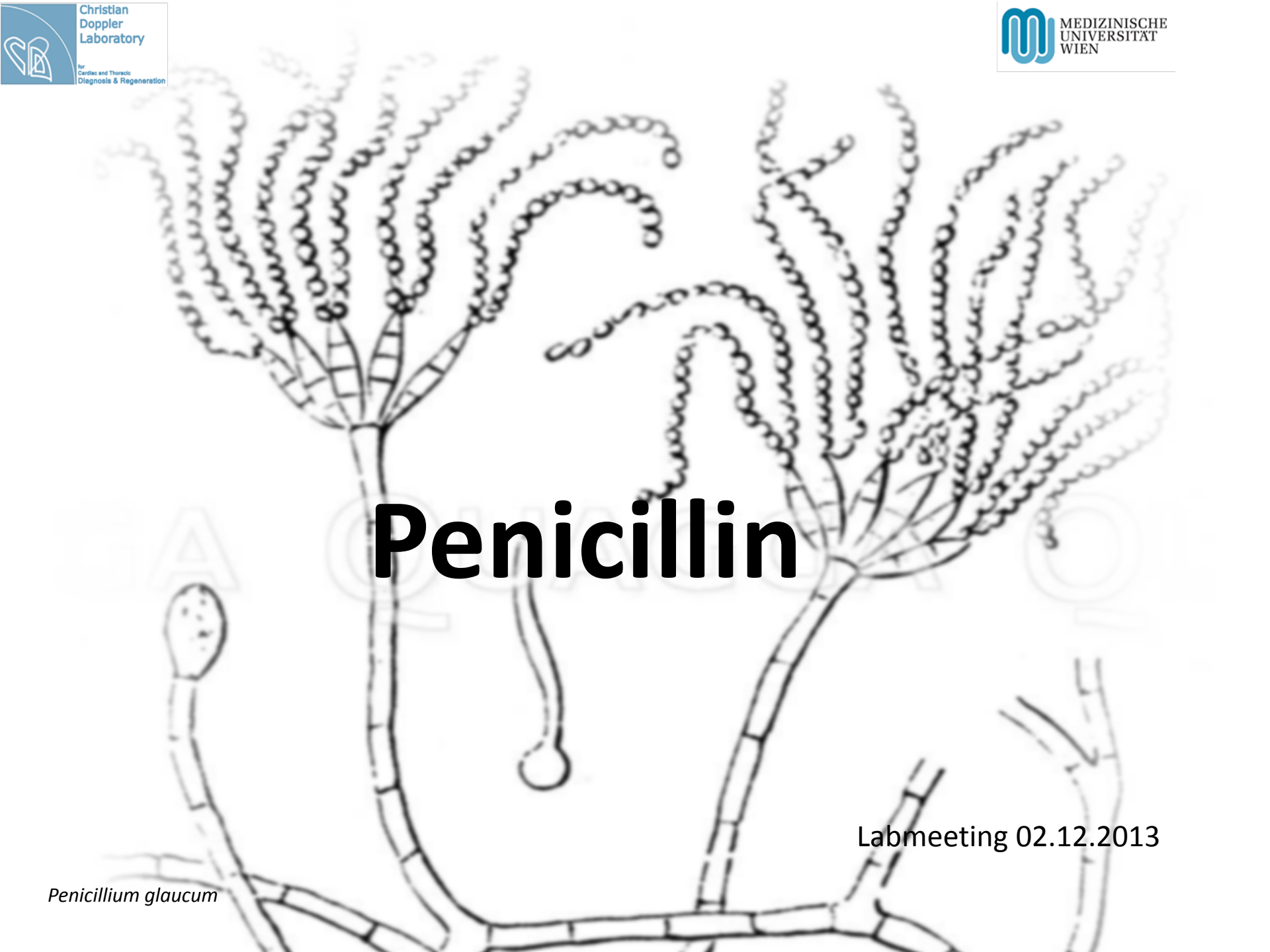


# Penicillin

Labmeeting 02.12.2013

*Penicillium glaucum*



# History of Antibiotics



350-550 AD traces of tetracycline have been found in human skeletal remains from ancient Sudanese Nubia

