My Antibiotics Days:
the ever-changing patterns of antimicrobial therapy

Emilio Bouza
Department of Microbiology and Infectious Diseases.
Hospital Gregorio Marañón
University of Madrid. Spain
Disclosures

Participation in meetings and advisory boards with:

- Pfizer,
- Novartis,
- Janssen,
- Baxter,
- McDonalds,
- Astellas,
- Wyeth Lederle,
- Optimer

Several Scientific Societies and non-profit foundations (Fundación de Ciencias de la Salud)

Research funds received from private and public origins:

- Pfizer,
- Astra-Zeneca,
- Novartis,
- Schering-Plough,
- and other pharmaceutical companies.
- FIS,
- CIBER Enf Respiratorias,
- REIPI,
- Mutua Madrileña,
- European Community funds,
- Fundación del Pino

Payment for conferences:

- Pfizer,
- Novartis,
- Astellas,
- Wyeth Lederle
- and other private and public sources

Nothing to disclose for this talk.
The title of my topic: 
“My antibiotics days.....”

Four Decades of Personal Relationships with Infectious Diseases and Antimicrobial Agents.
1970's

Phlebotomies to insert plastic catheters.
Ampicillin-Gentamicin the selection of choice.

1971-75
1970's

The difficulties of an stable IV line.

MRSA was practically unexistant

Ampicillin and Aminoglycosides: common choice
Bone-Marrow Transplantation: Carbenicillin-Gentamicin

1975-77
In 11 patients receiving transplants of allogeneic bone marrow, the graft was successful in six. Nine patients developed infections, and six died—five of septicaemia and one of Pneumocystis carinii pneumonia. Fifty individual infections occurred. Predisposing factors included severe underlying diseases, long-term exposure to resistant hospital organisms, heavy immunosuppressive therapy, and graft-versus-host disease. Gram-negative bacilli and Candida albicans were the most common causative organisms. In every instance of septicaemia identical organisms were isolated from blood cultures obtained on the clinical day and from bone marrow.
1970's: Neutropenia and sorrow

Pseudomonas aeruginosa: Antibiotics and more

Gentamicin: Clinical Use with Carbenicillin and In-Vitro Studies with Recent Isolates of Pseudomonas aeruginosa

Lowell S. Young

From the Infectious Disease Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, and Cornell University Medical College, New York

THE JOURNAL OF INFECTIOUS DISEASES • VOL. 126, NO. 3 • SEPTEMBER 1972
© 1972 by the University of Chicago. All rights reserved.

Human Immunity to Pseudomonas aeruginosa.
I. In-Vitro Interaction of Bacteria, Polymorphonuclear Leukocytes, and Serum Factors

Lowell S. Young and Donald Armstrong

From the Infectious Disease Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York
1970's: Neutropenia and sorrow

Combination of Carbenicillin and AGLx

In-Vitro Activity of Carbenicillin and Results of Treatment of Infections due to Pseudomonas with Carbenicillin Singly and in Combination with Gentamicin

Charles B. Smith,* James N. Wilfert, Peter E. Dans,† Thomas A. Kurrus, and Maxwell Finland

From the Thorndike Memorial Laboratory, Boston, Massachusetts; and the Department of Medicine, University of Michigan, Ann Arbor, Michigan

Vol. 284 No. 19 EMPIRIC THERAPY WITH CARBENICILLIN-GENTAMICIN—SCHIMPFF ET AL.

EMPIRIC THERAPY WITH CARBENICILLIN AND GENTAMICIN FOR FEBRILE PATIENTS WITH CANCER AND GRANULOCYTOPENIA*

Stephen Schimpff, M.D., Winston Satterlee, M.D., Viola Mae Young, Ph.D., and Arthur Serpick, M.D.
1970's

Trimethoprim-Sulfamethoxazole and the treatment of *P. carinii* pneumonia
1970's: *P. carinii* pneumonia (PCP)

TRIMETHOPRIM–SULFAMETHOXAZOLE TREATMENT OF *PNEUMOCYSTIS CARINII* PNEUMONIA IN ADULTS

William K. Lau, M.D., and Lowell S. Young, M.D.

*Pneumocystis carinii* pneumonia in the immunosuppressed patient is usually fatal if untreated.\(^1\)\(^-\)\(^3\) For several years, pentamidine isethionate or intravenous solution (80 mg of trimethoprim and 400 mg of sulfamethoxazole per 5-ml ampule) supplied by Roche Laboratories, Nutley, New Jersey.

Four of eight patients had a clinical response to co-trimoxazole, as evidenced by a rapid defervescence, resolution of pulmonary infiltrates and improvement in arterial oxygen tension. Defervescence was the most sensitive indicator of patient response, usually occurring between the second and fourth days of treat-
1970's: *P. carinii* pneumonia (PCP)

SUCCESSFUL CHEMOPROPHYLAXIS FOR *PNEUMOCYSTIS CARINII* PNEUMONITIS

Walter T. Hughes, M.D., Shirley Kuhn, R.N., Subhash Chaudhary, M.D., Sandor Feldman, M.D., Manuel Verzosa, M.D., Rhomesh J.A. Aur, M.D., Charles Pratt, M.D., and Stephen L. George, Ph.D.

Abstract  In a randomized, double-blind, placebo-controlled study to evaluate the efficacy of trimethoprim-sulfamethoxazole for the prevention of *Pneumocystis carinii* pneumonia, we studied 160 patients with cancer who were at high risk for this pneumonia over a two-year period. Seventeen of the 80 patients receiving a placebo acquired *P. carinii* pneumonia, whereas none of the 80 given 150 mg of trimethoprim and 750 mg of sulfamethoxazole per square meter per day had the infection (P<0.01). Bacterial sepsis, pneumonia other than that caused by *P. carinii*, acute otitis media, upper-respiratory-tract infections, sinusitis and cellulitis occurred less frequently in recipients of the drug than in the placebo group (P<0.01 in each case). Oral candidiasis was the only adverse effect encountered from trimethoprim-sulfamethoxazole administration. The study shows the combination to be highly effective in the prevention of *P. carinii* pneumonia. (N Engl J Med 297:1419-1426, 1977)

0/80  
SXT had PCP.

17/80  
Placebo had PCP.

Hughes WT. NEJM. 1977
My discovery of anaerobes: Oral Chloramphenicol
Sid Finegold. UCLA

Perfect anti-anaerobic spectrum
Total oral absorption
Gram positives
Gram negatives

Irreversible myelotoxicity perceived as irrelevant.
Choramphenicol: Oral and IV

PRELIMINARY REPORT ON THE USE OF CHLORAMPHENICOL (CHLOROMYCETIN) IN THE TREATMENT OF ACUTE GONORRHEAL URETHRITIS

By J. E. SmaDEL, C. A. BAILEY, and D. S. MANKIKAR

(From the Army Medical Department Research and Graduate School, the Commission on Immunization of the Army Epidemiological Board, Washington, D. C., and the Institute for Medical Research, Kuala Lumpur, Malaya)

THE JOURNAL OF INFECTIOUS DISEASES • VOL. 126, NO. 5 • MAY 1972
© 1972 by the University of Chicago. All rights reserved.

Treatment of Hemophilus influenzae Meningitis: A Comparison of Chloramphenicol and Tetracycline

Kenrad E. Nelson, Stuart Levin, