ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Conference on Reviving Old Antibiotics

22-24 Oct 2014, Vienna, Austria

Vienna

AIDA COOPERATION

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

EPASG ESCMID PK/PD OF ANTI-INFECTIVES STUDY GROUP
European Society of Clinical Microbiology and Infectious Diseases

ESGAP ESCMID STUDY GROUP FOR ANTIBIOTIC POLICIES
European Society of Clinical Microbiology and Infectious Diseases

U. Theuretzbacher
Center for Anti-Infective Agents, Vienna, Austria

Reviving old antibiotics – action in resistance strategies


World Health Organization

Draft outline of global action plan on antimicrobial resistance
June 2014

2.4 Building block-4: Identifying and closing critical gaps in knowledge needed to address AMR

The Advisory Group emphasised the importance of knowledge (information and data) in guiding all actions. The global action plan needs to address development and assessment of the evidence base for action, quality of data, and ability to monitor and evaluate progress. Surveillance, including the development and maintenance of laboratory capacity, should be given a high profile in the action plan.

Reviving old antibiotics – action in resistance strategies

Transatlantic Taskforce on Antimicrobial Resistance:
Progress report

May 2014

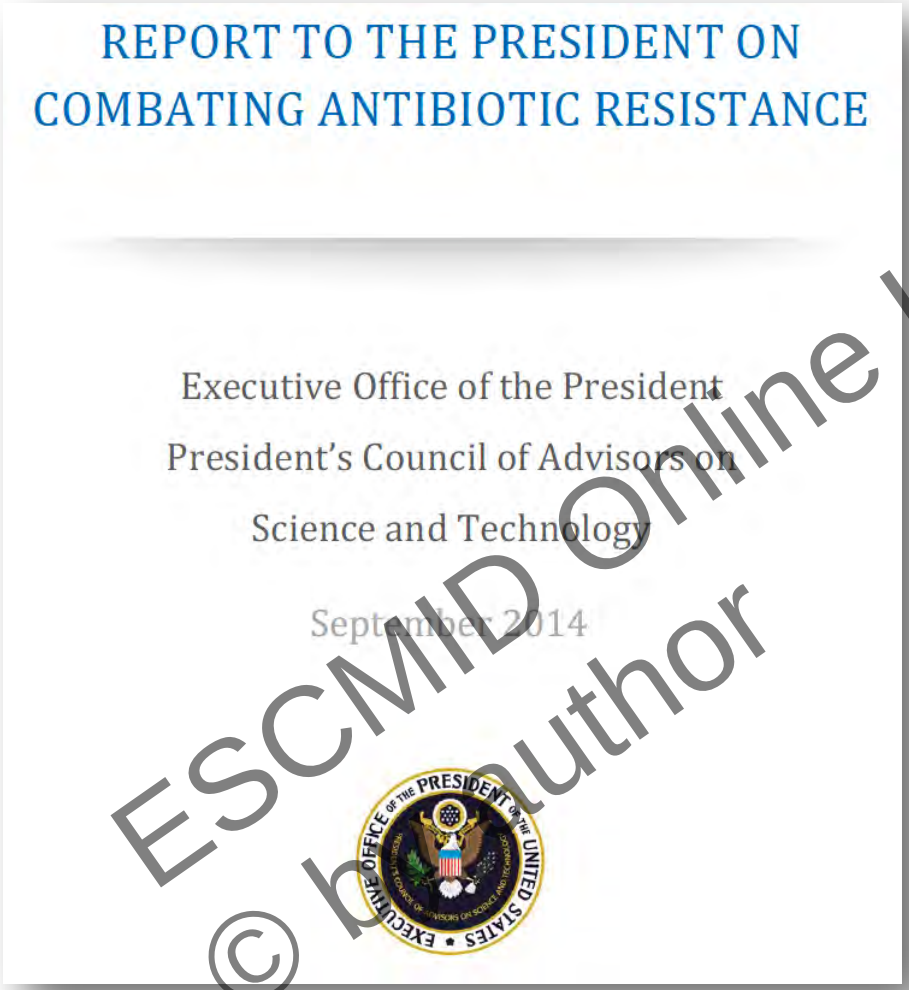
- **Campaigns to promote appropriate use in human medicine**

Issue: Campaigns to promote appropriate antimicrobial use must be periodically updated based on effectiveness data and societal factors

Recommendation 6: Establish an EU–US working group to assess the evidence for effectiveness of communications tools in promoting behaviour change to increase appropriate use and to develop joint priorities

- –Implementers: CDC and ECDC
- –Timeline: Within two years of adoption of recommendation

Reviving old antibiotics – action in resistance strategies


REPORT TO THE PRESIDENT ON
COMBATING ANTIBIOTIC RESISTANCE

Executive Office of the President
President's Council of Advisors on
Science and Technology

September 2014

(1) **improving our surveillance of the rise of antibiotic-resistant bacteria** to enable effective response, stop outbreaks, and limit the spread of antibiotic-resistant organisms,
and acting on surveillance data to implement appropriate infection control;
(2) **increasing the longevity of current antibiotics,** by improving the appropriate use of existing antibiotics, preventing the spread of antibiotic-resistant bacteria and scaling up proven interventions to decrease the rate at which microbes develop resistance to current antibiotics;
(3) **increasing the rate at which new antibiotics, as well as other interventions, are discovered and developed**.

Reviving old antibiotics

Reviving old antibiotics

STUDIES ON POLYMYXIN: ISOLATION AND IDENTIFICATION OF BACILLUS POLYMYXA AND DIFFERENTIATION OF POLYMYXIN FROM CERTAIN KNOWN ANTIBIOTICS

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Polymyxin is an antibiotic substance occurring in the culture filtrates of *Bacillus polymyxa*. The isolated substance is unique in its specificity for gram-negative bacteria. A summary of the more important results obtained during the course of several years, including chemotherapeutic and toxicity data, has been reported (Stansly, Shepherd, and White, 1947). The present contribution is concerned with the isolation and identification of the antibiotic-producing organism and some early findings which both characterized and distinguished polymyxin from certain known antibiotics.

Isolation of Bacillus polymyxa. *Bacillus polymyxa* was isolated from soil in the course of a program designed to find new antibiotics for the chemotherapy of gram-negative bacterial infections. The test organism used in this search was *Salmonella schottmuelleri*. Our method for isolating antibiotic-producing organisms with a specific type of activity involves the preparation of pour plates of soil dilutions using a variety of media and cultural conditions. The plates are subsequently sprayed with a suspension of the test organism by means of an apparatus designed for the purpose (Stansly, 1947).

Identification of Bacillus polymyxa. The identification of *Bacillus polymyxa* was established by following the key to the identification of aerobic sporeforming bacteria by Smith, Gordon, and Clark (1946). In the preliminary work,[1] edition 5 of Bergey's *Manual of Determinative Bacteriology* (1939) and the galley proofs of edition 6 were found helpful.

An 18-hour broth culture consisted of gram-negative rods with few or no gram-positive cells. Older cultures showed vegetative cells and oval spores either free or central to terminal in adhering and swollen sporangia. Broth cultures at 30 C were turbid and had a ropy sediment. Indole was not formed. Nitrates were reduced to nitrites. Hydrogen sulfide was not produced. Acid and gas were formed from glucose, lactose, and sucrose. Acid but no gas was produced from rhamnose and a slight amount of acid but no gas from sorbitol. Starch was hydrolyzed. Acid and gas were produced from litmus milk, which was coagulated and reduced.

The existence of oval spores, central to terminal, and sporangia frequently adhering and swollen, plus the predominant gram-negative nature of the vegeta-

[1] The authors are indebted to Dr. Walter C. Tobie and Miss Marion H. Cook for the preliminary work which led to the conclusion that the antibiotic-producing organism had characteristics intermediate between those of *Bacillus polymyxa* and *Bacillus macerans*.

California MEDICINE

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The Experimental and Clinical Use of Polymyxin, Chloromycetin, and Aureomycin

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SUMMARY

Polymyxin is an effective antibiotic for the treatment of severe infections produced by Ps. aeruginosa, H. pertussis, H. influenzae, E. coli, and A. aerogenes. Its toxicity to date precludes its general use in infections susceptible to its therapeutic effects.

Chloromycetin has been demonstrated to be an effective antibiotic agent for the treatment of rickettsial diseases and typhoid fever. It will undoubtedly prove effective in the treatment of other infections produced by certain Gram-negative micro-organisms and viral agents.

Aureomycin has been shown to be an active antibiotic agent against rickettsial diseases, primary atypical pneumonia, acute brucellosis, pneumococcal, streptococcal, and staphylococcal infections, urinary tract infections produced by E. coli, A. aerogenes and Strept. fecalis, certain types of infections of the eye, and in subacute bacterial endocarditis when the infecting agent is Strept. fecalis. Its clinical use in forms of extrapulmonary tuberculosis is in a completely experimental stage. It is not recommended in typhoid fever or in infections due to Ps. aeruginosa or P. vulgaris, and it seems to be ineffective in whooping cough.

To date, neither chloromycetin nor aureomycin has shown significant signs of systemic toxicity.

DURING the past 18 months, three new antibiotic agents, polymyxin,* chloromycetin,† and aureomycin,‡ have been described. The purpose of this presentation is to discuss certain observations which have been made regarding the antibacterial or bacteriostatic activity, the pharmacology and toxicity, the comparative effectiveness in experimental infections, and the potential clinical uses and value of these three compounds.

BACTERIAL AND BACTERIOSTATIC ACTIVITY

It can be said that, from the point of view of antibacterial activity, the polymyxins are definitely more effective *in vitro* than is streptomycin against certain Gram-negative bacteria. In our experience polymyxin D has from two to eighty times the activity of streptomycin against susceptible bacteria (see Table 1).

Furthermore, the activity of polymyxin is primarily bactericidal in the concentrations used, while that of streptomycin is bacteriostatic. Another point

*References 1, 4-6, 9-11, 26, 36, 46-48.
†References 3, 21, 32, 33, 40-44, 50, 53.
‡References 2, 7, 8, 12-20, 23-25, 27-31, 34, 35, 37-39, 45, 49, 51, 52.

Presented before the Alameda County Medical Association, Oakland, California, January 17, 1949.

From the Department of Preventive Medicine, The Johns Hopkins University School of Medicine. These investigations were supported by grants from the Abbott Laboratories; Eli Lilly and Company; Lederle Laboratories Division, American Cyanamid Company; Parke, Davis and Company; The Upjohn Company; and the Antibiotic Study Section, Division of Research Grants and Fellowships, The National Institutes of Health, Public Health Service of the Federal Security Agency. Polymyxin D and aureomycin were furnished by the Lederle Laboratory Division, American Cyanamid Company. Polymyxin B was supplied by Burroughs-Wellcome Company and chloromycetin by Parke, Davis and Company.