In traditional Chinese medicine a paste from chewed barley and mouldy apple was made and put on the surface of wounds



In the Jewish Talmud a therapeutic is mentioned that consist of mouldy corn soaked in water or date wine

In 1640 John Parkinson, London apothecary and King's herbalist advises that moulds have a curative effect when applied to infections



## MOULDS IN ANCIENT AND MORE RECENT MEDICINE

MILTON WAINWRIGHT

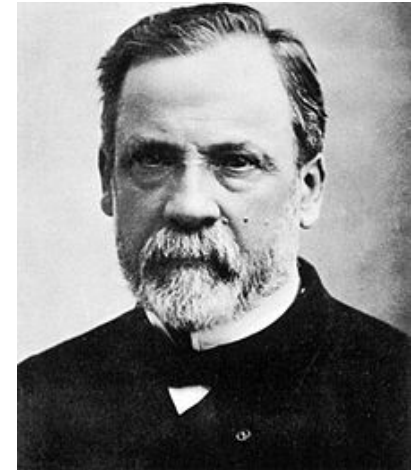
Department of Microbiology, University of Sheffield, Sheffield S10 2TN

## A Brief History of the Antibiotic Era: Lessons Learned and Challenges for the Future

Rustam I. Aminov; Frontiers in Microbiology. 2010; 1:134

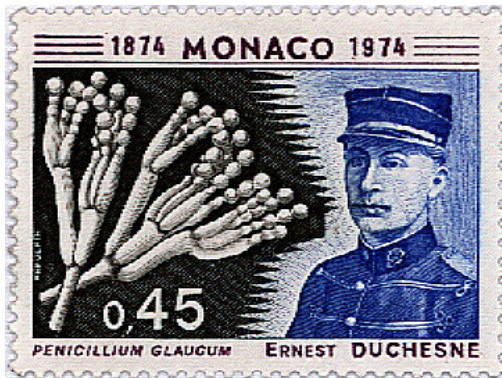
Jean Paul Vuillemin introduces the term „antibiosis“ meaning „against life“ in 1889

1877 Louis Pasteur observed that cultures of the anthrax bacilli, when contaminated with moulds, became inhibited



Louis Pasteur  
1822-1895

In 1893 Bartolomeo Gosio (1863-1944) is able to isolate Mycophenolic acid out of moulds from the genus penicillium and showed that it was able to inhibit the grow of bacillus anthracis. His work never found international recognition probably because it was written in italian and not translated



in 1897 Ernest Duchesne (1874-1912) submits the thesis for the doctorate degree: „ Contribution to the study of vital competition in micro-organisms: antagonism between moulds and microbes“

