

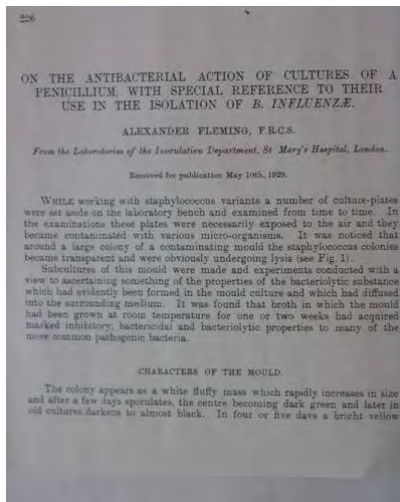
La pénicilline, agent de propagande

*Gilbert Shama
Loughborough University
United Kingdom*

CEMI 16
Colloque sur le Contrôle Epidémiologique des Maladies Infectieuses
Institut Pasteur le 13 mai 2011



An account of an accident at St Mary's Hospital, London.....



The re-discovery of penicillin....

PENICILLIN AS A CHEMOTHERAPEUTIC AGENT

BY
 E. CHAIN, F.R.D. CAMB. M. A. JENNINGS,
 H. W. FLOREY, B.M. OXFORD.
 M. B. ADELAIDE, J. ONS-ERWING,
 A. D. GARDNER, B.M. OXFORD.
 D.M. OXFORD, F.R.C.S. A. G. SANDERS,
 N. G. HEATLEY, F.R.D. CAMB. M.B. LONDON.
 (From the Sir William Dunn School of Pathology, Oxford)

In recent years interest in chemotherapeutic effects has been almost exclusively focused on the sulphonamides and their derivatives. There are, however, other possibilities, notably those connected with naturally occurring substances. It has been known for a long time that a number of bacteria and moulds inhibit the growth of pathogenic micro-organisms. Little, however, has been done to purify or to determine the properties of any of these substances. The antibacterial substances produced by *Pseudomonas pyocyanea* have been investigated in some detail, but without the isolation of any purified product of therapeutic value.

Recently, Dubos and collaborators (1939, 1940) have published interesting studies on the acquired bacterial antagonism of a soil bacterium which have led to the isolation from its culture medium of bactericidal substances active against a number of gram-positive micro-organisms.¹ Pneumococcal infections in mice were successfully treated with one of these substances, which, however, proved to be highly toxic to mice (Hotchkiss and Dubos 1940) and dogs (McLeod et al. 1940).

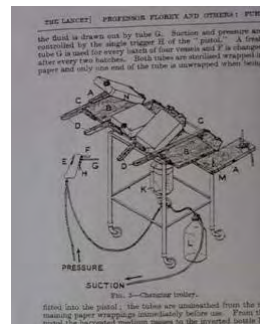
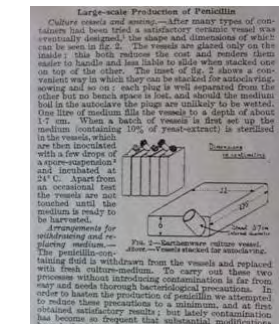
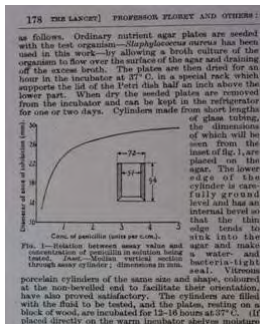
Following the work on tyrocyne in this laboratory it occurred to two of us (E. C. and H. W. F.) that it would be profitable to conduct a systematic investigation of the chemical and biological properties of the antibacterial

1. See *Lancet*, 1940, i, 1178.

The Lancet, August 1940

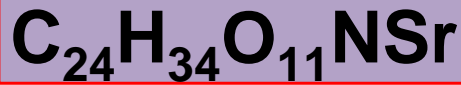
Everything you needed to know about producing penicillin but were afraid to ask.....

The Lancet, August 1941



Misinformation....?

Formula for strontium salt of Penicillin published in *Nature*, 1942



Penicillin in time of war.....

