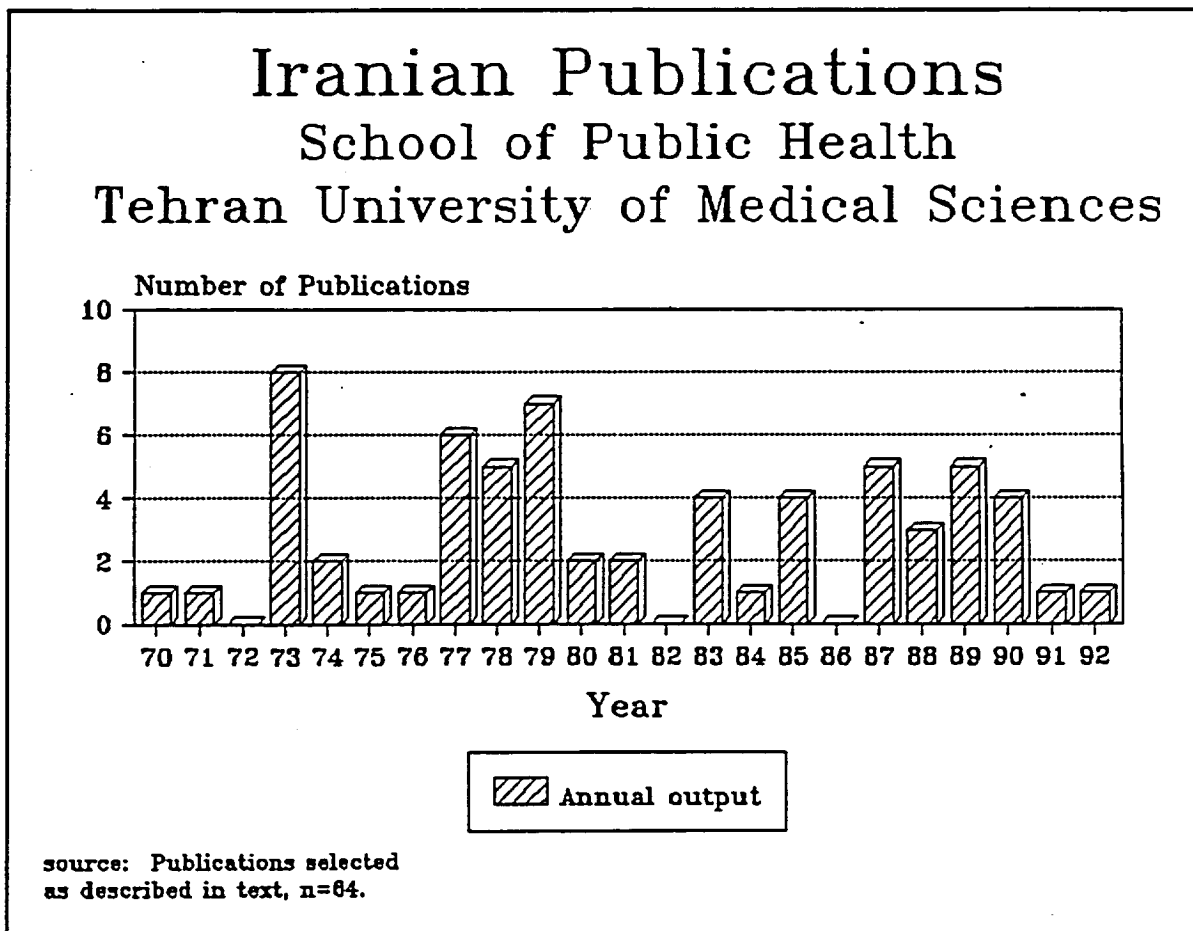


Figure 4. School of Public Health

Box 6 lists the main authors from the Institute. The full list of 116 authors from the School of Public Health and the list of publications are found in Annex C.

Afshar, A.
Edrissian, G. H.
Eshghy, N.
Ghorbani, M.
Imandel, K.
Javadian, E.
Manouchehri, A. V.
Mohammad, K.
Nadim, A.
Nasseri, K.
Sabbaghian, H.
Zaim, M.

Box 7 lists the research priorities observed in the publications from the School of Public Health. Compared to other Iranian laboratories examined in this study, especially those affiliated with universities, this appears to be a superior facility. It has modern equipment able to carry out sophisticated research related to highly pathogenic arboviruses such as Congo

6. Main Authors

Crimean Hemorrhagic Fever virus, Japanese Encephalitis virus and West-Nile virus. Some of these viruses would normally require the most

stringent biosafety levels if they were being handled experimentally. This centre also reported work on highly pathogenic bacteria, such as the bacteria that cause anthrax and brucellosis. However, most of the research published from this centre that deals with

Anthrax
Biological Control of Insects
Botulism
Brucellosis
Cholera
Congo Crimean Hemorrhagic Fever
Japanese Encephalitis
Vaccines and Immunization
West-Nile Virus

7. Research Priorities

pathogenic microorganisms is concerned with serological and epidemiological survey of diseases in Iran. The nature of the research reported in the studies makes it appear that the manipulations do not require high-level containment facilities. It is not clear whether such facilities were or were not available; or whether the types of research, where a high level of containment would be required, were not reported.

3.5 Razi State Vaccine and Serum Institute, Tehran

The Razi State Vaccine and Serum Institute is located in Tehran. It published 59 papers in the time period under study. Annex D contains the bibliographic information of the publications from the Razi State Vaccine and Serum Institute, Tehran and the 73 authors of the publications. Box 8 lists the main authors of publications from the Razi State Vaccine and Serum Institute, Tehran. These authors have published 3 or more publications. Many authors have published at least several papers from this Institute, indicating more continuity in research.

Box 9 lists the research priorities of publications from the Razi Institute. These include surveys of endemic diseases in Iran and potential treatments. From the published research, this facility appears to have extensive facilities for experimental work. A major area of research and development concerns vaccines for human and animal disease. Of particular importance is research described in a publication dealing with large scale productions and standardization of vaccine to *Clostridium perfringens*. It was reported that many millions of doses of vaccine are prepared each year.

Aarabi, I.
Ahourai, P.
Ardehali, M.
Bahrami, S.
Darakhshan, H.
Ebadi, A.
Farzanpay, R.
Hashemi, Fesharki R.
Kamali, M.
Latifi, M.
Mahinpour, M.
Mirchamsy, H.
Nazari, P.
Shafiyi, A.
Zowghi, E.

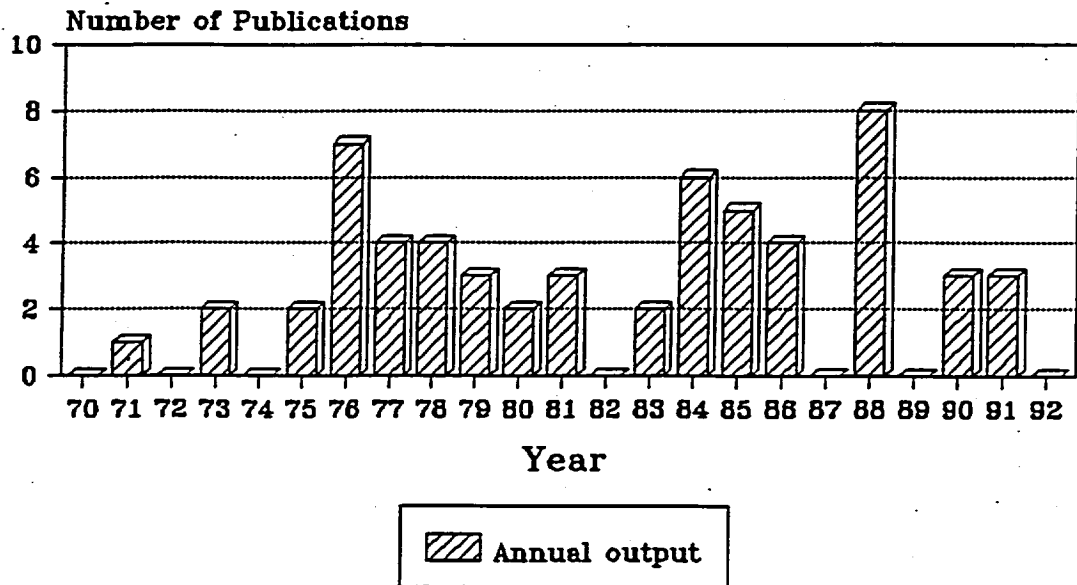
8. Main Authors

Anthrax
Brucella melitensis
Brucella vaccine
Brucellosis
Clostridium perfringens vaccine
(large-scale production)
Mesobuthus eupeus venom
Pit Viper venom
Rinderpest virus

9. Research Priorities

Iranian Publications

Razi State Vaccine and Serum Institute Tehran



source: Publications selected as described in text, n=59.

Figure 5. Razi Institute

Figure 5 shows the time course of the publication output. The output of the Razi Institute shows great fluctuations in some years. While there is a reasonably steady output of publications from 1975 to 1981, there are no publications in 1982. Publications pick up again in 1983 peaking in 1984, falling to no publications in 1987. In 1988, there were 8 publications, while in 1989 there are no publications. In 1990-1991 there are 3 publications each year. In 1992, there are no publications reported from this Institute.

The Razi Institute is a superior centre in terms of the types of research and development reported.

3.6 Plant Pest and Disease Research Laboratory, Tehran

The Plant Pest and Disease Research Laboratory in Tehran published 49 papers on research subjects selected by this study. Box 10 lists the main authors from this laboratory. Annex E contains the bibliographic citations of these publications. It also lists all 40 authors shown on the publications. Box 11 lists the research priorities of publications from the Plant Pest and Disease Research Laboratory. These studies include research on *Pyricularia oryzae*, the fungus which causes rice blast disease, and *Fusarium* species which can produce mycotoxins (common agricultural problems).

Barooti, S.
Ershad, D.
Fassihiani, A.
Izadyar, M.
Saber, M.
Torabi, M.
Zad, J.

Figure 6 shows the time course of publications from the Plant Pest and Disease Research Laboratory. There were no publications before 1976. Starting in 1976, there is a small increase in publications which peaks in 1978. This tapers off to no publications in 1983. Starting in 1984, there is a large increase in publications which is maintained for 3 years. In 1989, there are 10 publications.