1909 Paul Ehrlich discovered arsphenamine, the first synthetic antibiotic as a treatment for syphilis

**„Abtöten der Parasiten ohne erhebliche Schädigung des Organismus,...,wir müssen chemisch zielen lernen“**

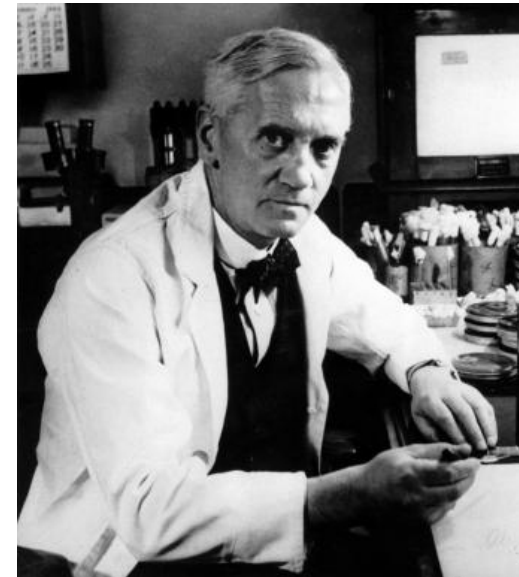


Paul Ehrlich (1854-1915)  
Nobel Prize in Medicine 1908

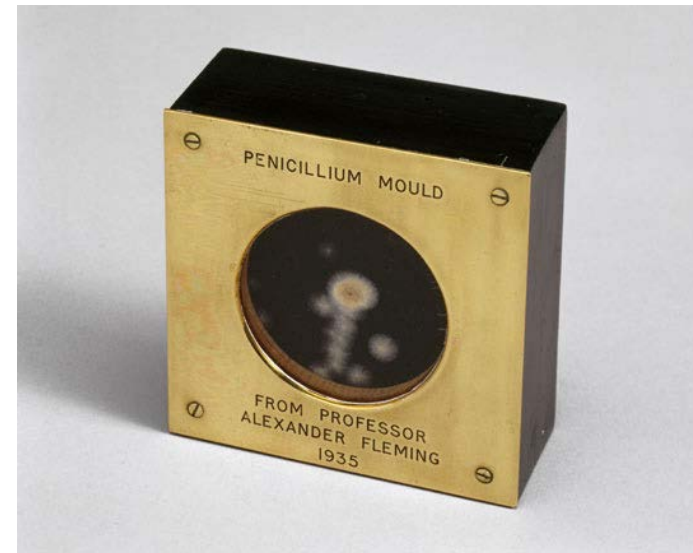
## Sir Alexander Fleming

**“When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionise all medicine by discovering the world's first antibiotic, or bacteria killer. But I suppose that was exactly what I did.”**

Fleming was born on 6 August 1881 at Lochfield farm, Scotland as the third of the four children. In 1903 he enrolled at St Mary's Hospital Medical School and qualified with a bachelor degree from the school with distinction in 1906. He became assistant bacteriologist to Sir Almroth Wright, a pioneer in vaccine therapy and immunology.



In 1928, while working on influenza virus, he observed that mould had developed accidentally on a staphylococcus culture plate and that the mould had created a bacteria-free circle around itself. He was inspired to further experiment and he found that a mould culture prevented growth of staphylococci, even when diluted 800 times.



In 1939 Ernst Chain began, with Howard Florey, a systematic study of antibacterial substances produced by micro-organisms. This led to his best known work, the reinvestigation of penicillin, which had been described by Sir Alexander Fleming nine years earlier, and to the discovery of its chemotherapeutic action. Later he worked on the isolation and elucidation of the chemical structure of penicillin and other natural antibiotics.



Ernst Boris Chain  
(1906-1979)



Sir Howard Walter Florey  
(1898-1968)

Fleming, Florey and Chain jointly received the Nobel Prize in Medicine in 1945.

