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DISCOVERY, DUPLICATION, AND DOCUMENTATION A CASE STUDY.

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[Data on the rate of discovery of antibiotics and the frequency of rediscovery of known antibiotics, from different organisms, in different countries, during the period 1907–1967, are presented. The problems in deeming a rediscovery of a known antibiotic as unnecessary wastage of research potential and the role of documentation in this complex situation are mentioned. The duplication of discoveries reported in a country is the highest in the reports published in that country itself (Self-Duplication). It is also found that the number of cases of self-duplication is the highest in the same year as the publication of the original report. The curve for self-duplication has alternate peaks and troughs for the first ten years of the discovery and then falls off. The emergence of the two specialities — Biochemical Engineering and Biochemical Technology — mainly from the work on antibiotics, is pointed out. The structure of these two subjects as represented in the Colon Classification is discussed.]

1 Documentation

11 OBJECTIVE

An essential objective of documentation is to bring into use nascent micro subjects by specialist readers, pinpointed exhaustively, and expeditiously.

12 Kinds of Service

Different kinds of documentation service may be required to meet the different demands of specialist readers. For example it may include

1 Serving with a frequently published advance documentation list for current-awareness;

2 Preparing abstracts on demand or in anticipation;
3 Preparing reports of the state-of-art in a subject;
4 Preparing trend reports;
5 Drawing from available data;
6 *Ad hoc* collection of data; and
7 Preparing digests.

The overall purpose of such services is to reduce to a minimum *unintended* and *unnecessary duplication* of work by specialist readers and thereby helping to conserve intellectual potential.

3 Factors Affecting Efficiency of Documentation

The objective of documentation and the need for the provision of the different kinds of service mentioned in Sec 11 and 12 respectively, are now generally accepted. For the purpose of this paper, in any case, it is assumed that they are accepted. The efficiency of documentation service will be affected by the documentation techniques used. Further, the organisation and development of the services will require information on factors such as the following:

1 The kinds of research — pure, applied, and developmental — dominant at a particular time or in a particular context, in different subjects;
2 The variation in the dominant form of research from time to time;
3 The methodology used in the research in the different subjects;
4 The mode of development of subjects through each kind of research;
5 The role of information retrieved from documents, in each kind of research, at different stages;
6 The pattern of use of documents by different specialist groups;
7 The production and availability of different media of publication of research results;
8 Other modes of communication among specialists; and
9 The impact of various social forces on each of the above factors.

4 Scope of the Paper

In recent years, a number of studies on some of the factors mentioned in Sec 2, have been made. They have been found helpful to the documentalists in developing documentation systems. This paper presents data on the duplication of the discovery of antibiotics. The problems involved in deeming a discovery as an unnecessary and unintended duplication of effort in the research on antibiotics are discussed.

3 Research on Antibiotics

31 Antibiotic: Definition

An Antibiotic is an organic substance produced by livi organisms. In very low concentrations it inhibits the grow or kills microorganisms susceptible to it. In current usage t term is restricted to the substances produced by microorgani and excludes those produced by higher plants and animals. T definition also limits the term to naturally occurring substanc and excludes synthetically prepared correlates.

32 Team-Research

Antibiosis — the situation in which an organism lives i antagonism to the life of another — has been well known fro the days of Louis Pasteur, if not earlier. In the early part of th present century, a crude preparation of an antibiotic call Pyocyanase from *Pseudomonas aeruginosa* was used in the trea ment of diphtheria. Reports on antibiotic activity of bacter and fungi and the isolation from some of them crystalline co pounds having such activity, have appeared in the periodicals i the early years of this century. However, the extensive use o research on, and the large-scale commercial production of an biotics did not take place until after World War II. The iso lation, evaluation, and demonstration of the therapeutic use o an antibiotic requires the cooperative efforts of specialists i different subjects — such as, microbiology, chemistry, pharmac logy, and therapeutics. Therefore, even Alexander Fleming' report on penicillin in the *British journal of experimental pathology* in 1929 and a fairly good abstract of it in the *Biologic abstracts* of that year, did not make any immediate impact o the scientific world. The team work on penicillin could be org nised only about 1938, when Fleming, E B Chain, and Howa Florey joined hands to form the Oxford Group. Even the in the earlier stages the interest in the product, as Chain put i appears to have been largely to study the biochemistry of micr organisms. The important point is that the break-through i antibiotic production might not have occurred at that time b for the team effort. In 1945 Fleming, Florey and Chain receiv the Nobel Prize for the work.

33 Rapid Developments

However, once the therapeutic value of penicillin w established it gave a tremendous impetus to the research on t isolation of antibiotics. A variety of fungi and other organis were experimented upon. The discovery of antibiotics effecti against microorganisms not susceptible to penicillin was of spec interest. The isolation of Streptomycin from the cultures of

pecies of *Streptomyces* in 1943 and the demonstration of its ffectiveness against mycobacteria causing tuberculosis, set the ace for the exploitation of Actinomycetes. The discovery of road-spectrum antibiotics such as the Tetracyclines, and of thers with specific use, such as Chloramphenicol and Nystatin, ere further incentives. Thus, in the last two decades, much of e experiments in the isolation of new antibiotics has been con-rned with the Actinomycetes. By 1960, over 500 named anti-otics had been isolated and a dozen of them had gone on large-ale production.

More Team Work

The large scale industrial production of an antibiotic for ommercial distribution requires the cooperative efforts of other pecialists, such as the fermentation technologist, the chemical ngineer, the pharmaceutist, the quality control expert, and the ckaging specialist. The first large-scale production of peni-llin itself is an example of international cooperation between ecia i t in the United Kingdom and the United States.