10. Main Authors

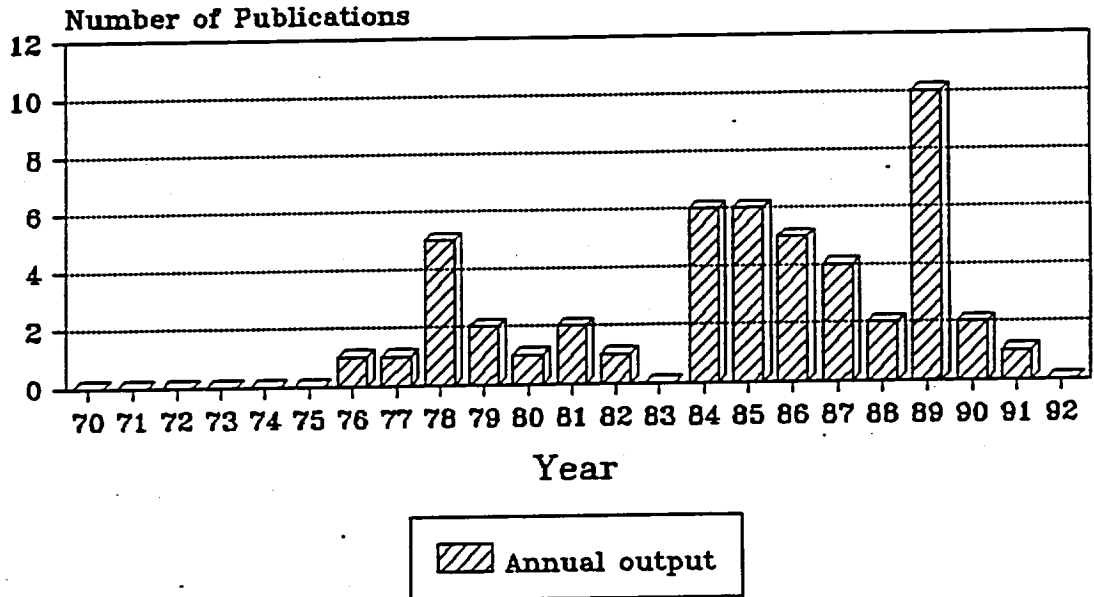
This research centre appears to be one of the main sites in Iran that deals with agricultural problems. As well, it appears to be a well-equipped laboratory that publishes significant research.

Aflatoxins
Fusarium oxysporum
Pyricularia oryzae
Mycotoxins

11. Research Priorities

Iranian Publications

Plant Pest and Disease Research Laboratory, Tehran



source: Publications selected as described in text, n=49.

Figure 6. Plant Pest and Disease Research Laboratory

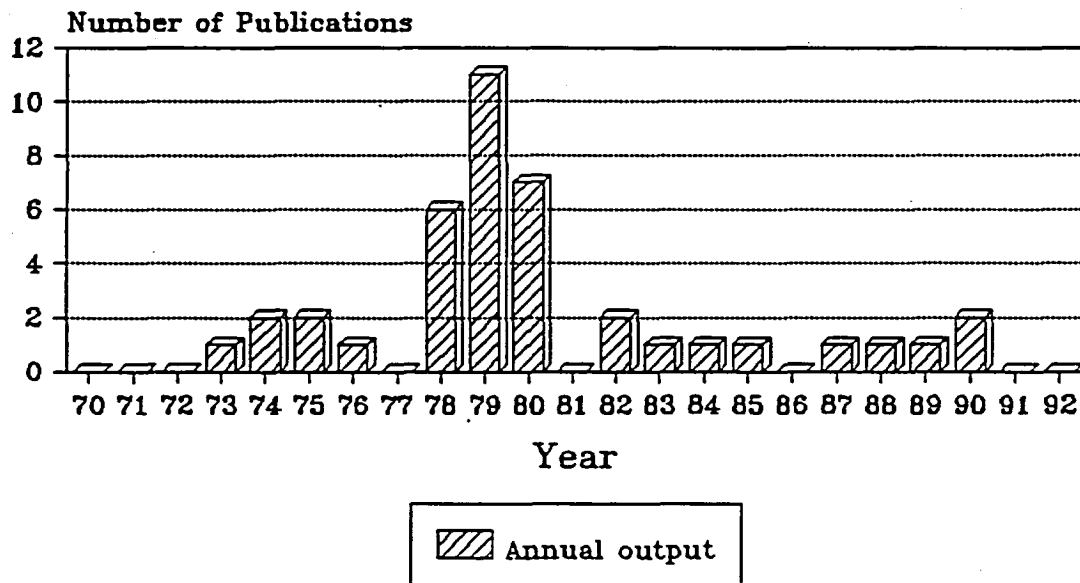
3.7 Department of Medicine, Shiraz University, Shiraz

The Department of Medicine, Shiraz University in Shiraz published 40 papers selected by this study. Annex F contains the bibliographic citations of these publications. It also lists all 75 authors shown on the publications. Box 12 lists the main authors from the Department of Medicine, Shiraz University. Figure 7 shows the

Azadeh, B.
Dar, M.S.
Dutz, W.
Kohout, E.
Zirvi, K.A.

12. Main Authors

Iranian Publications Department of Medicine Shiraz University, Shiraz



source: Publications selected as described in text, n=40.

Figure 7. Department of Medicine, Shiraz University

pattern of publications from the Department of Medicine, Shiraz University. It shows great fluctuations from a peak in 1979 to no publications in 1981.

Box 13 lists the research priorities of publications from the Department of Medicine, Shiraz University. Anthrax and brucellosis are the subjects of research from this laboratory.

-
- Anthrax
 - Brucella melitensis*
 - Curare
 - Scorpion-venoms
 - Thyroliberin
 - Typhoid fever
 - Prolactin
-

13. Research Priorities

3.8 Faculty of Veterinary Medicine, University of Tehran, Tehran .

The Faculty of Veterinary Medicine, University of Tehran, Tehran published 34 papers between 1978 and 1982 dealing with industrial microbiology and food contamination. Annex G contains the bibliographic citations and list of authors. Box 14 lists the main authors from this department. Figure 8 shows the time course of the publications from this research centre.

Gharagozlou, M. J.
Hosseinioun, M.
Keyhani, M.
Nadalian, M.
Samadieh, B.
Shimi, A.
Tabatabayi, A. H.
Tadjebakhche, H.

14. Main Authors

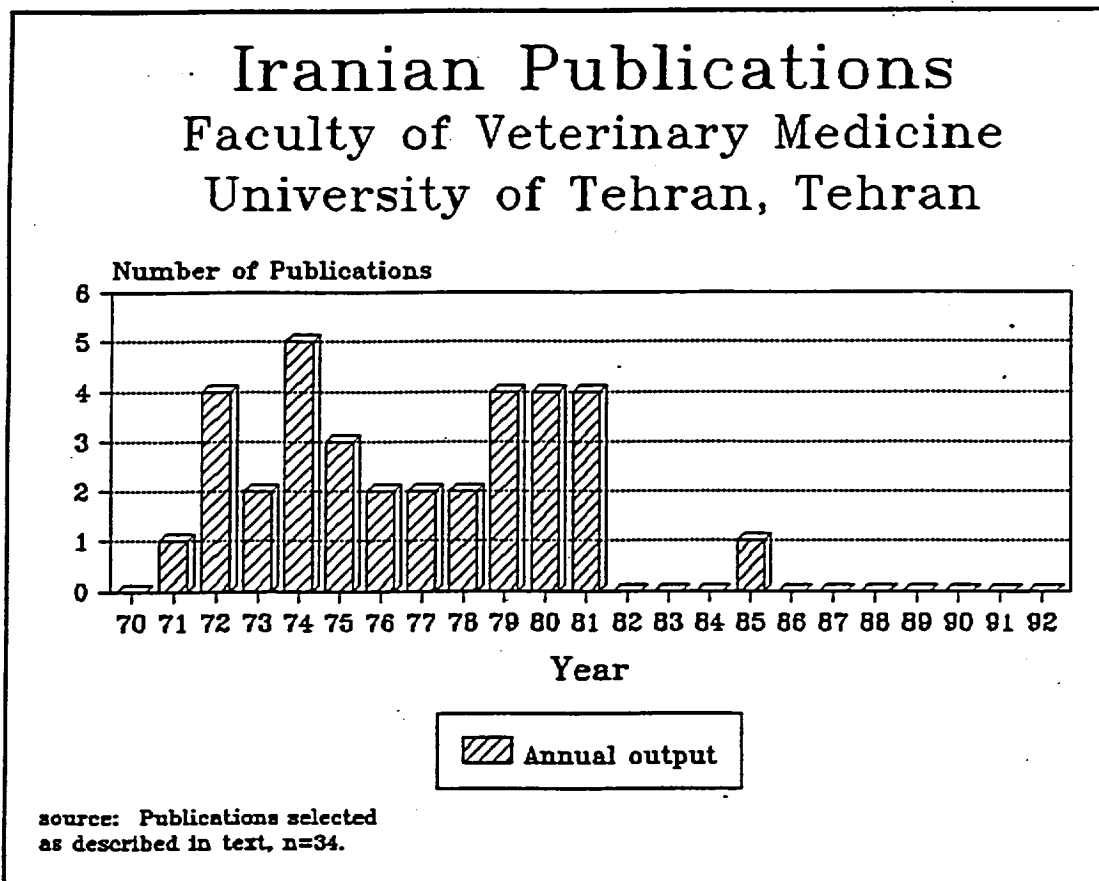


Figure 8. Faculty of Veterinary Medicine, University of Tehran

Box 15 lists the research priorities in the publications.

No publications have been found from this centre since 1985.

Brucella melitensis
Foot-and-Mouth Disease
Influenza virus

15. Research Priorities

3.9 Pasteur Institute, Tehran

The Pasteur Institute, located in Tehran, published 26 papers during the time period of this study. Most of the research was published between 1978 and 1981. Box 16 lists the main authors of this work. Annex H contains the bibliographic information of the publications from the Pasteur Institute. As well, it contains a list of all 43 scientific personnel shown as authors in the publications. Box 17 lists the research priorities which include the pathogenic bacteria and their toxins.

Figure 9 shows the time course of the publications. Most publications are found in the period 1972 to 1981. No publications are found in 1982 to 1984. There is a sharp increase in 1988 to 1990. The Pasteur Institute is superior centre in terms of the types of research and development reported.