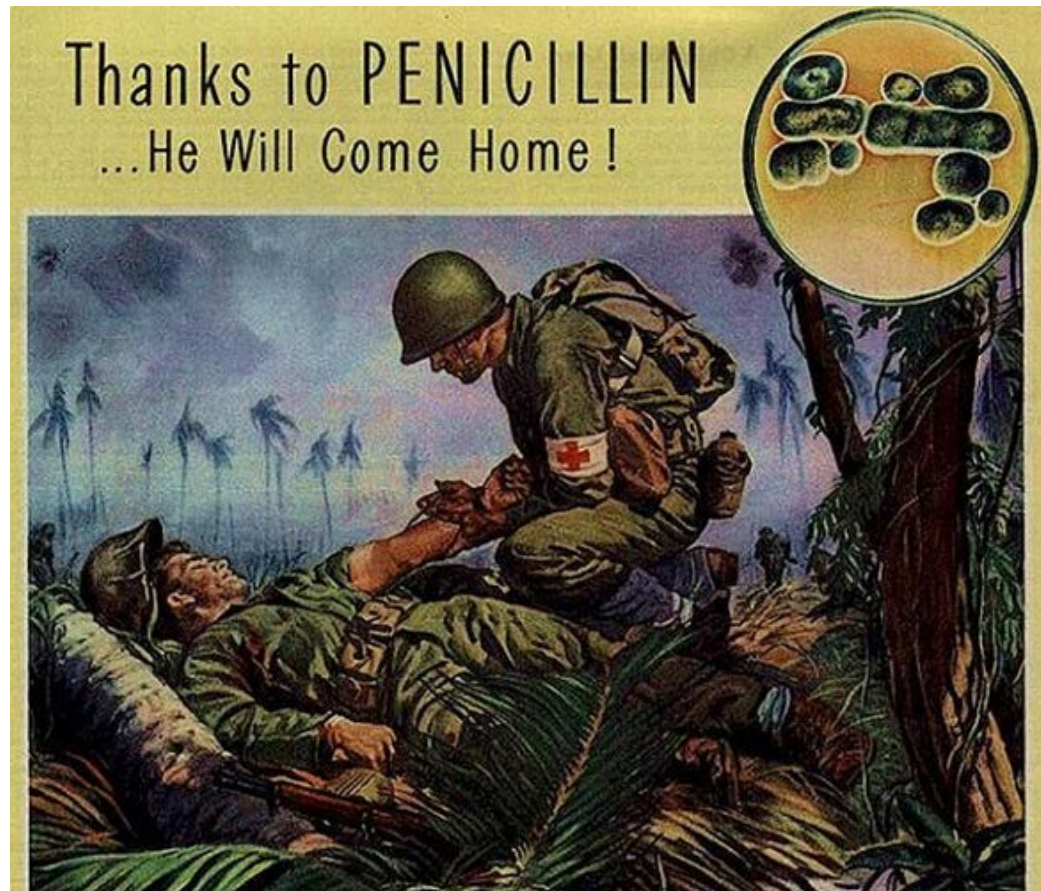




## Penicillin production in the beginning



Glass flasks and milk churns used for making early forms of penicillin



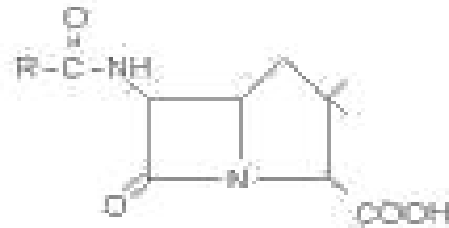
The United States to produce 2.3 million doses in time for the invasion of Normandy in the spring of 1944