1940

- Dunkirk
- Start of the 'Blitz'

1941

- Stalemate in the W. Desert

1942

- Fall of Singapore

Penicillin in the media

THE TIMES



First Article in The Times

27th August, 1942

Letters to THE TIMES



Sir Almost Right

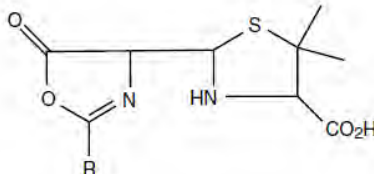
"...a laurel wreath for
Professor Alexander
Fleming for the
discovery of penicillin"



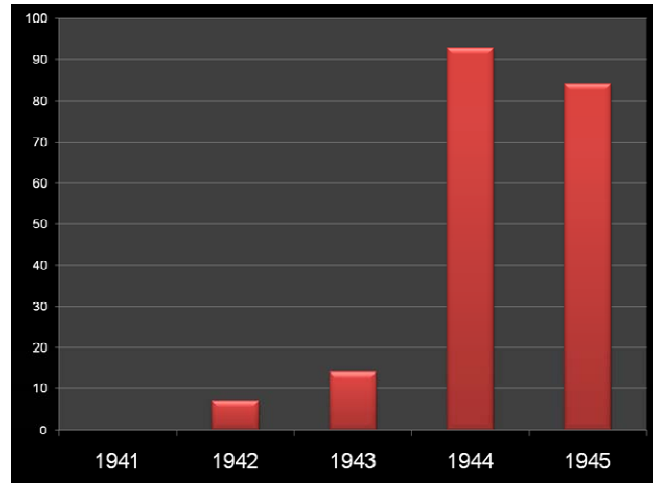
31st August, 1942



Robert Robinson,
Waynflete Professor
of Chemistry,
University of Oxford



Number of Citations in *The Times*



English Language Broadcasts

'Ariel in Wartime' – 4th September, 1942

'Marching On' – 15th October, 1942

'Penicillin' – 2nd September, 1943

'Producing the Drug Penicillin' – 22nd
October, 1943

'Penicillin' – 20th December, 1943

'Science Notebook' – 10th April, 1944

The Listener

Published every Thursday by The British Broadcasting Corporation



British battleship firing a 16-inch gun, great gunners offered a large part in sinking the *Princes* which they tried to sweep the Allies back into the sea at Salerno.

The Naval Campaign in the Mediterranean
(see page 129)

Unwanted Publicity....

“....a flood of pathetic letters
from Western Australia to
Saskatchewan.....”

Letter

HW Florey to the BBC, October 1942

Ici Londres....

- French Language Broadcasts

'Medical News 10' – 21st July, 1943

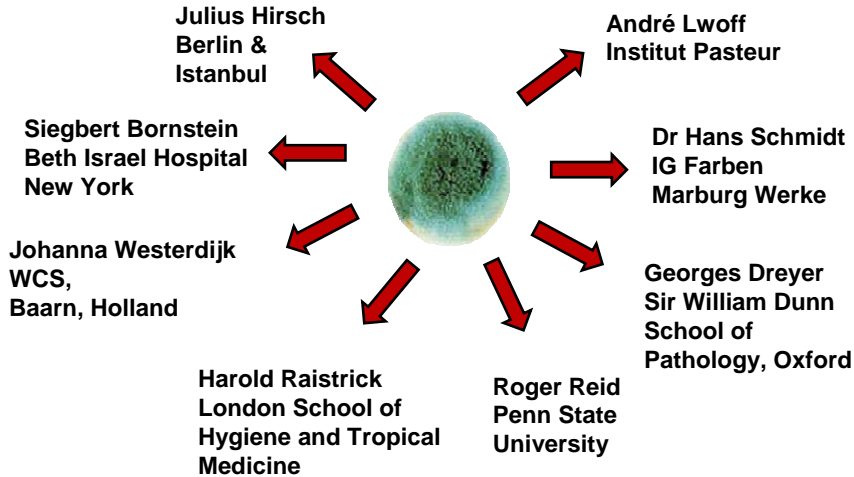
'Medical News 17' – 29th September, 1943

'Une Grande Decouverte de la Science Anglaise'
– 17th February, 1944





Transmission of *P. notatum* cultures – Pre 1940



Distribution of *P. notatum* NCTC 4222 after the outbreak of war.

Division of Industrial Chemistry
Council for Scientific & Industrial
Research, East Melbourne,
Australia.

Indian Inst. of Science.
Bangalore, India

The British Council

S.A. Brewing Co. Ltd.,
Adelaide, S. Australia.