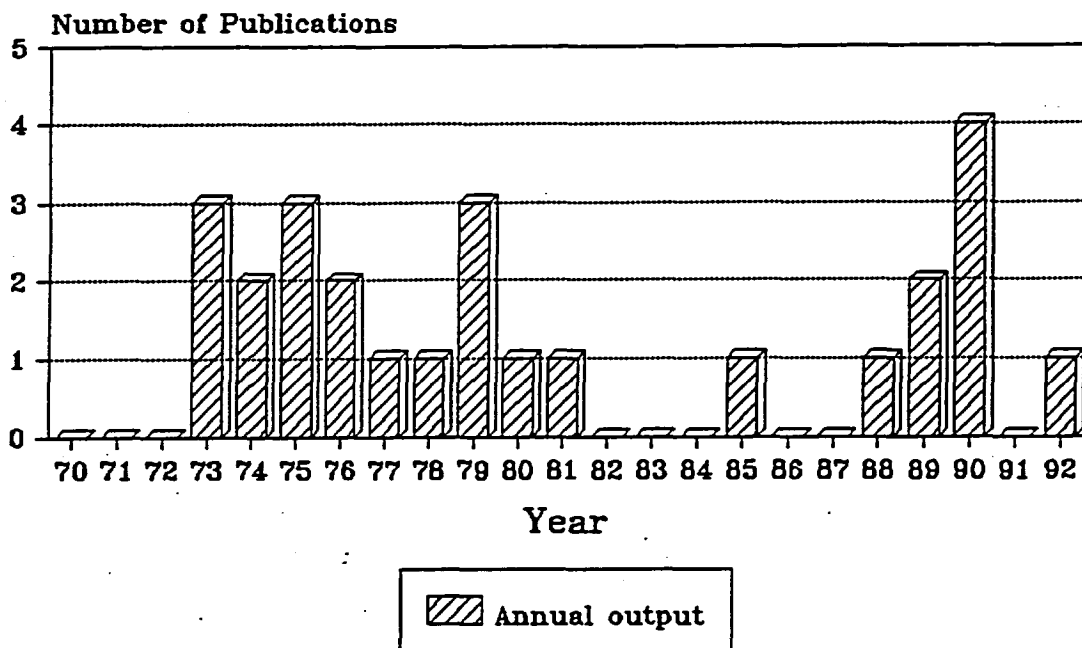
Bahmanyar, M.
De, Almeida, C. R.
Jafari, A.
Karimi, Y.
Katouli, M.

16. Main Authors

Cytotoxins
Yersinia pestis
Enterotoxins
Meliodosis
Plague
Rabies vaccine
Salmonella typhi
Tularaemia

17. Research priorities

Iranian Publications Pasteur Institute, Tehran



source: Publications selected as described in text, n=28.

Figure 9. Pasteur Institute, Tehran

3.10 Institute of Biochemistry and Biophysics, University of Tehran, Tehran

The Institute of Biochemistry and Biophysics, University of Tehran, Tehran published 22 papers. Annex I lists the publications and the 26 authors involved. Box 18 lists the main authors that have published on these topics. Box 19 lists the research priorities

Djavadi, O. L.
Goliaei, B.
Keyhani, E.
Rabbani, A.

18. Main Authors

from this laboratory. A topic of research that stands out is a recent series of papers on the polypeptide Colony Stimulating Factor, which is a hormone bioregulator. Figure 9 shows the time course of

Enzymology
Prostaglandins
Bioregulators

19. Research Priorities

publications from this laboratory. Unlike most other Iranian laboratories, there is a trend of increasing number of publications in 1990 to 1992. This Institute is a leading Iranian laboratory in cell and molecular biology. The published material focuses on basic as opposed to applied research.

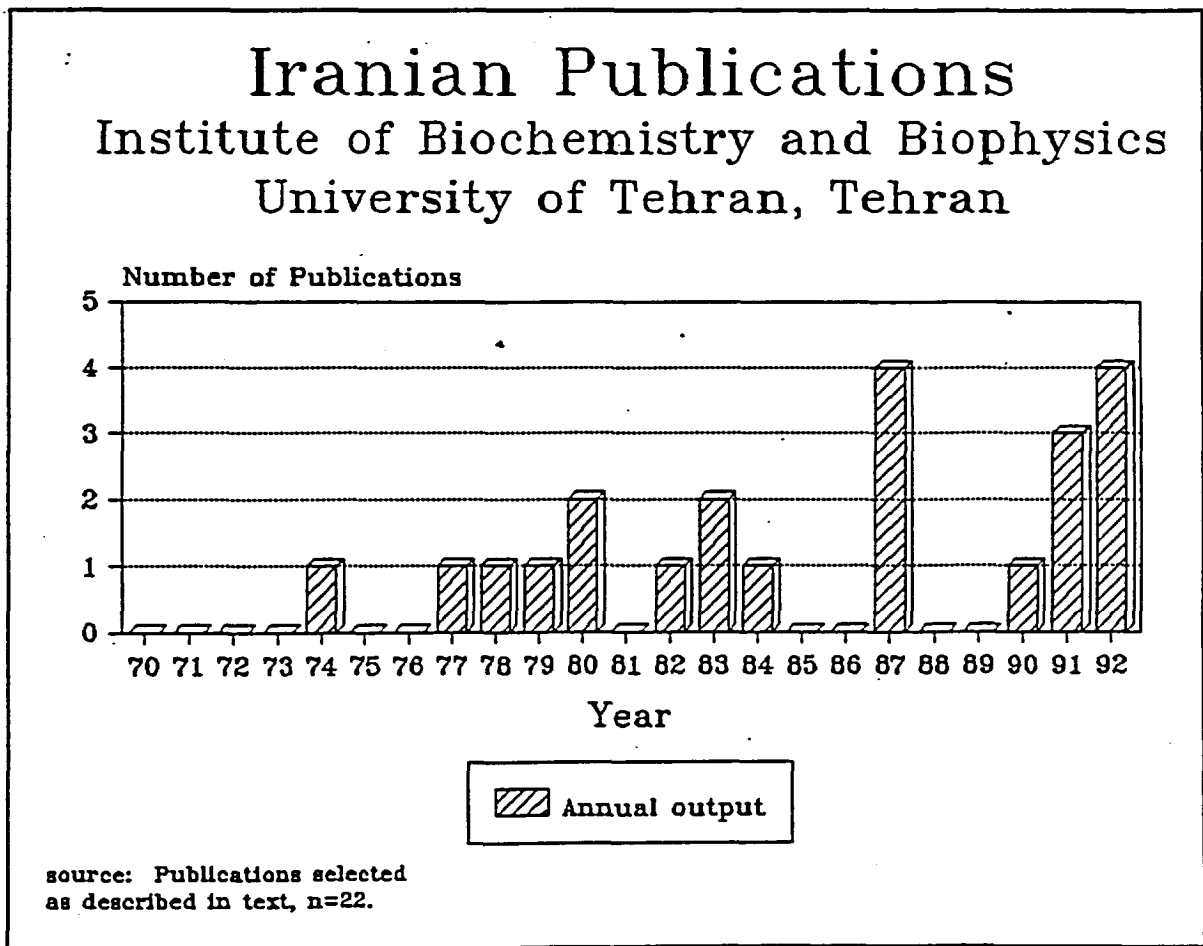


Figure 10. Institute of Biochemistry and Biophysics, Tehran

3.11 School of Medicine, Isfahan University, Isfahan

The School of Medicine, Isfahan University, is located in the city Isfahan (also spelled Esfahan). It published 22 papers between 1970 and 1992. Annex J lists these papers and the 50 authors of these publications. Box 20 gives the main authors of the School of Medicine. Figure 11 gives the time course of the publications from this centre.

Emtiazi, G.
Feiz, J.
Ghafghazi, T.
Miralai, M.
Sabbaghian, H.

20. Main Authors

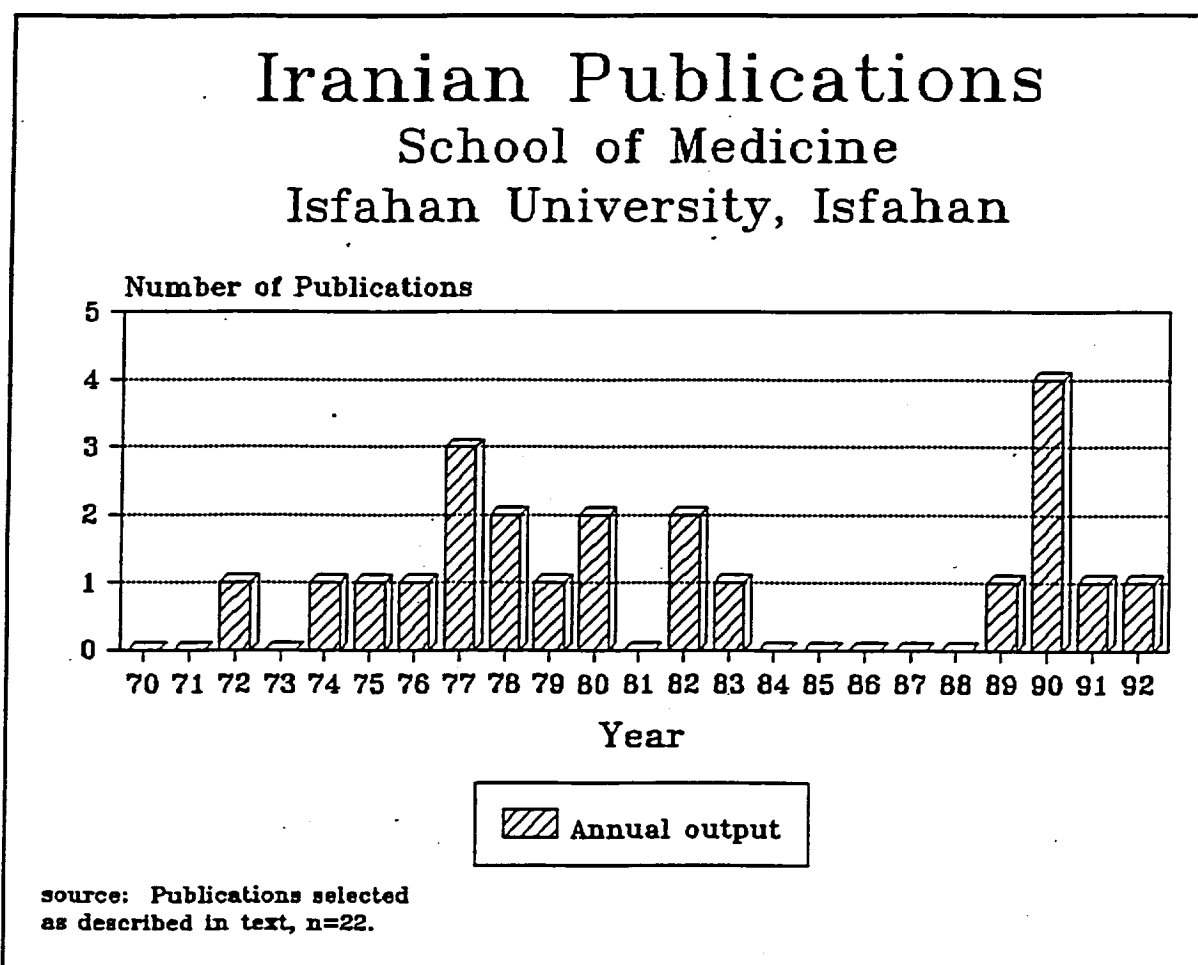


Figure 11. School of Medicine, Isfahan

Box 21 lists the research topics including various pathogenic bacteria such those which cause brucellosis and typhoid fever. As well, clinical and biological effects of mustard gas on victims of chemical warfare attacks were described in publications.