Varied Research

The isolation of new antibiotics from different species f microorganisms and from different strains of species already use; the production, by artificial means, of mutants giving gher yields of useful antibiotics; the chemistry and the modifi-tion of the chemical structure of an antibiotic to reduce its xicity or for other therapeutic benefits; the formulation of harmaceutical preparations for protracted action or for particular e such as, for the treatment of infections in children; the genetics d the biochemistry of microorganisms; the process of anti-osis; the mode of development of resistance of microorganism antibiotics, and the mode of action and the pharmacodynamics f antibiotics, are among the many subjects investigated in several ountries in the last two decades. There is continued interest isolate antibiotics with a wider spectrum of activity, lesser xicity and fewer side reactions, antibiotics for the treatment of fections caused by virus, fungi, and protozoa, and those effective ainst malignant tumours.

New Specialities

In the industrial production of antibiotics engineers and emical technologists gained considerable knowledge of the ctors affecting large-scale fermentation. Subjects such as, bio-emical engineering and biochemical technology have become lds of specialisation at an advanced level.

37 SCATTER AND SEEPAGE OF REPORTS

Till after World War II, the number of documents on antibiotics was comparatively few. Several of the earlier papers were published in British periodicals, such as the *British journal of experimental pathology* and the *Biochemical journal*. With the dramatic post-war developments in research, production and use of antibiotics, particularly in the USA and Japan, the time appeared to be ripe to have periodicals in which the research worker could find most of the reports on the subject. To facilitate this, the following periodicals were started:

Japan

Journal of penicillin (1944).
Journal of antibiotics (1948–52), split as
Journal of antibiotics, Series A (1953) ; and
Journal of antibiotics, Series B (1953).

USA

Antibiotics and chemotherapy (1951).
Antibiotic medicine (1955–56), continued as
Antibiotic medicine and clinical therapy (1956).
Antibiotics (Translation of *Antibiotiki* (USSR)) (1959).

USSR

Antibiotiki; *sbornik* etc. (1948).
Antibiotiki (Ministerstvo zdravookhranenia SSSR) (1956).

Serials carrying papers contributed to seminars and conferences on antibiotics, and review of the progress in the field were also started. These include:

Antibiotics annual (New York) (1953–54).
Antibiotica et chemotherapia. Fortschritte (Basel) (1954).
Antibiotics monographs (New York) (1955–59).

Several state-of-art and review articles also appeared. Compilations of data on antibiotics also increased in number.

By the mid-1950's, even these media could not contain all that was being published in the field. Papers on the microbiological aspects of antibiotics were published in periodicals primarily devoted to microbiology; those dealing with the chemistry in periodicals devoted to chemistry; periodicals in biochemistry also had their share; the chemical engineering aspects were reported in periodicals in chemical engineering, and in the newly started periodicals in biochemical engineering and biochemical technology; and the articles on the pharmacological and therapeutic aspects were distributed in a large number of medical periodicals.

4 Duplication of Discovery

41 Contributing Factors

The efforts to cultivate and develop a subject by specialists in different parts of the world can result in the duplication of work. The tremendous burst of activity in the post-war period, in the isolation and production of antibiotics has naturally resulted in some apparent duplication of research in the field, such as the rediscovery of a known antibiotic. Further, as already mentioned in Sec 37, the scatter and seepage of current reports of antibiotics in a large number of periodicals and other kinds of documents in different languages has not been conducive to efficient communication between research workers. This also has added to duplication of effort. However, the rediscovery of an antibiotic cannot always deemed to be a true case of duplication. This is discussed in the succeeding sections.

42 Problems in Anticipating Results

In a research to isolate a new antibiotic, the result is difficult to anticipate. On the one hand, one and the same species of a microorganism may yield more than one antibiotic, depending upon the culture conditions etc.

For example, from cultures of *Streptomyces griseus* the following antibiotics have been isolated:

Actidione	Eurotin	Phagolessin
Antimycin A	Fermizin	Pseudostreptomycin
Actinomycin C	Globismycin	Rhodomycetin
Actinomycin X	Grisein	Streptocin
Antibiotic A-9828	Griseococdin	Streptovitacin
Antibiotic SK-229	Griseoviridin	Viomycin
Candicidin	Grisonomycin	Viractin
Chromomycin	Holomycin	Viridogrisein
Danubomycin	Mannosidostreptomycin	

On the other hand, one and the same antibiotic may be derived from different species of a microorganism. For example, Oxytetracycline has been extracted from the cultures of the following species of *Streptomyces*:

Actinomyces varsoviensis	*S capuensis*	*S rimosus*
Streptomyces sp A-140	*S gilvus*	*S ticinesis*
S albofaciens	*S henetus*	*S utilis*
S armillatus	*S platensis*	*S vendargensis*

There are also cases of an antibiotic being got from the cultures of fungi as well as of actinomycetes. Examples are:

Helvolic acid	Cephalosporin N
Nebularine	Mycelin
Beta-Nitropropionic acid	

Similarly, Prodigiosin has been extracted from the cultures of *Bacillus prodigiosus* (a bacterium) and also of a *Streptomyces* sp.

Thus, one may start with a species of microorganism not already worked upon and yet it may lead to a known antibiotic. On the other hand, one may start with a species already worked upon and yet get a new product.

There is another complication. Until after a product is isolated and its physical, chemical and biological properties compared with those of antibiotics already known, one cannot be sure whether it is something new or a rediscovery.

Again, even if an investigation leads to a known compound, and if the compound has therapeutic use, and the new source for it yields a larger quantity of it at a lesser cost under a given set of conditions, then the research has been worthwhile. In fact, such work may be deliberately taken up.

Further, the isolation of a known compound from a species of microorganism may throw light on the metabolic properties of different species or even other genera of an organism or of even different organisms. Here too, the research effort cannot be said to have been a waste.