N.Z. Government, Strand W.C.

School of Pathology, T.C.D., Eire.

Aktiebolaget Marvella
Stockholm, Sweden.

Imperial Mycologist, New Delhi,
India.

Guinness Brewery, Dublin, Eire.

Dept. of Pathology, Univ. Coll. Dublin, Eire.

Ministry of Agriculture, Belfast, N. Ireland.

Laboratorio Fidelis, Lisbon, Portugal

Alexr. Lipworth Pty. Co., Johannesburg, S.
Africa.

Bakubhai Ambalal & Co., Bombay, India.

South African Inst. For Medical Research,
Johannesburg.

Clinsearch Laboratories, Johannesburg, S.
Africa.

Information Wars in France

Jean Gérard
Secretary General
Maison de la Chimie

Frédéric Joliot-Curie
Centre National de la
Recherche Scientifique

Access to the best
microfilming
facilities, paper
and printing
presses

Jean Wyart
Crossed between
Occupied and
Unoccupied Zones

Primarily French-
German exchanges
of scientific literature

Access to Anglo-
American Material
Bulletin Analytique

Information Cascade in the French Pharmaceutical Industry

Applications to WCS, Baarn for
cultures of *P. notatum*

Laboratoires du Dr Roussel – 7th July, 1943

Etablissements Byla – 23rd September, 1943

Maison L Frere – 3rd February, 1944

Publish and be damned...?

Nitti, F. (1944). Un nouveau traitement des infections microbiennes par un produit élaboré par les moisissures: la pénicilline. *Le Progrès Médical*. No. 1, 10th **January**, 10-12.

Martin, R., Sureau, B., and Vittoz, A. (1944) Un cas de méningite a pneumocoques sulfamido-résistants traitée par la pénicilline. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris*, Nos. 11 & 12, 17 **March**, 117-120.

Martin, R., and Sureau, B. (1944). La pénicilline et ses applications thérapeutiques. *Paris Médical*. 10th **June**, 115- 119.

'Wervelwind' Leaflet Dropped over N. Holland by the RAF 24/25th April, 1944



Thanks to PENICILLIN
...He Will Come Home!



FROM ORDINARY MOLD —
The Greatest Healing Agent of this War!

On the quiet, green moldy surface which, when Penicillium notatum in the laboratory grows, the substance which is Penicillin is born. The more drugs the antibiotic substance known as penicillin can be made from directly from a pure of Schenley's penicillin. Schenley Laboratories have the only way of making penicillin, when the great need for it came.

When the antibiotic bodies of this war have reached to pages of other pills in a busy bank, the general idea came to them. It was to use the mold in the laboratory, and to make it into a more useful weapon than any other of a weapon that can be used in the way of a weapon.

From day, penicillin is producing some remarkable acts of healing on some of the soldiers. Thousands of men will never have the infection which would not have been a chance. There will never and none of the present drug is now available for certain war — were on the level of present of drug use.

A pure and production of penicillin was difficult, until Today, due to specially devised methods of manufacturing, as set by Schenley Laboratories, Inc., and the other have developed by the government to make penicillin, it is available in increasing quantity and progressively lower cost.

SCHENLEY LABORATORIES, INC.
Producers of PENICILLIN-Schenley

Me too.....

Vol 22
Ze. 44, Heft 16/17
27. April 1943

VONKENNEL, KIMMIG u. LEMBEKE, Wirksame Substanzen aus Pilzen. — DÖGL, Natriumgehalt des Serums.

**DIE MYCOINE, EINE NEUE GRUPPE
THERAPEUTISCH WIRKSAMER SUBSTANZEN
AUS PILZEN.**

Von
J. VONKENNEL, J. KIMMIG und A. LEMBEKE.
Aus der Arbeitsgemeinschaft der Kieler Universitätsklinik.