Aflatoxins
Brucellosis
Brucella melitensis
Prolactin
Mustard gas effects
Typhoid fever

21. Research Priorities

3.12 Faculty of Agriculture, University of Tehran, Tehran

The Faculty of Agriculture, University of Tehran, is located in Tehran. It published 21 research papers. Annex K lists the papers and 17 authors from this Centre. Box 22 lists the main authors. Box 23 lists the research topics from the publications of Faculty of Agriculture. Fungi are a main topic of research. This includes fungi pathogenic to animals, such as aflatoxins; and fungi pathogenic to plants, such as *Pyricularia oryzae*. Figure 12 shows the time course of publications from this research centre. There are 5 publications in 1987, which was the peak output. There were no publications reported from this Faculty in 1991 or 1992.

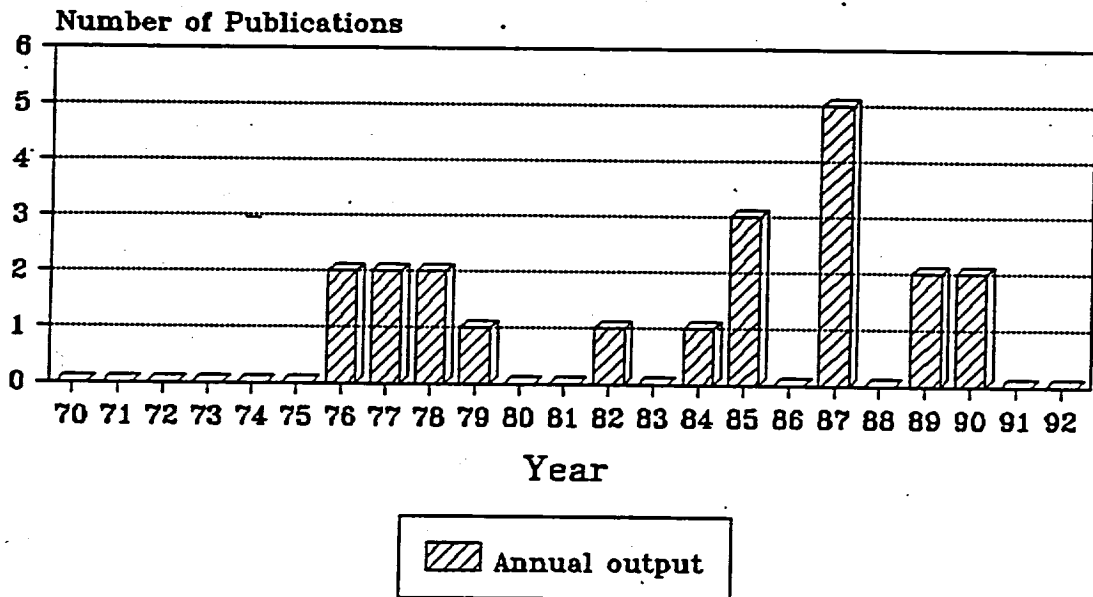
Charifi, Tehrani A.
Hedjaroude, G. A.
Okhovat, M.
Zad, J.

22. Main Authors

Aspergillus flavus
Brucellosis
Pyricularia oryzae

23. Research Priorities

Iranian Publications Faculty of Agriculture University of Tehran, Tehran



source: Publications selected as described in text, n=21.

Figure 12. Faculty of Agriculture, Tehran

3.13 Iranian National Blood Transfusion Service, Tehran

The Iranian National Blood Transfusion Service is located in Tehran. It published 19 papers in the scientific literature between 1970 and 1992. Annex L lists these papers and their 26 authors. Box 24 lists the main authors. Figure 13 shows a time course of the publications. Most of the papers were published between 1976 and 1980.

Ala, F.
Anaraki, F.
Farzadegan, H.
Foroozanfar, N.
Harbour, C.
Shamszad, M.
Sharma, M. K.

24. Main Authors

No publications are found from 1981 to 1985. Some work has been published in 1992. Box 25 lists the main research topics. The research described in these papers concerns hepatitis virus and tetanus toxoid. A recent paper, published in 1990, deals with biochemical effects of sulfur mustard in people attacked with chemical weapons.

Hepatitis b
Tetanus toxoid

25. Research Priorities

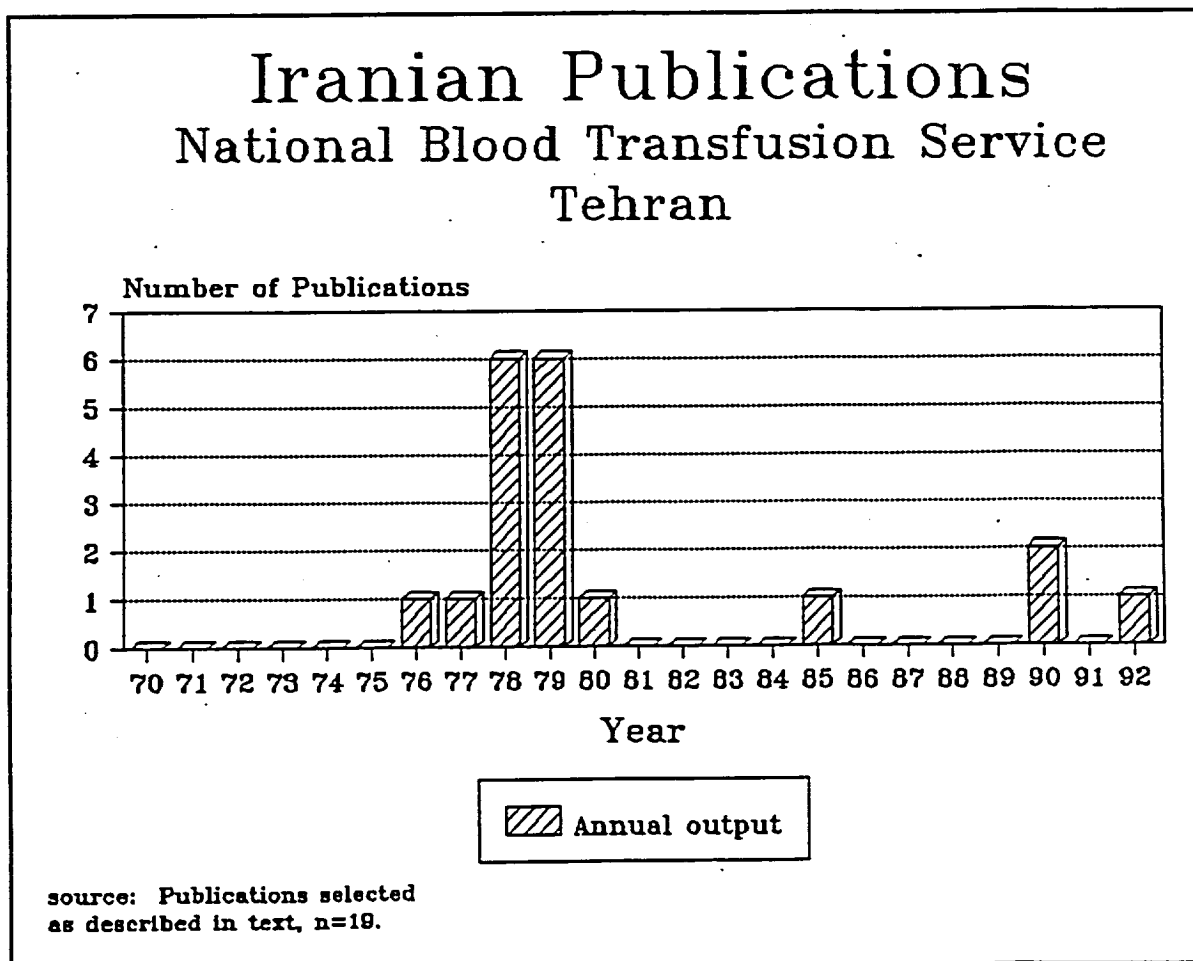


Figure 13. Iranian National Blood Transfusion Service, Tehran

3.14 College of Agriculture, Isfahan University, Isfahan

The College of Agriculture, Isfahan University, is located in Isfahan. It published 17 papers. Annex M contains the bibliographic information of the publications from the College of Agriculture. As well, it contains a list of all 17 scientific personnel listed as authors

Bahar, M.
Danesh, D.
Emami, A.
Mojtahedi, H.
Suzangar, M.