Thus, a research effort may be said to have been unfruitful only if the sole objective was to isolate a new antibiotic with certain specific properties and the research did not yield the desired result.

43 Full Extent of Duplication not Known

431 *Discontinuance of Research*

It is not always a simple academic curiosity to study the biochemical mechanism of a microorganism that is involved in its culture for antibiotic production. In many a case, especially in an industry-oriented research, the isolation of therapeutically useful antibiotic and its producibility on a large scale are primary considerations. In such a case, the research on an antibiotic may not be continued till its properties are compared with those of other known antibiotics. The research may be discontinued for several reasons after a compound has been isolated. Such reasons may include the following: the compound

1 Shows no better activity than other therapeutic agents in use; or

2 Is found too toxic even in the preliminary laboratory trials on animals; or

3 Is very difficult to extract; or

4 Involves considerable cost to extract; or

5 Does not have the desirable physical and chemical

properties suitable for its conversion into a useful commercial pharmaceutical; or

6 Has two or more of the above deficiencies.

432 *Priority Claim*

On the other hand, claims for priority of investigations may be a reason for reporting on a compound even before all the investigations on it are completed.

433 *Secrecy*

Compared to what has been said in the preceding sections, the public report on a promising antibiotic, in the usual media, may be delayed for several years after its discovery until the patenting possibilities are thoroughly investigated.

On account of these factors, in actuality, perhaps, there are many more duplicate discoveries than those reported in the usual media of publication.

44 HELP FROM DOCUMENTATION

It is in this complex context that documentation has to be done in antibiotics research and development. The objective of documentation has already been mentioned in Sec 11. Documentation may not be able to prevent the rediscovery of a known antibiotic. It can, however,

1 Help to identify or differentiate a newly isolated compound; and thereby

2 Facilitate decision to continue or discontinue further work on a compound when it is found to have properties similar to a known compound.

These are a few specific roles of documentation in antibiotics research leading to economy therein. They are in addition to the general function of keeping the specialists abreast of the wavefront of thought in the subjects of interest to them.

This paper does not go into the question of deciding whether the research resulting in the isolation of a known antibiotic has some benefit or it. It only gives data on the number of times one and the same compound has been claimed to have been a new discovery but subsequently found not to be so.

5 Procedure

51 SOURCE DOCUMENT

About ten years ago, I was associated with the library of an antibiotics research and a production centre. At that time, data on the physical, chemical and biological properties of antibiotics were collected from various primary and secondary document sources. To facilitate the work on and the identification of compounds isolated in the laboratory, an index to the data

was developed. This work has been continued and recently a fairly comprehensive list of antibiotics has been compiled by that library [Rao (G S), Banmur (B B), and Purandare (G M). Index to antibiotics producing microorganisms. (Hindustan antibiotics bulletin. 10, N 1; 1967 August; 7–122)]. This *Index* has been used in the present studies on the duplication of discovery of antibiotics.

52 TRANSFER OF ENTRIES TO SLIPS

Each of the entries in the *Index* was transferred on to a slip to facilitate their arrangement and rearrangement in the different sequences required for the study.

53 CRITERIA FOR A DUPLICATE

An antibiotic was considered a duplicate discovery if it had been identified with another antibiotic already known and reported so in published documents (as notified in the *Index*) whether the compounds were produced by the same or by different species of microorganisms. In some cases, there are several reports on an antibiotic before it is identified as a known compound. The number of duplications is counted as one only in each such case.

54 COUNTRY OF REPORT

This paper is essentially concerned with the role of documentation in minimising unitended and unnecessary duplication of research work. The periodical and patent are among the most widely used media of communication in the field under consideration. An article in a periodical published in USA is taken as a report in USA even though the work reported might have been done in some other country. Similarly, a patent taken in UK is taken as a report in UK even though the innovation for which the patent is granted might have been done in some other country.

54 PERIOD COVERED

The period covered in this study is 60 years — from the middle of 1907 to about the middle of 1967.

6 Data on the Number of Antibiotics

61 PERIOD-WISE ANALYSIS

Tables 1 and 2 give data on the number of antibiotics reported during the period 1907 to 1967 divided into six 10-year blocks. The data are divided among three broad groups of microorganisms producing the antibiotics. The data are also visualised in the graph in Fig. 1.

TABLE 1. NUMBER OF ANTIBIOTICS (PERIOD-WISE)

Period		Antibiotics from						Total (c+e+g)	Cumul Total
		Bacteria		Algae, Fungi, Lichen		Actino-mycetes			
a	Years b	N c	Cumul Total d	N e	Cumul Total f	N g	Cumul Total h	j	k
1	1907–16	0	0	8	8	1	1	9	9
2	1917–26	1	1	2	10	0	1	3	12
3	1927–36	4	5	28	38	0	1	32	44
4	1937–46	22	27	79	117	15	16	116	160
5	1947–56	57	84	175	292	375	391	606	766
6	1957–67	33	117	148	440	767	1157	948	1714

TABLE 2. PERCENTAGE

Period	Percentage of Antibiotics from							
	Bacteria		Algae, Fungi, Lichen		Actinomycetes		All organisms	
Years b	% c	Cumul% d	% e	Cumul% f	% g	Cumul% h	% j	Cumul% k
1907–16	—	—	1·8	1·8	—	—	0·5	0·5
1917–26	0·9	0·9	0·5	2·3	—	—	0·2	0·7
1927–36	3·4	4·3	6·4	8·7	—	—	1·9	2·6
1937–46	18·8	23·1	17·8	26·5	—	—	6·8	9·4
1947–56	48·7	71·8	39·9	66·4	32·5	32·5	35·4	44·8
1957–67	28·2	100·0	33·6	100·0	66·3	98·8	55·3	100·1