Im Jahre 1929 isolierte FLEMING eine bactericide Substanz aus dem Schimmelpilz *Penicillium notatum*. Dieses „Penicillin“ erwies sich im Kulturversuch als wirksam gegen Gram-positive und Gram-negative Eiterkokken und gegen anaerobe Sporenbildner, nicht dagegen auf coli- und typhus-ähnliche Keime sowie hämolysierende Farbstoffbildner. Mit der Isolierung des wirksamen Prinzips beschäftigte sich RAISTRICK erfolglos. Durch die Arbeiten von ABRAHAM, CHAIN, FLETCHER, GARDNER, HEATLEY und JENNINGS erhielt das Thema einen neuen Auftrieb. Es gelang diesen Autoren durch eine sinnvolle Methode die wirksame Substanz anzureichern und als Bariumsalz zur Kristallisation zu bringen. Da die Toxizitätsbestimmungen im tierischen und menschlichen Organismus eine auffallend gute Verträglichkeit ergaben, während das Wachstum vieler Krankheitserreger noch in Verdünnungen von 10^{-6} bis 2×10^{-7} gehemmt wird, muß dem Penicillin ein äußerst günstiger therapeutischer Index zugeschrieben werden. Bemerkenswert ist die Beobachtung, daß auch Erreger erfaßt werden, die außerhalb des Wirkungsbereichs der Sulfanilamide liegen. Auch ist bisher keine zum Penicillin interferierende Substanz bekannt geworden — ähnlich wie die *o*-Aminobenzoesäure zu den Sulf-

röhrchen gebracht. Belastungsaxanogramm nach 24 Stunden.

Über die notwendigen methodischen Voraussetzungen Isolierung der Mycoine wird eine weitere Arbeit berichtet.

Ein Identitätsnachweis der verschiedenen Mycoine war uns bisher nicht möglich, so daß noch nicht entschieden ist, ob es sich um chemisch einheitliche Verbindungen handelt.

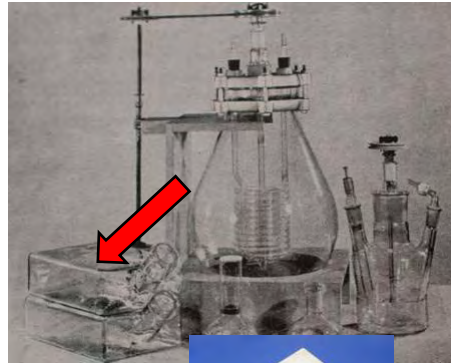
Nachdem die bakteriologischen Prüfungen auch für die Mycoine eine direkte Wirkung annehmen ließen, haben wir in der Klinik die lokale Anwendung versucht und bei sekundär infizierten Ulcera eine ausgezeichnete Reinigungskraft festgestellt.

Für das Penicillin dürfte neben der lokalen noch die parenterale Anwendung aussichtsreich sein. Da dieses Mycoine aus *Penicillium*arten seine Aktivität in stark saurem bis stark alkalischem Milieu verliert, war von der peroralen Verabreichung keine Wirkung zu erwarten, was auch der vorliegende Versuch bestätigte.



Abb. 2.

Vorsprung durch (englische) technik



Advertisement – The Observer 16th April, 1944



FLASK FOR

Most people know that the wonderful new drug Penicillin is obtained from a sugar liquid on which fungus has been bred. The mould has to be "cultured" in a special flask capable of withstanding reacting conditions. In collaboration with the laboratory furnishers, Messrs. Townson & Mercer Limited, Chance research workers produced the

flask you see above from their famous "Hyall" heat-resisting glass. Though this time we helped to put a drug on the market, our talents usually lie in the other direction, and anyone interested in looking up a demand for his product can count on the help of our Research Department, when it's a question of glass.

CHANCE GLASS FOR SCIENCE, INDUSTRY & THE HOME

CHANCE BROTHERS LIMITED · GLASSMAKERS SINCE 1824 · HEAD OFFICE: SMETHWICK, BIRMINGHAM · LONDON OFFICE: 10, PRINCES ST., WESTMINSTER, S.W.1

STAMPS
PHILATES of all countries please for each also really good collectors DON'T MISS: with STEPHEN FENNERSON & CO., LTD., Limited Valuers, Leominster.

Printed for the Proprietors by the Assoc. Press, Limited, 410, St. Paul Street, London, E.C.4. Reprints also published by The Observer, Leamington, 1944, at 12, Tudor-street, London, E.C.4, England.

Homemade Penicillin?



Chemical Synthesis of Penicillin

39 Laboratories

- Commercial Organizations
- Universities
- Government Agencies
- Private Foundations

Expenditure by pharmaceutical and chemical companies alone
~ \$3 million

Second in scale only to the Manhattan project