26. Main Authors

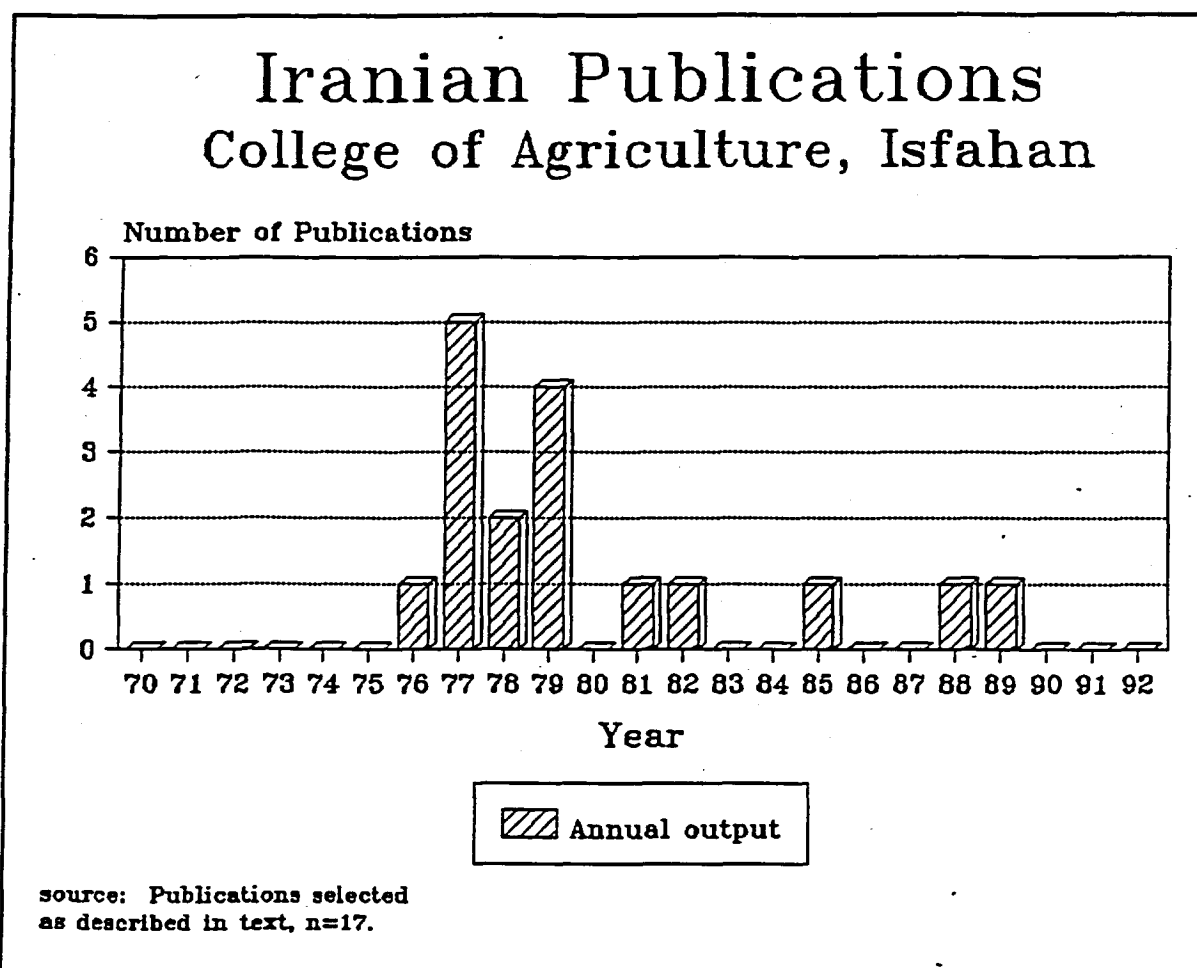


Figure 14. College of Agriculture, Tehran

in the publications. Figure 14 shows the time course of the publications.

The main body of research was published between 1976 and 1979. There have been sporadic publications until 1992. Box 27 shows the main research topics which emphasize fungal toxins such as mycotoxins and aflatoxins.

Aflatoxins
Aspergillus flavus
Mycotoxins

27. Research Priorities

3.15 Department of Plant Protection, College of Agriculture, Shiraz University, Shiraz

The Department of Plant Protection, College of Agriculture, Shiraz University, is located in Shiraz. It published 17 papers. Annex N contains the bibliographic information of the publications from the Department of Plant Protection. As well, it contains a list of all 12 scientific personnel listed as authors in the publications.

Banihashemi, Z.
Fatemi, J.
Izadpanah, K.
Rahimian, M. K.

28. Main Authors

Box 28 lists the main authors. Box 29 lists the main research topics. Figure 15 shows the time course of publications. Many publications are found in the period 1977 to 1982. There are no publications during 1983 to 1986. There is a sharp increase in publications in 1989.

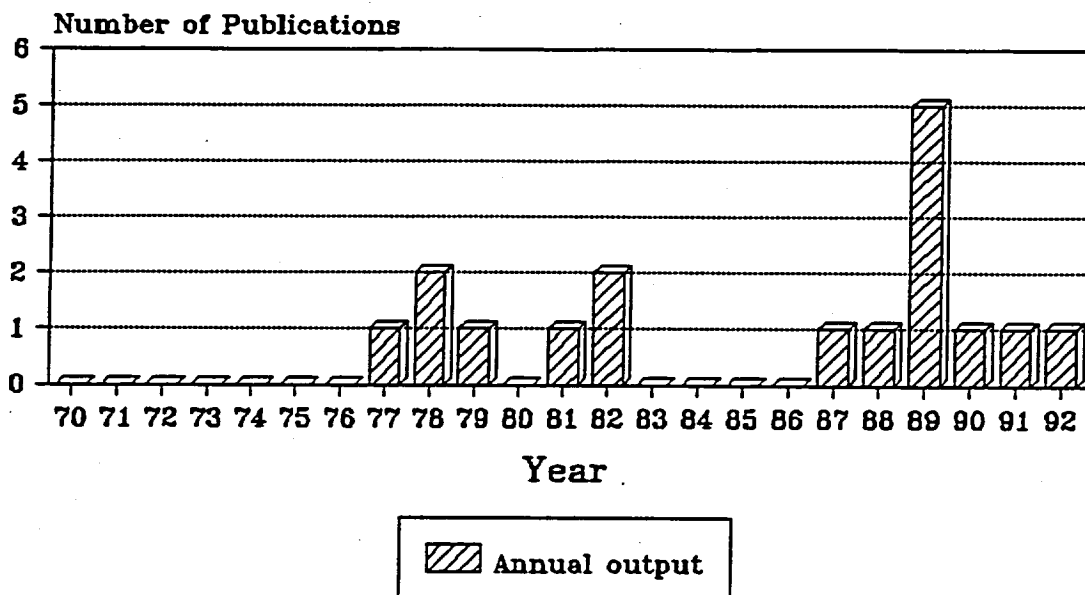
Plant viruses
Rice Blast Pathogen

29. Research Priorities

Iranian Publications

Department of Plant Protection

Shiraz University, Shiraz



source: Publications selected as described in text, n=17.

Figure 15. Department of Plant Protection, Shiraz

3.16 Department of Microbiology, Shiraz University, Shiraz

The Department of Microbiology, Shiraz University, in Shiraz published 16 papers. Annex O contains the bibliographic information of the publications from the Department of Microbiology. As well, it contains a list of all 30 scientific personnel shown as authors in the publications. Box 30 gives the

Ardehali, S.
Behforouz, N. C.
Kabiri, M.
Kohanteb, J.
Rezai, H. R.

30. Main Authors

main authors. Box 31 gives the main research topics. Figure 16 gives the time course of the publications. Most of the papers were published between the years 1977 and 1981, after which time there have been occasional publications. In 1992, there were no publications from this laboratory.

Antibiotics
 Immunization
 Immunology

31. Research Priorities

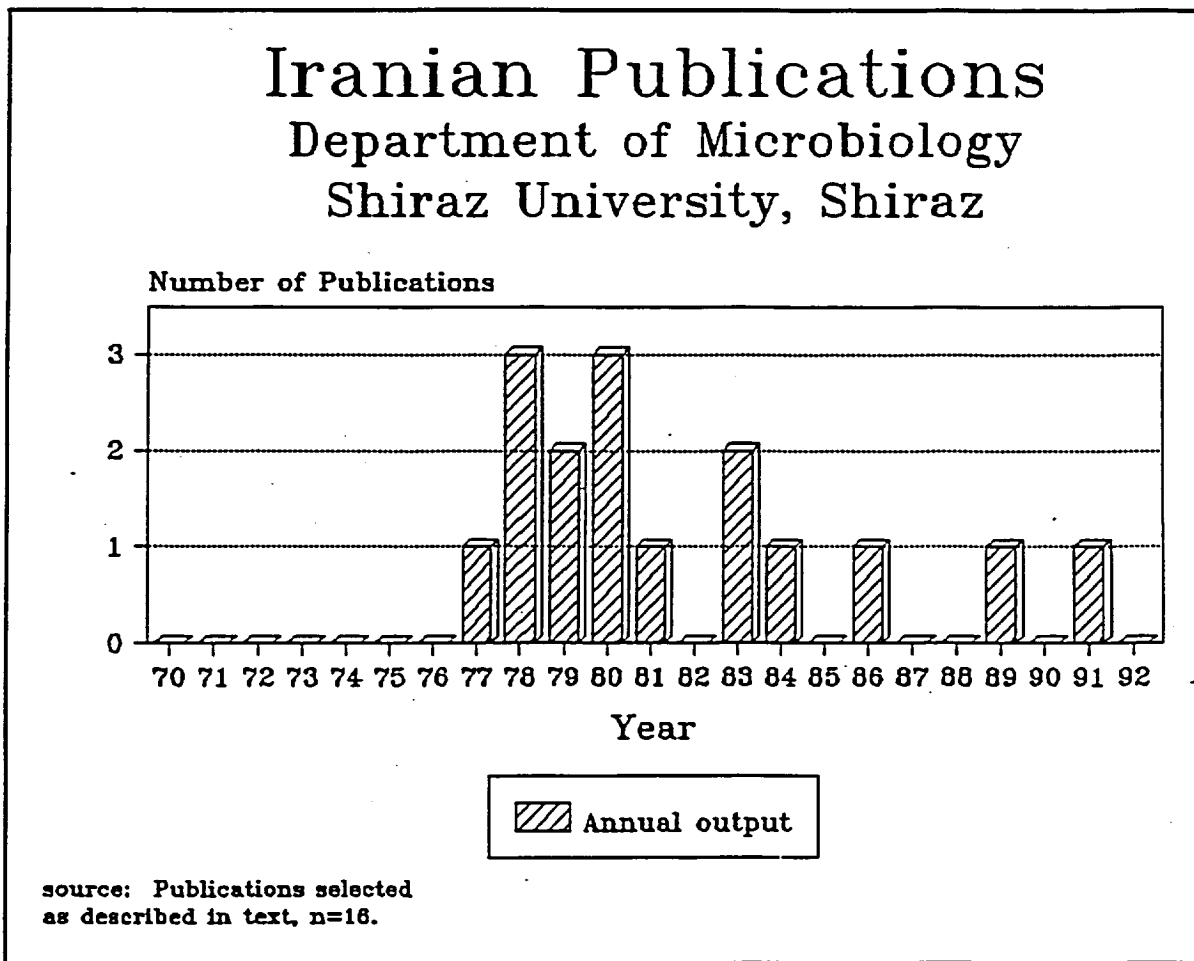


Figure 16. Department of Microbiology, Shiraz

3.17 Department of Biology, Faculty of Science, University of Tehran, Tehran

The Department of Biology, Faculty of Science, University of Tehran, Tehran published 14 papers. Annex P contains the bibliographic information of the publications. As well, it contains a list of all 19 scientific personnel listed as authors in the publications. Box 32 lists the main authors. Box 33 lists the main research topics. Most publications from the Department of Biology were reported between the years 1977 and 1983. There have been no papers published since 1989.