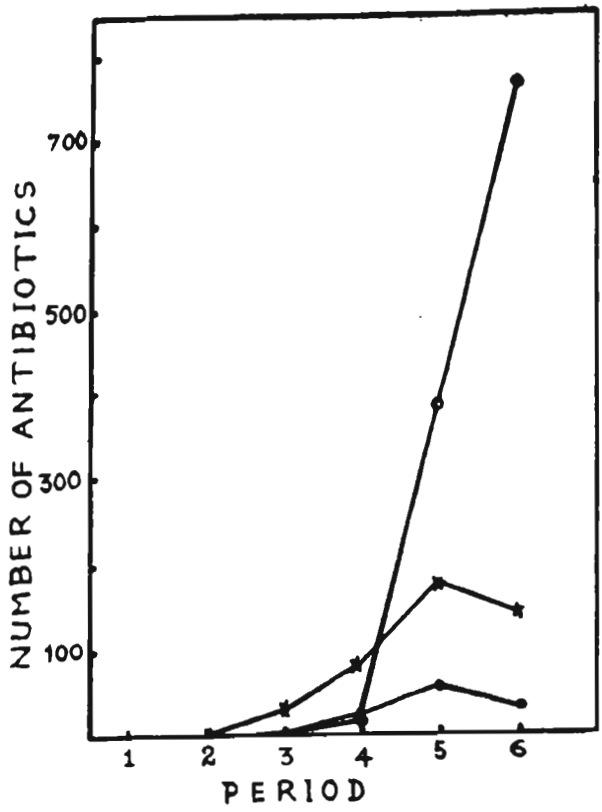

FIG 1. Number of Antibiotics (Period-wise).

•—•—• Antibiotics from Bacteria
x—x—x Antibiotics from Algae, Fungi, Lichen.
o—o—o Antibiotics from Actinomycetes.

611 *Annotation*

1 The first report of an antibiotic from bacteria appeared in Germany in 1924; the first report of an antibiotic from fungi appeared in Japan in 1907; and the first report of an antibiotic from Actinomycetes appeared in Germany in 1908.

2 Over 96 per cent of the reports were published during the latter half of the 60-year period — that is, 1937–67.

3 Out of the total of 1714 antibiotics, 67·5 per cent were those isolated from Actinomycetes, 25·7 per cent those from algae, fungi and lichen, and 6·8 per cent from bacteria.

62 RATE OF DISCOVERY

Table 3 gives data on the rate of discovery of antibiotics from each of the three groups of microorganisms. The rate

ven as the ratio of the number of antibiotics reported during wo consecutive 10-year periods. Since, during the war period, 914–19, little work was reported, the entire two ten-year periods, 907–26, is taken as a single period for the purpose of calculation f the rate. The data are also visualised in the form of a graph n Fig. 2.

ABLE 3. RATE OF DISCOVERY

SN	Antibiotics from	Ratio of the N of Antibiotics reported during the periods			
		1907–26 and 1927–36 (Period 1)	1927–36 and 1937–46 (Period 2)	1937–46 and 1947–56 (Period 3)	1947–56 and 1957–67 (Period 4)
a	b	c	d	e	f
1	Bacteria	4	5·5	2·6	0·6
2	Algae, Fungi, Lichen	2·8	2·8	2·2	0·8
3	Actinomycetes	—	—	25·0	2·5
4	All organisms	2·7	3·6	5·2	1·6

21 *Annotation*

1 In the case of antibiotics from bacteria, and algae, ngi and lichen, the rate of discovery has generally increased aching a maximum during 1937–46, and then declined.

2 The work on antibiotics from Actinomycetes may be id to have accelerated about 1943 when Streptomycin was ported from a *Streptomyces* sp. Therefore, the data on dis- very for the periods earlier to 1937–46 is negligible. Though e peak-rate value is comparatively much higher for Actino- ycetes antibiotics, the pattern of the rate-curve is similar to that r the rate-curves for antibiotics from bacteria, and from algae, ngi and lichen.

3 The pattern of the curves depicts a phenomenon familiar many fields of research. A piece of seminal research or a eak-through stimulates a considerable amount of pure, applied, d developmental research in the field. After a time, the field ts sort of saturated and research may be directed towards greener stures as it were. A few persons may persevere in the old area d some fundamental research may lead to another break-through.

That would again provide for productive pure, applied, and developmental research for a time. And so on the pattern may be repeated.

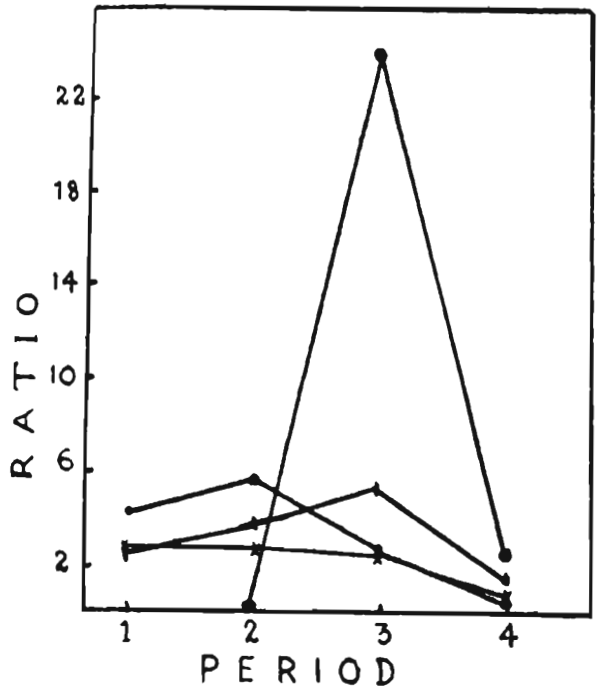

FIG 2. Rate of Discovery.