# Mechanism of action

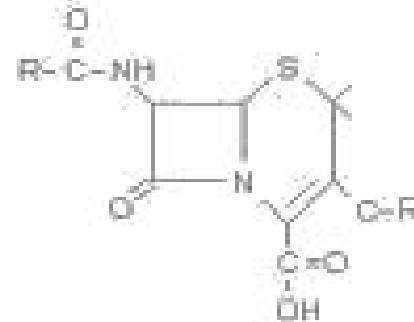


## $\beta$ -Lactam antibiotic

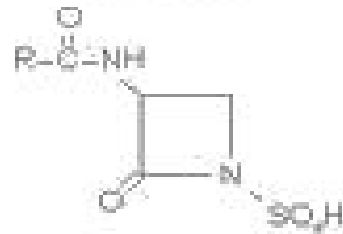
**PENICILLINS**



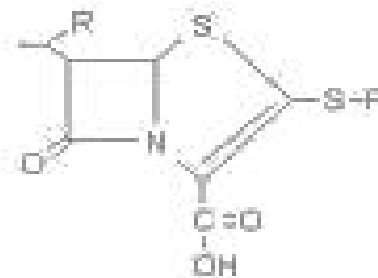
**CEPHALOSPORINS**



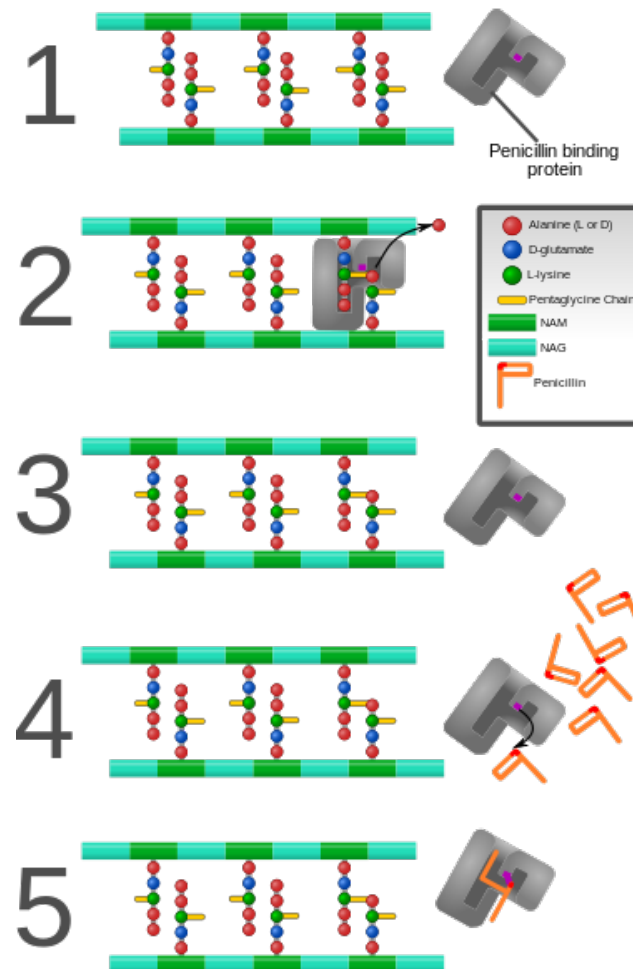
**MONOBACTAMS**



**CARBAPENEMS**



Penicillin intervenes in the metabolism of the bacteria and blocks the synthesis of the bacterial cell wall



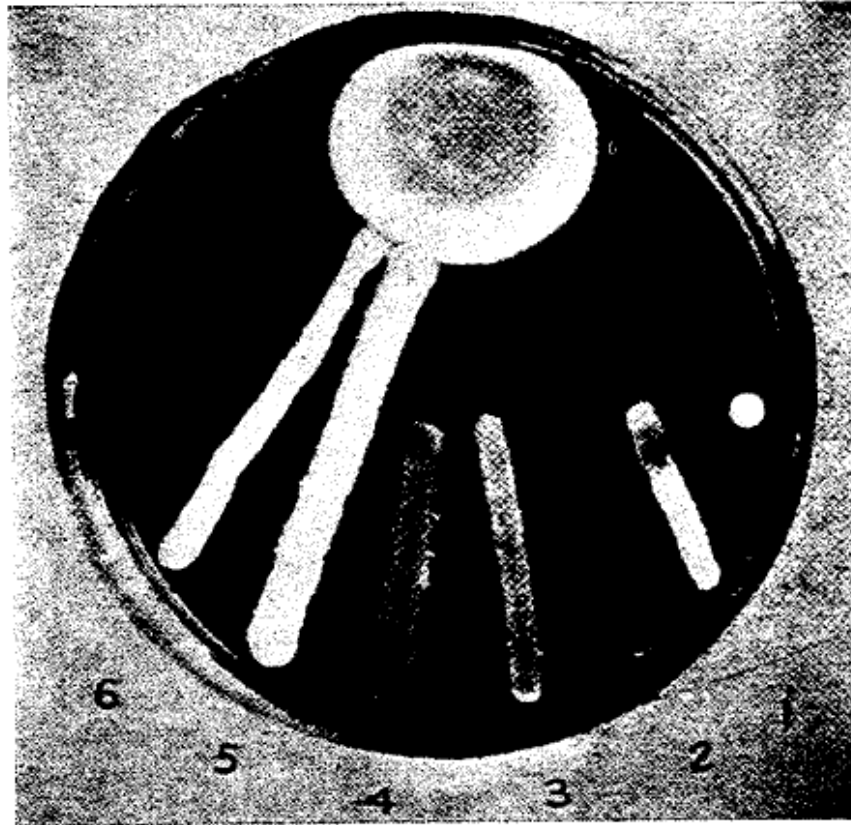


Fig. 2. Different bacteria streaked radially to a four-day-old colony of *Penicillium notatum* on agar.