Ala, F.
Malekzadeh, F.
Mortazavi, M. S. M.
Rahbar, S.

32. Main Authors

Bacillus anthracis
Fermentation

33. Research Priorities

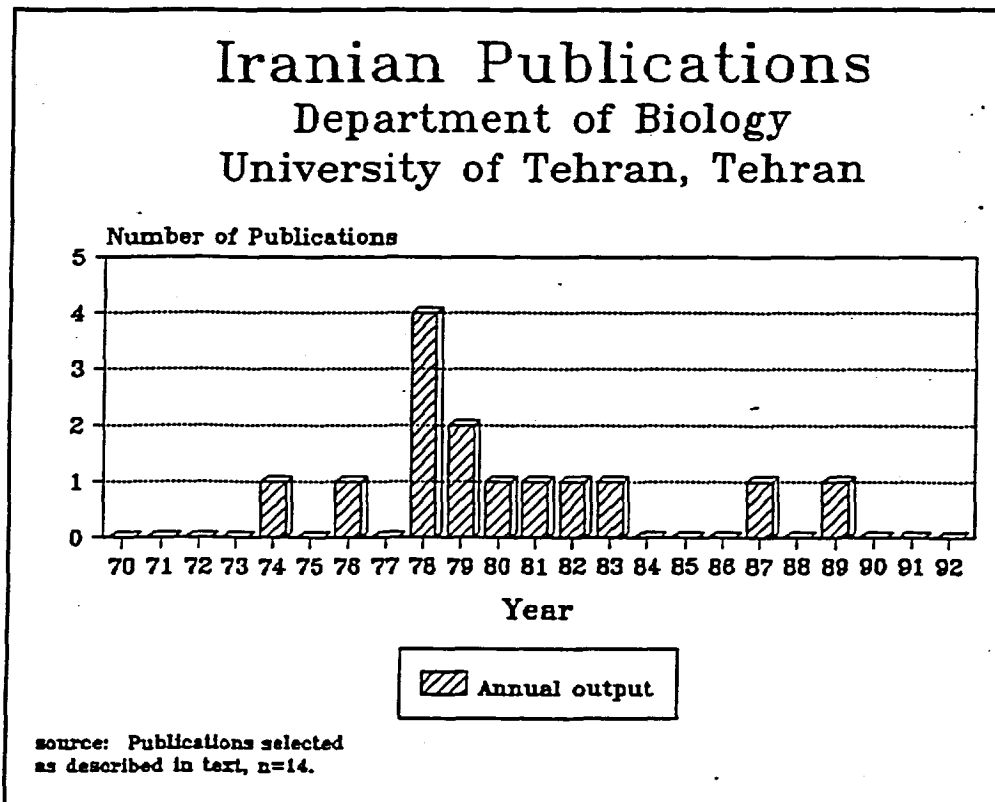


Figure 17. Department of Biology, Tehran

3.18 Mashad Medical Sciences University, Mashad

The Mashad Medical Sciences University, at Mashad published 12 papers. Annex Q contains the bibliographic information of the publications. As well, it contains a list of all 13 scientific personnel listed as authors in the publications. Box 34 lists the main authors. Box 35 lists the main research topics. Figure 18 shows the time course of the publications. There have been several clusters of publications, the last of which occurred between the years 1989 and 1991.

Al-Saadi, D.
Kianmehr, H.

34. Main Authors

Brucellosis
Chemotherapy-antibac
terial

35. Research Priorities

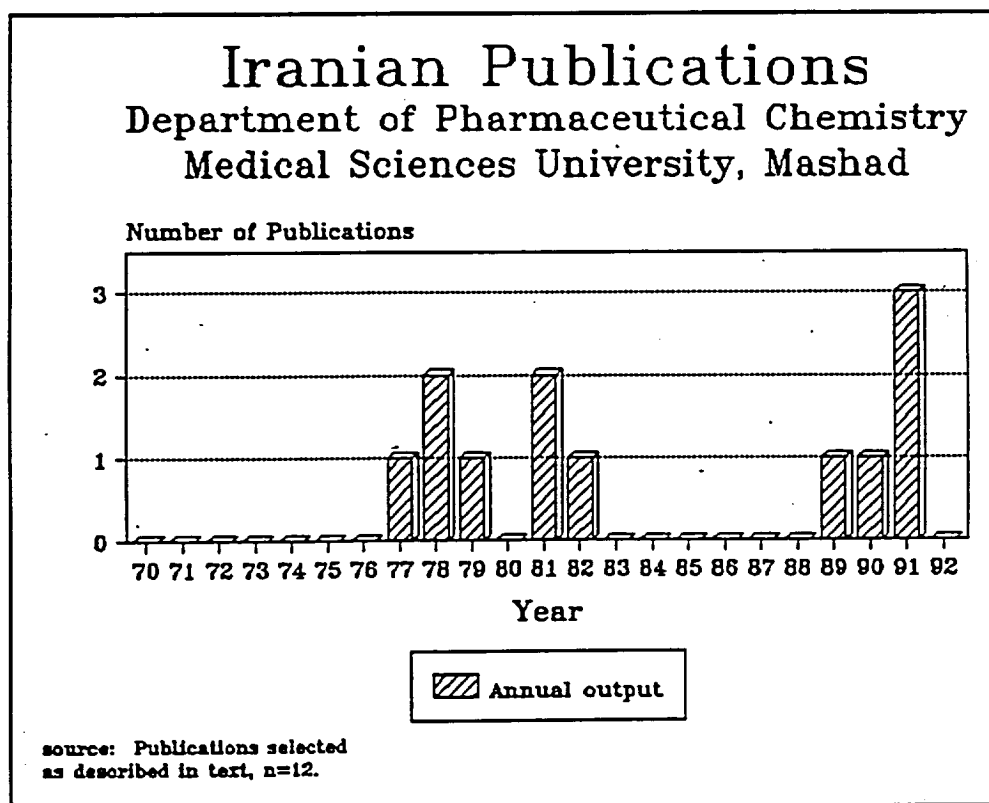


Figure 18. Mashad Medical School, Mashad

3.19 Pharmaceutical Research Centre, Darou-Pakhsh Company, Tehran

The Pharmaceutical Research Centre, Darou-Pakhsh Company, in Tehran published 10 papers. Annex R contains the bibliographic information of the publications from the Pharmaceutical Research Centre. As well, it contains a list of all 14 scientific personnel shown as authors in the publications. Box 36 lists the main authors. Figure 19 shows the time course of the publications.

Akhtar, K. F.
Amini, S.
Eshghi, L.
Khoyi, M. A.
Mahmoudian, M.
Nouhnejade, P.
Rezaei, E.
Salehian, P.

36. Main Authors

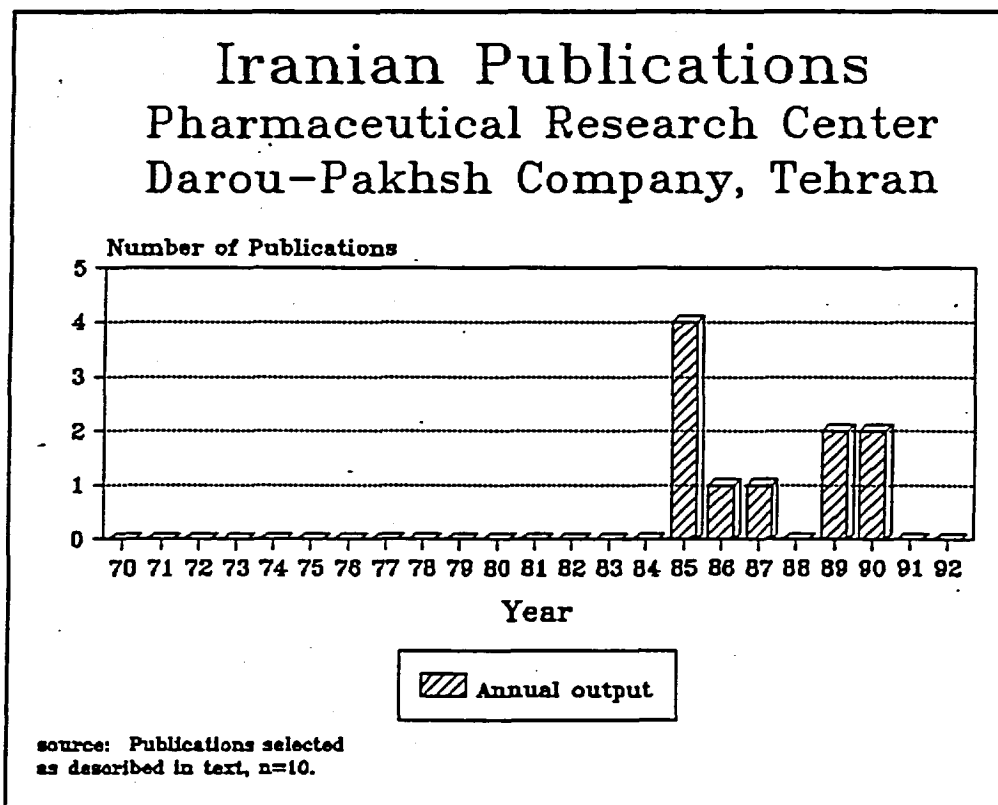


Figure 19. Pharmaceutical Research Center, Tehran

Box 37 lists the main research topics.

There were no publications from this laboratory before 1985. As well, in the last two years there have been no papers published from the Pharmaceutical Research Center.

Bacillus cereus
Insulin
Growth Hormone
Salmonella-typhi
chemotherapy-antibacterial
chemotherapy-antifungal

37. Research Priorities

3.20 School of Veterinary Medicine, Shiraz University, Shiraz

The School of Veterinary Medicine, Shiraz University, in Shiraz published 10 papers. Annex S contains the bibliographic information of the publications from the School of Veterinary Medicine. As well, it contains a list of all 12 scientific personnel listed as authors in the publications. Box 38 lists the main authors. Box 39 lists the main research topics. Figure 20 gives a time course of the publications.

Muhammed, S. I.
Tadayon, R. A.