•—•—• Antibiotics from Bacteria.
x—x—x Antibiotics from Algae, Fungi, Lichens
o—o—o Antibiotics from Actinomycetes.
I—I—I Antibiotics from all organisms.

63 COUNTRY-WISE ANALYSIS

Table 4 gives data on the number of antibiotics produced by each of the three groups of organisms as reported in different countries during the period 1907–67.

631 *Annotation*

1 Out of the total of 1714 antibiotics, over 70 per cent have been reported in the three countries Japan, UK and USA taken together. The category 'Other countries' includes twenty countries with an average of about 1·5 reports per country.

2 Japan has reported the highest percentage (28·5) of antibiotics. It is closely followed by USA with 27·6 per cent.

TABLE 4. NUMBER OF ANTIBIOTICS (COUNTRY-WISE)

SN	Country	Antibiotics from						Total c+e+g	h × 100 / 1714
		Bacteria		Algae, Fungi, Lichen		Actino-mycetes			
		N	c×100 / 117	N	e×100 / 440	N	g×100 / 1157		
a	b	c	d	e	f	g	h	j	k
1	Germany	3	2·6	15	3·4	84	7·3	102	6·0
2	Japan	18	15·7	70	18·1	400	34·6	488	28·5
3	UK	31	26·6	147	33·4	68	5·9	246	14·3
4	USA	41	35·0	96	21·9	336	29·9	473	27·6
5	USSR	1	—	10	—	86	7·4	97	5·7
6	Other countries	23	20·0	102	23·2	183	15·8	308·	17·9
		117	99·9	440	100·0	1157	99·9	1714	100·0

ranks third with about half as many reports as Japan. Germany and USSR each with about 6 per cent rank immediately after UK.

3 Nearly 82 per cent of the antibiotics reported in Japan are those produced by Actinomycetes. In the reports in USA also the number of antibiotics from Actinomycetes is high, though the percentage (71) is less compared with that of Japan. Among all the countries, excluding each of the countries in the "Other countries" group, UK has reported the fewest number of antibiotics from the Actinomycetes.

4 Over 73 per cent of all antibiotics from algae, fungi, and lichen have been reported in Japan, UK and USA taken together. UK has reported the highest percentage (33·4) of antibiotics from these microorganisms; and out of all the antibiotics reported in UK, 60 per cent have come from them. The number of antibiotics from this group of microorganisms reported in Japan and USA taken together is only about 6 per cent more than that for UK.

5 Over 77 per cent of all antibiotics from bacteria have been reported in Japan, UK and USA taken together. USA

has reported the highest percentage (35) of antibiotics from bacteria; then rank UK and Japan in that sequence.

7 Data on Duplication

71 Period-wise Analysis

Tables 4 and 5 give data on the number of antibiotics reported and the number identified as duplicate discoveries, during each of the ten-year periods from 1907 to 1967. The data from the Tables are also visualised in Figs 3 and 4.

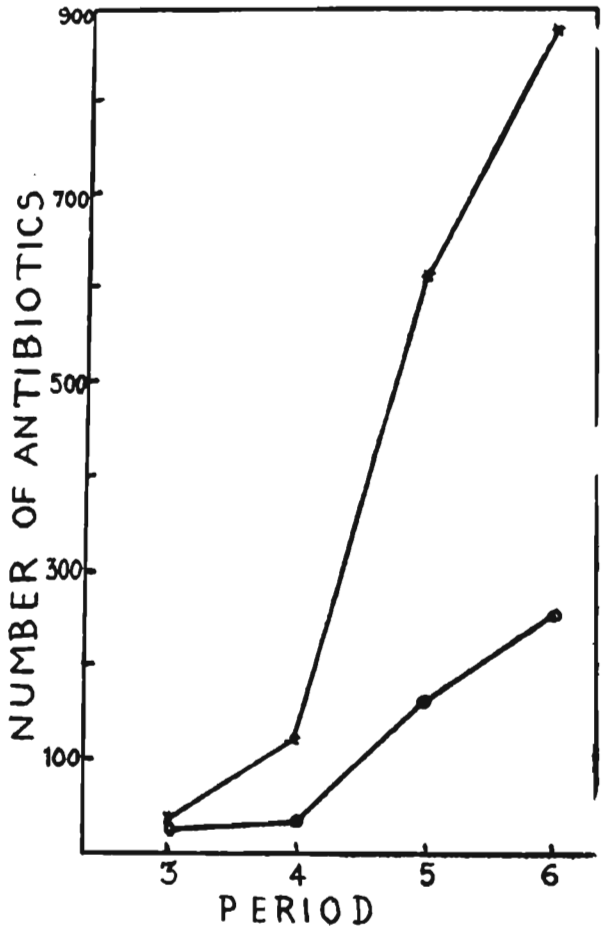

Fig 3. Duplicate Discoveries (Period-wise).

x—x—x Number of Antibiotics reported.

o—o—o Number of Duplication reports.