The bacteria are: (1) *Staphylococcus*; (2) *Streptococcus* (haemolytic); (3) *B. diphtheriae*; (4) *B. anthracis*; (5) *B. typhosus*; (6) *B. coli*.

Gruppe	Wirkungsschwerpunkt								
Substanz	Strepto- kokken	Pneumo- kokken	S. aureus	Haem. Infl.	E. coli	Entero- kokken	Proteus	P. aerug.	B. fragilis

### Penicillin G und Derivate

Penicillin G, V	+++	+++	-	-	-	-	-	-	-
Propicillin	+++	+++	-	-	-	-	-	-	-
Azidocillin	+++	+++	-	+	-	-	-	-	-

- Penicillin G: nicht säurefest (nur parenteral), Penicillin V: säurefest (Oralpenicilline)
- nicht stabil gegen  $\beta$ -Laktamasen

### Isoxazolympenicilline

Oxacillin	++	+	+++	-	-	-	-	-	-
Dicloxacillin	++	+	+++	-	-	-	-	-	-
Flucloxacillin	++	+	+++	-	-	-	-	-	-

- säurefest und  $\beta$ -Laktamasefest, Staphylokokkenpenicilline

### Aminopenicilline

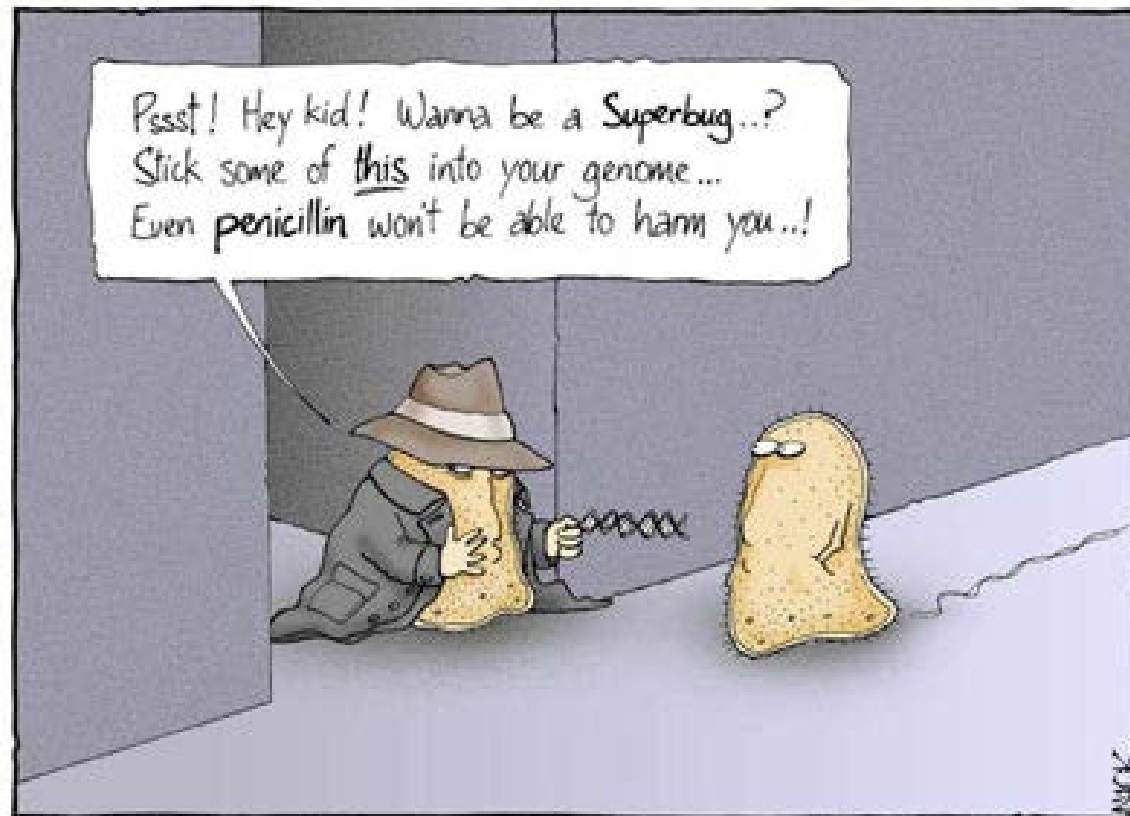
Ampicillin(-Ester)	+++	+++	-	++	±	++	-	-	-
Amoxicillin	+++	+++	-	++	±	++	-	-	-
Amoxicillin/ Clavulansäure	+++	+++	+++	+++	++	++	±	-	++
Ampicillin/ Sulbactam	+++	+++	+++	+++	++	++	±	-	++