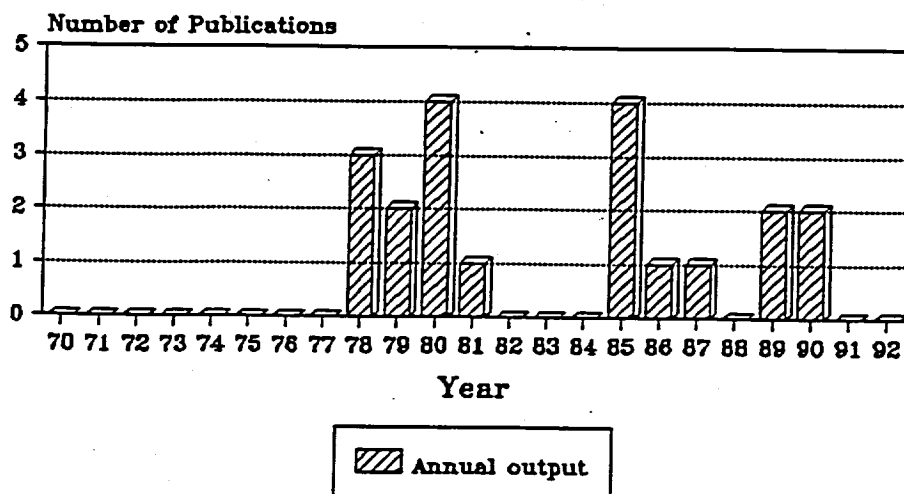
38. Main Authors

Brucellosis
Brucella melitensis
Pesticides

39. Research Priorities

The School of Veterinary Medicine had three clusters of publications. In 1991-1992, there were no publications from this centre. The nature of the work reported dealt with applied veterinary problems such as brucellosis. Other published work was concerned with pesticide applications.

Iranian Publications School of Veterinary Medicine Shiraz University, Shiraz



source: Publications selected as described in text, n=10.

Figure 20. School of Veterinary Medicine, Shiraz

3.21 Other Iranian Publications

This section contains research publications from other Iranian centres. Annex T contains the bibliographic citations of research publications from other institutes and laboratories that published biological and toxin research from Iran. This includes research laboratories with few publications, as well as publications in which no institutional affiliation was given. Box 40 lists authors with multiple publications. Box 41 lists various agents that have been the subject of research at other Iranian centres.

Arshady, Reza
 Aryanpur, I.
 Aynéhchi, Y.
 Babadoost, M.
 Bakhtavar, F.
 Daneshwar, A.
 Etebarian, H. R.
 Hakimelahi, G. H.
 Karim, G.
 Marandian, M. H.
 Parvaneh, V.
 Rahimian, H.
 Sadeghi, E.
 Shafiee, A.
 Shakibi, J.
 Soltanabadi, A.
 Upadhyay, R. R.

Aerosols
 Aflatoxins
Bacillus anthracis
 Antibiotics
 Aspergillus
 Endotoxin
 Fusarium
 Gastrin
 Oxytocin
 Pesticides
 Q fever
 Scorpion Venom
 Snake Venom
 Smallpox vaccine
 Peptide Synthesis
 Tetanus toxin
 Vaccines

40. Main Authors

41. Research Priorities



Figure 21. Other Iranian Publications

3.22 Iranian Fungal Toxin Publications

Figure 22 shows the time course of Iranian publications dealing with fungal toxins from all research centres identified in this study. Fungal toxins include mycotoxins and aflatoxins. Twenty-two publications are found within the period 1975 to 1982. From 1983 to 1992, there are only 3 publications from all Iranian sources.

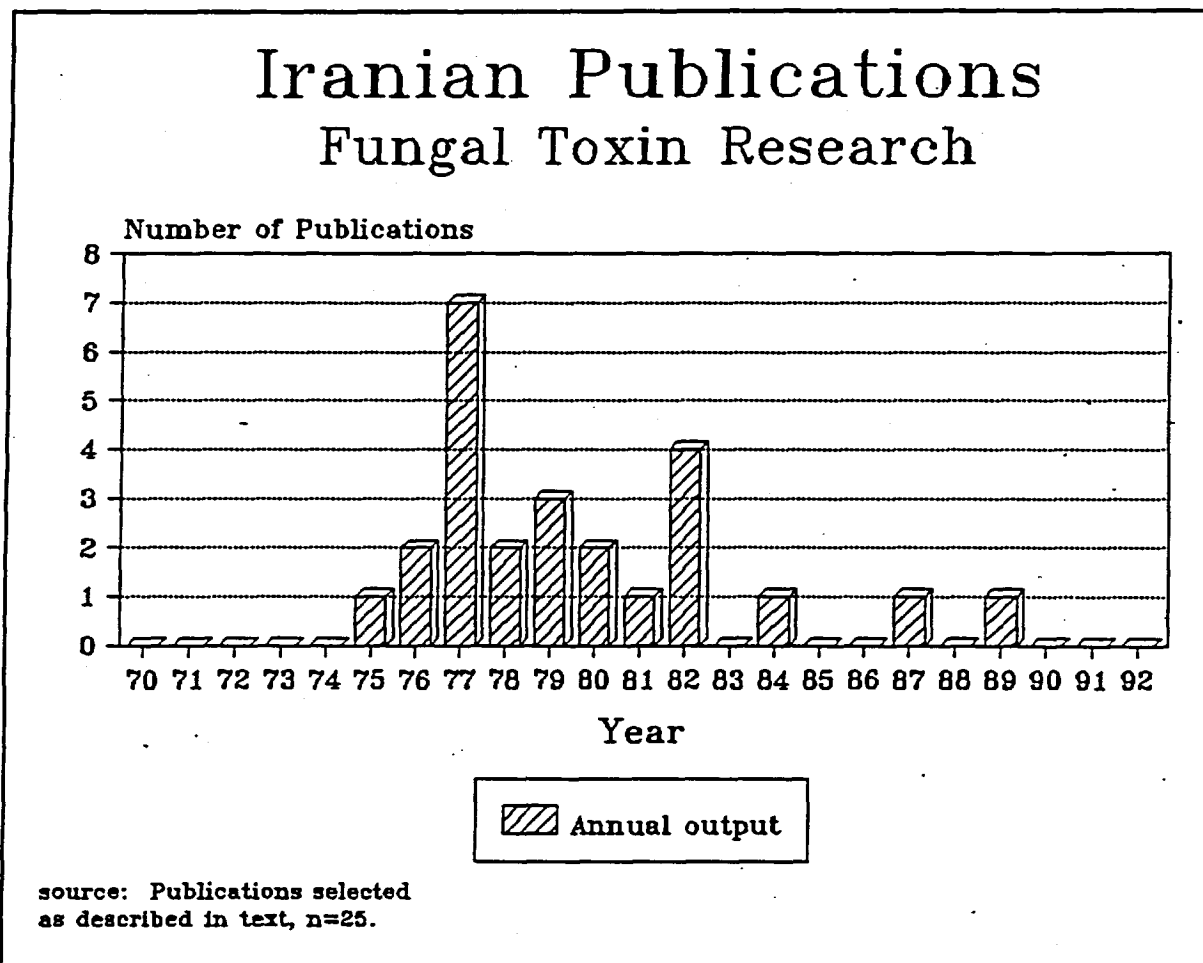


Figure 22. Iranian Fungal Toxin Publications

3.23 Iranian Brucellosis Publications

Figure 23 shows the time course of all Iranian publications dealing with brucellosis published by centres identified by this study. During most of the time period under consideration, research was published on brucellosis. However, in the peak of research activity in other subject areas in 1979, there are no publications on brucellosis. Publications on brucellosis decreased in 1989 to 1992 as well.

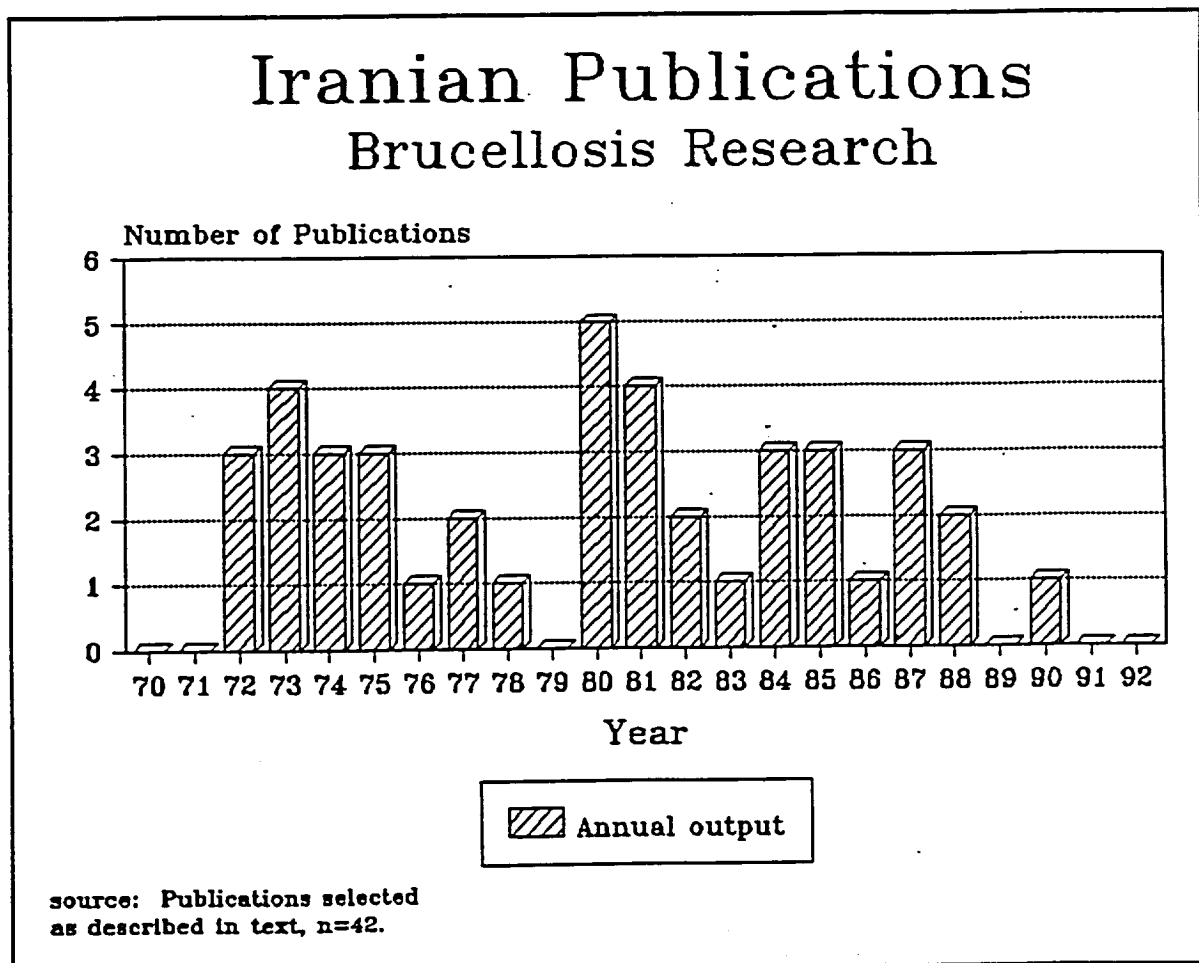


Figure 23. Iranian Brucellosis Publications

3.24 Iranian Anthrax Publications

Figure 24 shows the time course of the ten Iranian publications dealing with anthrax published by centres identified by this study. There are no publications since 1985.