TABLE 5. DUPLICATE DISCOVERIES (PERIOD-WISE)

Period		N reported	Cumul total	N of duplicate reports	Cumul Total	c — e	Cumul Total
N	Years						
a	b	c	d	e	f		h
1	1907–16	9	9	4	4	5	5
2	1917–26	3	12	1	5	2	7
3	1927–36	32	44	16	21	16	23
4	1937–46	116	160	34	55	82	105
5	1947–56	606	766	163	218	443	548
6	1957–67	948	1714	252	470	696	1244

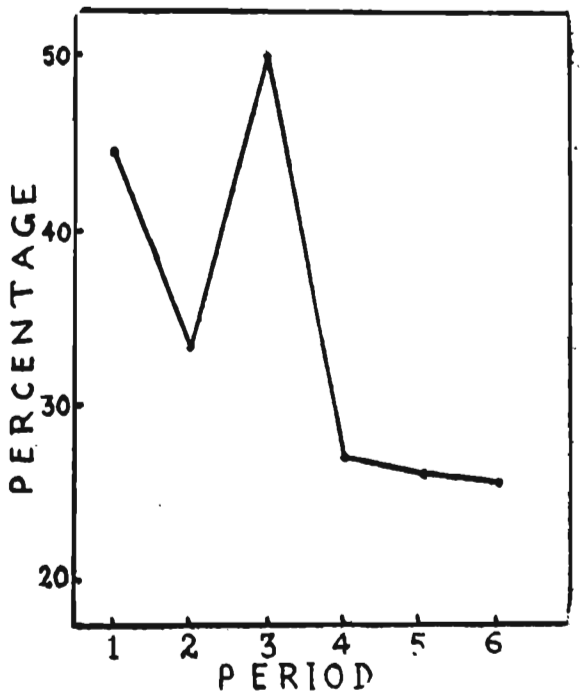

FIG 4. Percentage of Duplicate Discoveries.

TABLE 6. PERCENTAGE OF DUPLICATE DISCOVERIES

Period		N reported	N of duplicates	d×100 / c	c×100 / 470
N	Years				
a	b	c	d	e	f
1	1907–16	9	4	44·4	0·9
2	1917–26	3	1	33·3	0·2
3	1927–36	32	16	50·0	3·4
4	1937–46	116	34	28·3	7·2
5	1947–56	606	163	26·9	34·7
6	1957–67	948	252	26·6	53·6
		1714	470	27·4	100·0

711 *Annotation*

1 About 27 per cent, out of the total of 1714 antibiotics reported during the 60-year period 1907–67, were on antibiotics known earlier to the date of report (*See also* Sec 73).

2 The highest percentage (50) of duplication was during 1927–36. There was a steep drop to 28 per cent in the next period 1937–46, and almost a levelling off at about 26 per cent in the subsequent two periods.

3 Out of a total of 470 duplicate reports, over 83 per cent have been published during the 20-year period 1947–67 and about 54 per cent during the 10-year period 1957–67.

72 RATE OF DUPLICATION

Table 7 gives data on the rate of duplication, from period to period. The rate is given as the ratio of the number of duplicate reports during two consecutive 10-year periods. The entire 20-year period 1907–26 is, however, taken as a single period for the purpose of this calculation as the number of reports was comparatively small. The data are also visualised in the form of a graph in Fig. 5.

721 *Annotation*

1 Starting from a higher value in period 1, the rate of duplication declined in period 2, again rose to reach a peak value in period 3, and then declined to the lowest value in period 4.

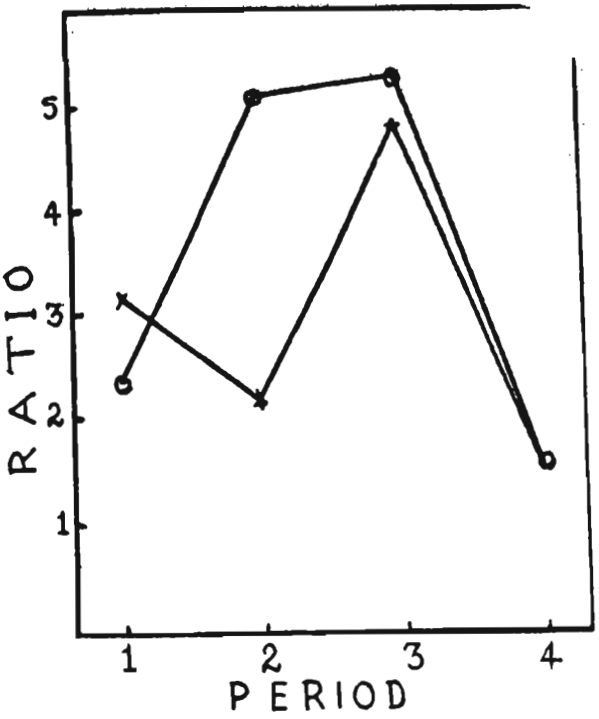

FIG 5. Rate of Duplication.

x—x—x Ratio of Duplication.
o—o—o Ratio of non-duplicates.

TABLE 7. RATE OF DUPLICATION

	Period	Ratio of the N of reports		c/d
N	Years	Non-duplicates	Duplicates	
a	b	c	d	e
1	1907–26 and 1927–36	2·3	3·2	0·7
2	1927–36 and 1937–46	5·1	2·1	2·4
3	1937–46 and 1947–56	5·3	4·8	1·1
4	1947–56 and 1957–67	1·6	1·6	1·0

2 The rate of non-duplication, on the other hand, has steadily increased from period 1 reaching a peak value in period 3, and then declined steeply.

3 The ratio of the rate of non-duplication to duplication (*See* col d of Table 6), started at a minimum in period 1, reached a peak value in period 2 and has levelled off at a lower value in periods 3 and 4.

73 FREQUENCY OF DUPLICATION

Table 8 gives data on the cases of single and multiple duplications. The data in col d are visualised in Fig 6.