- säurefest, nicht stabil gegen  $\beta$ -Laktamasen (orale Breitspektrumpenicilline)

### Acylaminopenicilline

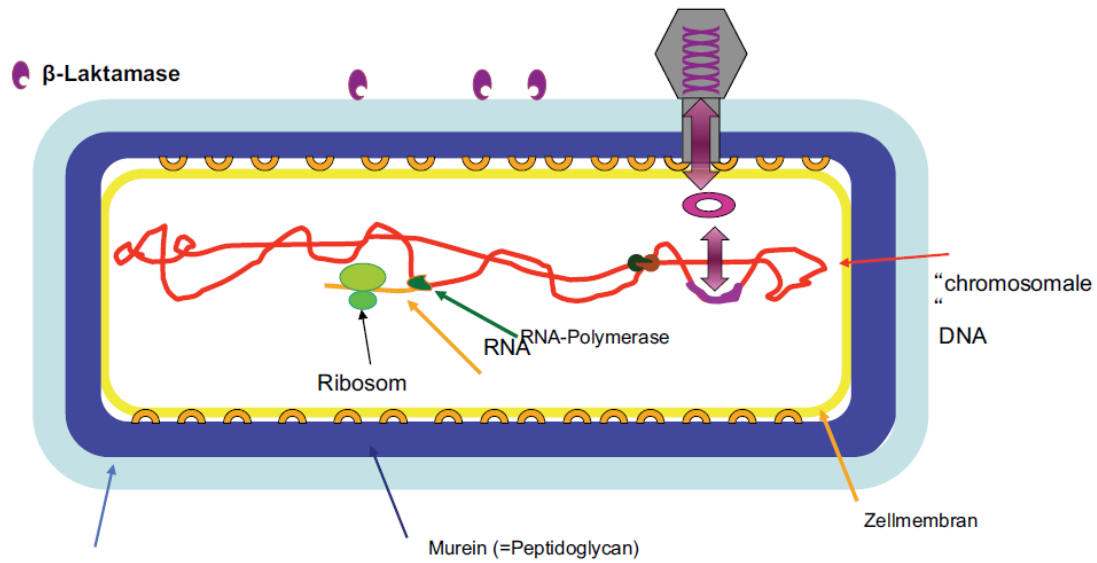
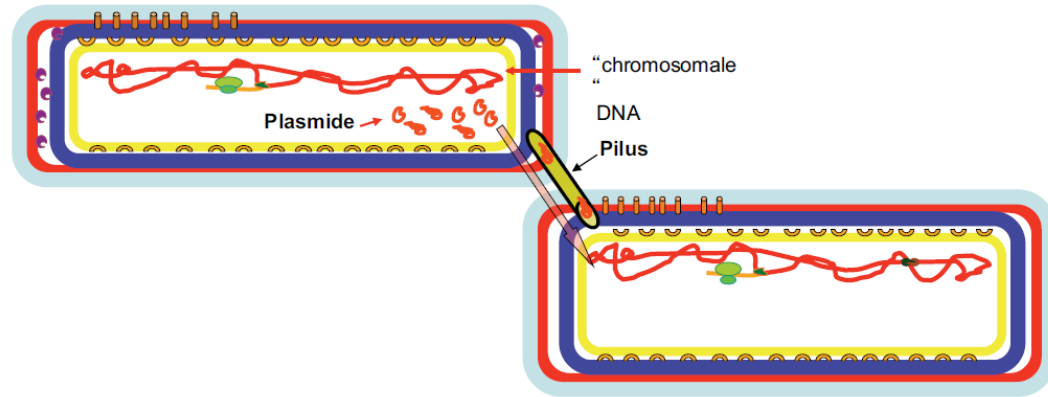
Mezlocillin	+++	+++	-	+++	+	++	±	-	+
Piperacillin	+++	+++	-	+++	+	+	±	++	+
Piperacillin/ Tazobactam	+++	+++	+++	+++	+++	+	+++	+++	+++