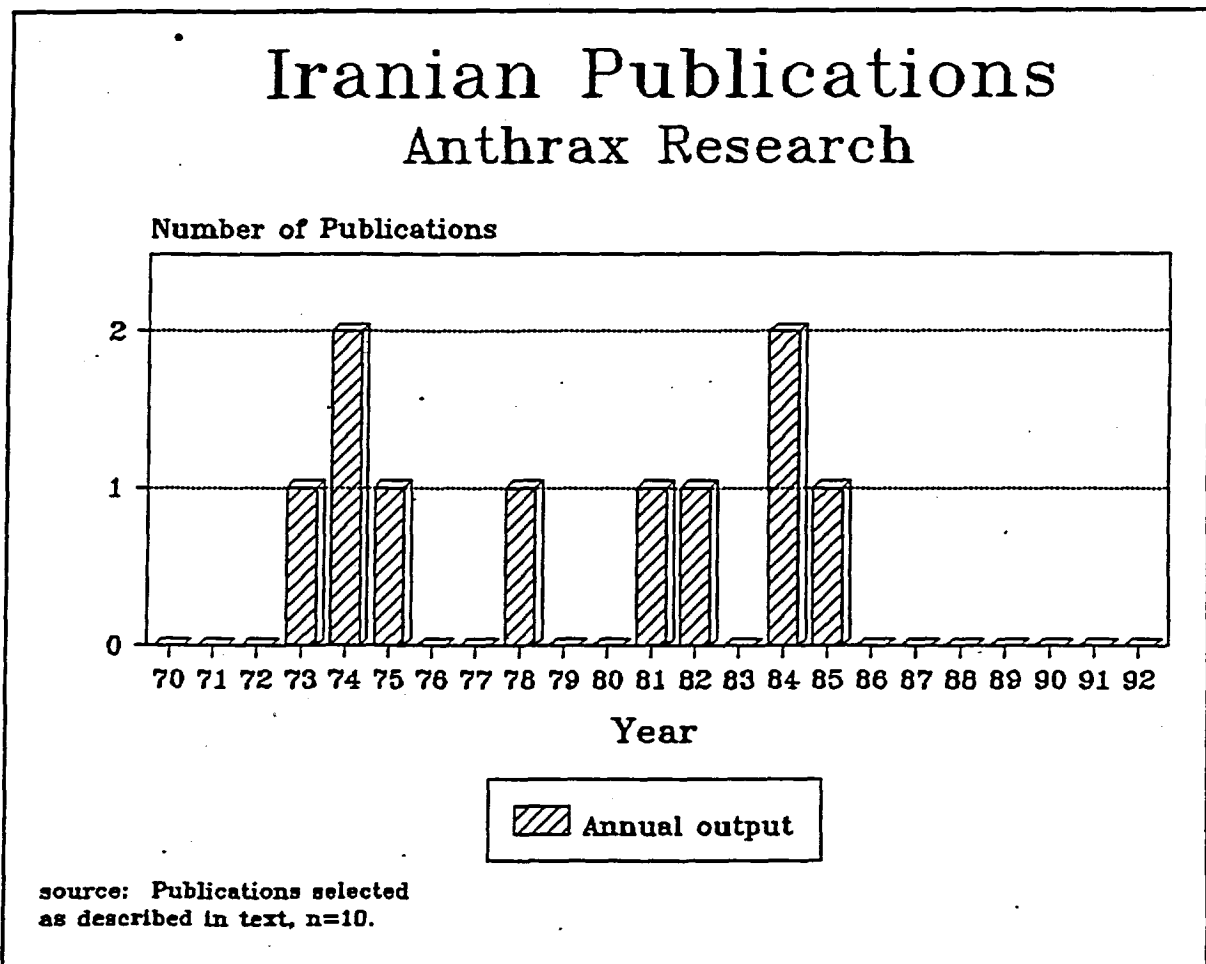


Figure 24. Iranian Anthrax Publications

3.25 Iranian Neurotoxin Publications

With regard to research on neurotoxins, only a single paper on botulism was found from Iran in the research publications from 1970 to 1992. This paper dealt with a large outbreak of botulism type E poisoning. There was none on botulinum toxin itself. During this period, 3 publications dealt with vaccination against tetanus toxin. Two publications dealt with saxitoxin and two dealt with tetrodotoxin. (5 other papers dealt with various venoms from scorpions and snakes.) There is an apparent lack of publications in the area of neurotoxins in general.

4.0. CONCLUDING REMARKS

4.1 Sites of Biological and Toxin Research

This study examined the open scientific literature to determine the patterns, locations and apparent nature of Iranian biological and toxin research. In regard to these objectives, the following observations can be made.

Judging from the published research, there seemed to be some differences between the nature and quality of research at Iranian government laboratories and the laboratories located at universities. When examining the range of experimental procedures, equipment and publication output per institute, the government laboratories appear to have the more sophisticated resources in relation to the types of biological and toxin research that this study focused on.

The main sites of research were: the Faculty of Medicine, University of Tehran; the School of Public Health, Tehran University of Medical Sciences; and the Razi State Vaccine and Serum Institute; all in Tehran. While the first two above-mentioned research centres published the most papers, they were not necessarily involved in the most advanced research. This distinction appears to have belonged to the following three research institutes: the Razi State Vaccine and Serum Institute; the Pasteur Institute; and the Institute of Biochemistry and Biophysics, University of Tehran; all in Tehran. This conclusion is based on the nature of the published research, and on the inference of the types of equipment needed to conduct that research. Also notable for the advanced level of research and development was the

Pharmaceutical Research Centre, Darou-Pakhsh Company, in Tehran. However, this Institute has had a much smaller output of published papers, with only 10 publications published during the years 1985 to 1990.

While there were varying levels of sophistication in the Iranian centres of research, no significant evidence was found of a genetic engineering or recombinant DNA research program.

The Razi Institute reported the capability to make 20 million doses of *Clostridium perfringens* vaccine for veterinary purposes on an annual basis in Iran. This is clearly a very large-scale effort in vaccine production.

4.2 Patterns of Publications

One of the basic findings of this study is that Iranian research publications grew dramatically in the 1970s, peaking in 1978 and then falling to a low output in the early 1980s. While there was a subsequent recovery in 1988 to 1990, the levels of research publications did not return to the level of 1978. The pattern found in this study of Iranian biological and toxin research can be compared to the pattern that other studies have found for Iran's neighbour, Iraq. (The major trend in Iraqi biological research reported in other studies can be described as follows. Initially, there was low number of publications which showed a major increase from 1979 to 1981. After this peak of publications, there was a decrease during 1983 to 1985. Following this, there was another large increase. This is in some contrast to Iran which did not have a subsequent resurgence in research publications

between 1988 and 1990.)

In order to have an increase in research output, significant resources must be committed. Laboratories must be built or equipped, and researchers must be employed or re-assigned. Once new laboratories are set-up, research must be initiated and completed, and then published. This results in a significant lag between a change in research priorities and that change becoming evident in publications in the open literature. Therefore, the increased publications first observed around 1974, may reflect a change in research priorities decided upon around 1970.

The sudden decreases seen in publications may also reflect changes in research priorities, shortages due to the war effort, or other factors.

4.3 Gaps in the Publications

In some cases, when examining the open scientific literature, what is not found may also be of interest. The following section will examine several topics that appeared to be under-represented or totally lacking in the Iranian scientific literature.

Two potential warfare agents that are often mentioned in relation to concerns about biological and toxin warfare are *Bacillus anthracis* and the botulinum neurotoxin A. These two agents, respectively, cause anthrax and botulism. Anthrax causes fever, shock and, if inhaled, has a mortality rate of between 80 to 100 percent. Botulism, often fatal, causes vomiting, convulsions, and paralysis and can be serious problem in developing countries. While anthrax appears to be major health problem, there have been only 10 publications

from Iran between 1973 and 1985. Since 1985 there have been no publications dealing with anthrax from Iran. Another bacterium of interest from the point of view of public health is *Francisella tularensis*, which causes tularemia. It was the subject of 3 publications in the open scientific literature. (In contrast, brucellosis, another health problem in Iran, has been the subject of 42 publications which have been spread out over the period 1972 to 1990.)

It has already been mentioned in this paper that reported work on botulinum toxin and other neurotoxins would suggest an apparent lack of interest. The same might be said about research on fungal toxins, over the past decade, though presumably such toxins remain a health hazard in Iran.

It is noteworthy that there do not appear to be any major government biological facilities that do not publish in the open literature.

ANNEX A

Major Iranian Laboratories Publishing Biological Research

Faculty of Medicine, University of Tehran, Tehran

School of Public Health, Tehran University of Medical Sciences, Tehran

Razi State Vaccine and Serum Institute, Tehran

Plant Pest and Disease Research Laboratory, Tehran

Department of Medicine, Shiraz University, Shiraz

Faculty of Veterinary Medicine, University of Tehran, Tehran

Pasteur Institute, Tehran

Institute of Biochemistry and Biophysics, University of Tehran, Tehran

School of Medicine, Isfahan University, Isfahan

Faculty of Agriculture, University of Tehran, Tehran

Iranian National Blood Transfusion Service, Tehran

College of Agriculture, Isfahan University, Isfahan

Department of Plant Protection, College of Agriculture, Shiraz University, Shiraz

Department of Microbiology, Shiraz University, Shiraz

Department of Biology, Faculty of Science, University of Tehran, Tehran

Mashad Medical Sciences University, Mashad

Pharmaceutical Research Center, Darou-Pakhsh Company, Tehran

School of Veterinary Medicine, Shiraz University, Shiraz

The following Annexes contain an alphabetical bibliography and an author list of the publications of the above-mentioned Iranian research laboratories.

ANNEX B

Faculty of Medicine, University of Tehran, Tehran

Bibliography

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ANNEX C

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ANNEX D

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ANNEX G

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