TABLE 8. NUMBER AND PERCENTAGE OF DUPLICATIONS

N of Times Reported	N of Anti-biotics	Cumul Total	N of Times Duplicated	b×d	Cumul Total	% of Dupli-cation
a	b	c	d	e	f	g
1	1244	1244	—	—	—	—
2	115	1359	1	115	115	24·5
3	34	1393	2	68	183	7·1
4	22	1415	3	66	249	4·7
5	9	1424	4	36	285	2·0
6	7	1431	5	35	320	1·5
7	5	1436	6	30	350	1·1
8	2	1438	7	14	364	0·4
9	2	1440	8	16	380	0·4
10	2	1442	9	18	398	0·4
11	2	1444	10	20	418	0·4
12	2	1446	11	22	440	0·4
13	1	1447	12	12	452	0·2
14	—	1447	13	—	452	—
15	—	1447	14	—	452	—
16	—	1447	15	—	452	—
17	—	1447	16	—	452	—
18	—	1447	17	—	452	—
19	1	1448	18	18	470	0·2

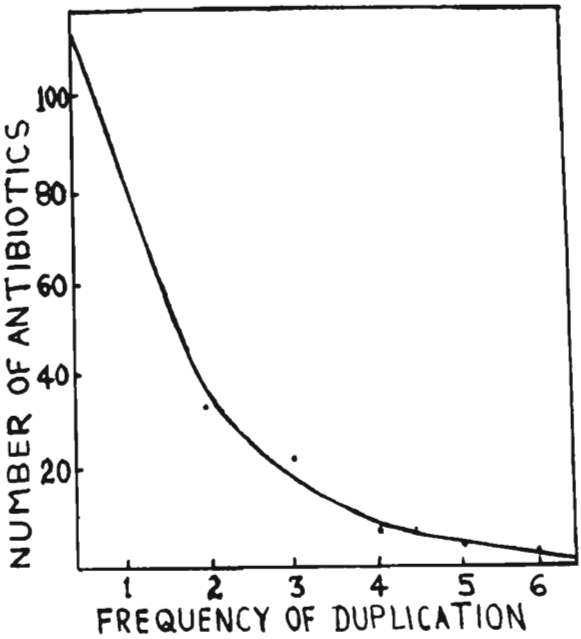

FIG 6. Frequency of Duplication (*See* Table 8, Col *d*).

731 *Annotation*

1 Out of the total of 1714 reports of discovery of antibiotics, 470 are reports of duplications involving 204 antibiotics.

2 The average number of times one and the same antibiotic has been reported from different microorganisms was 2·3. The maximum number of times one and the same antibiotic was reported from different microorganisms was 18.

3 The duplication curve is ogive.

74 COUNTRY-WISE DUPLICATION

Table 9 gives data on the number of duplication reports published in different countries.

741 *Annotation*

1 UK has the highest figures for duplication, followed by Japan, Germany, USA and USSR in that sequence.

2 UK has a larger proportion of duplication of antibiotics from fungi. For Japan and USA the highest proportion of duplication is among antibiotics from the Actinomycetes. This finding correlates with the data that UK has reported the largest number of antibiotics from algae, fungi and lichen whereas Japan and USA have worked largely with the Actinomycetes (*See* Table 3 in Sec 63).

TABLE 9. DUPLICATION: COUNTRY-WISE ANALYSIS

SN	Country	Number of antibiotics			$\frac{d \times 100}{c}$
		Reported	Duplication reports	c − d	
a	b	c	d	e	f
1	Germany	102	26	76	25·5
2	Japan	488	137	351	28·0
3	UK	246	99	147	40·2
4	USA	473	112	361	23·7
5	USSR	97	21	76	21·7
6	Other countries	308	75	233	24·3
		1714	470	1244	27·3

75 COUNTRY-TO-COUNTRY DUPLICATION

Tables 10 and 11 give data on the number of antibiotics reported in one country and the number of reports of rediscovery of the same antibiotics in other countries.

TABLE 10. DUPLICATION REPORTS (COUNTRY-TO-COUNTRY)

G = Germany J = Japan

SN	First report		N of duplication reports in						Total
	Country	N	G	J	UK	USA	USSR	Other	d to j
a	b	c	d	e	f	g	h	j	k
1	Germany	15	15	3	5	3	3	3	32
2	Japan	46	4	65	10	13	1	7	100
3	UK	38	—	6	53	12	2	12	85
4	USA	70	7	54	26	85	10	27	209
5	USSR	5	—	—	—	—	5	—	5
6	Other countries	30	—	9	5	1	—	24	39
		204	26	137	99	114	21	73	470

ABLE 11. RATIO OF DUPLICATION (COUNTRY-TO-COUNTRY)

SN	First report		Ratio of the N of first reports in the country in col b and N of duplications in	
	Country	N	Same country	All other countries
a	b	c	d	e
1	Germany	15	1·0	1·2
2	Japan	46	1·4	0·8
3	UK	38	1·4	0·9
4	USA	70	1·2	1·8
5	USSR	5	1·0	—

51 *Annotation*

1 Out of the 204 antibiotics duplicated, USA has the ighest percentage (34) of first reports, followed by Japan with 2·5 per cent, and UK with 18 per cent.

2 Out of the 470 reports of duplication, Japan has the ighest percentage (29·2), followed by USA and UK with 24·2 er cent and 21 per cent respectively.

3 The duplication of the discoveries reported in a country s the highest in the reports published in that country (self-dupli- ation). This is true of each of the countries studied, including ach of those grouped under 'Other countries'. Among the easons for this phenomenon may be the comparatively greater acility of communication among the research teams within a ountry, availability of media for publication etc.

4 The ratio of the number of discoveries in a country to he number of duplicate reports in the same country is about ·2. There is only a little variation from one country to another n this respect.

5 In respect of the first reports of USA, Japan has reported he highest number of duplications, second only to the report of uplications in USA itself. On the other hand, in respect of the irst reports of every other country, the number of reports of uplications in each of the outside countries is quite small com- ared to the number of reports of duplications within the country itself.

76 TIME-LAPSE IN DUPLICATION

Table 12 gives data on the number of reports of dupli- tion in relation to the number of years between the original rep and the duplication reports.