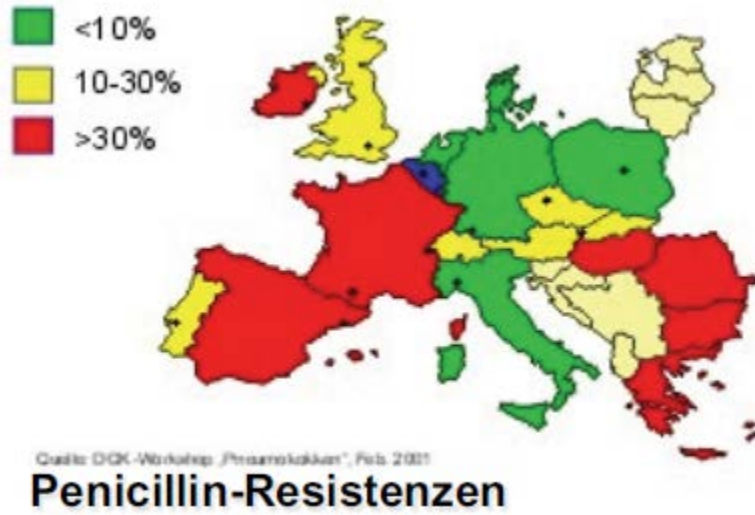
- gegen gramnegative Problemkeime (Pseudomonas-, Proteus-Arten)
- nicht säurefest, nicht stabil gegen  $\beta$ -Laktamasen (parenterale Breitspektrumpenicilline)



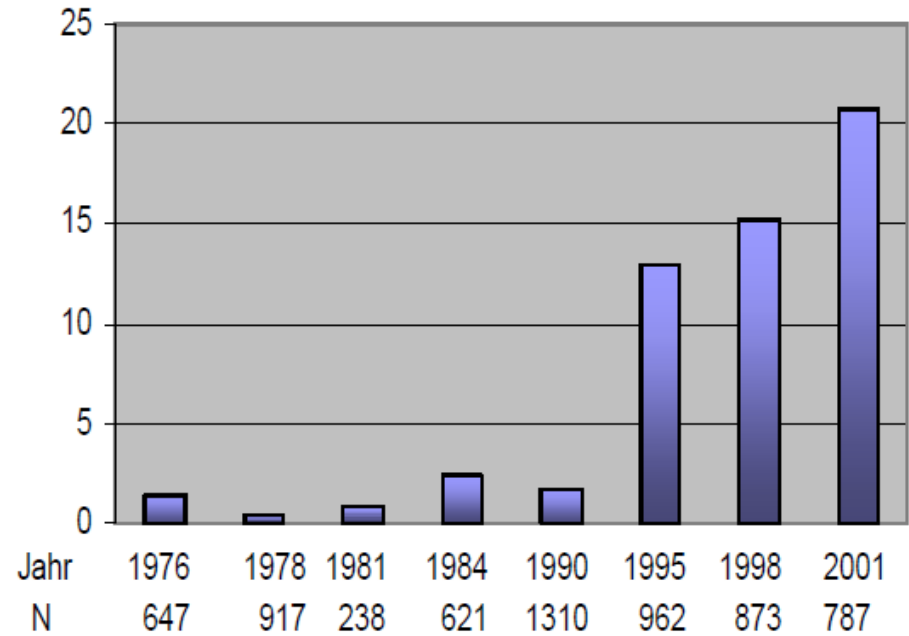
It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.







MRSA (%)



**Danke für die  
Aufmerksamkeit**