TABLE 12. TIME-LAPSE IN DUPLICATION

Duplication in year	N of reports in		Total	$\frac{b \times 100}{d}$	$\frac{c \times}{d}$
	Same country	Other countries			
a	b	c	d	e	f
0	61	15	76	80·2	19·8
1	12	23	35	34·2	65·8
2	32	14	46	69·5	30·5
3	15	27	42	35·7	64·3
4	18	21	39	46·1	53·9
5	17	11	28	60·7	39·3
6	11	18	29	37·8	62·2
7	4	16	20	20·0	80·0
8	4	12	16	25·0	75·0
9	6	10	16	37·5	62·5
10	11	8	19	57·8	42·2
>10	29	75	104	27·8	72·2
	220	250	470	47·0	53·0

761 *Annotation*

1 The number of reports of 'self-duplication' is the highe in the same year as the publication of the original report.

2 The curve for the percentage of such 'self-duplicatio has alternate peaks and troughs till the eighth year when it touch the lowest level and then rises steadily, declining after the ten year.

77 THERAPEUTICALLY USEFUL ANTIBIOTICS

771 *From Bacteria*

The first antibiotic from bacteria was reported in 192 and the first one with therapeutic value (Gramicidin/Tyrothric

1939. A second such useful antibiotic (Bacitracin) was reported in 1945. These two products have been manufactured on a commercial scale, and used to some extent, in the treatment of infections.

772 *From Fungi*

The first antibiotic from fungi was reported in 1907; and the first one of therapeutic value (Penicillin) in 1929. It went into large-scale production and use only in the 1940's. Another antibiotic with potential clinical use (Cephabsporin N) was discovered in 1951. It attracted the attention of research workers and doctors in the 1960's.

773 *From Actinomycetes*

The first antibiotic from Actinomycetes was reported in 1908, but a second one came up only thirty years later in 1937. The first clinically useful antibiotic (Streptomycin) was reported in 1943. For fifteen years thereafter the rate of production of antibiotics with therapeutic value from Streptomyces has been almost one per year. Most of them have gone into large-scale commercial production. However, in the last decade the rate of discovery of useful antibiotics from *Streptomyces* has been comparatively low.

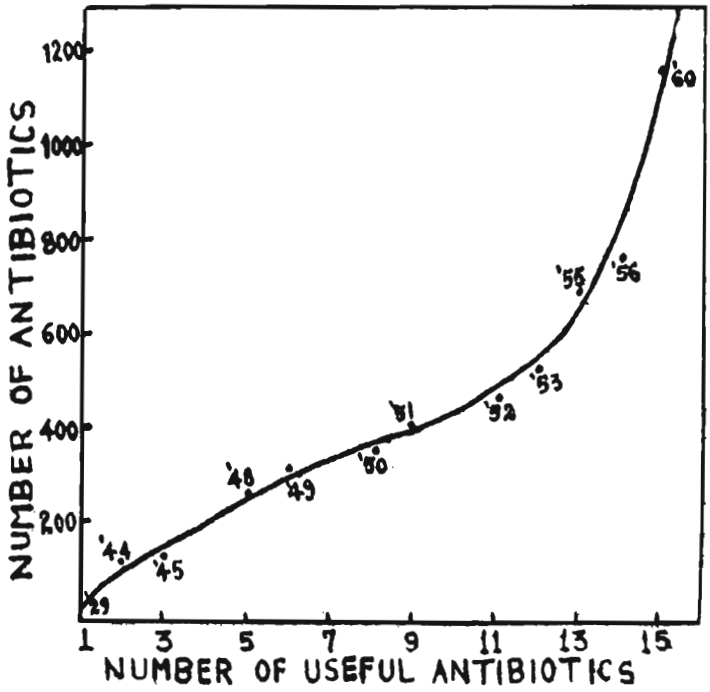

FIG 7. Rate of Discovery of Useful Antibiotics.

774 *Problems*

In Sec 32, 33 and 43 some of the problems in the isolation and development of a useful antibiotic have been mentioned. To be taken up for large-scale production an antibiotic should prove itself better than any of the existing pharmaceuticals in some aspect or other. Therefore, as one compound becomes accepted as therapeutically useful and goes into large-scale production, it becomes increasingly more difficult for subsequent compounds to be similarly accepted and manufactured (*See* Fig 7).

8 Summary

1 The rate of discovery of antibiotics from different organisms, in different countries, during the period 1907 to 19[illegible] has been worked out. The frequency of rediscovery of known antibiotics has also been studied.

2 The problems in deeming a rediscovery of a known antibiotic as unnecessary wastage of research potential have been pointed out (*See* Sec 4). The role of documentation in the complex situation as it obtains in the research in antibiotics has been mentioned (*See* Sec 44). Such problems are likely to arise in the research in other specific subjects also.

3 It has been noted that the duplication of the discoveries reported in a country is the highest in the reports published in that country itself (Self-Duplication) (*See* Sec 75). This phenomenon could be examined in other subjects.

4 It has been further noted that cases of self-duplication are highest in the same year as the publication of the original report. The curve for self-duplication has alternate peaks and troughs for the first ten years of a discovery and then falls off (*See* Sec 76).

5 The emergence of two specialities — Biochemical Engineering and Biochemical Technology — has been mentioned (*See* Sec 36). Till 1966, in CC a subject such as Biochemical Engineering was deemed as a Facet relation between the two subjects brought together — that is, Technology of biochemical production and Engineering. In 1967, the new Phase relation 'Application' (Connecting Digit '0e') was created. More recently [Ranganathan (S R). Basic subjects and their kinds. Lib Sci 5; 1968; Paper C] such a subject has been considered as a 'Specials Basic Subject'. The successive changes of Class Number for the two subjects are as follows:

Year	Biochemical Engineering	Biochemical Technology
Till 1966	F9G: (D)	F9G
1967	F9G0eD	F9G
1968	D9NE	F9NE

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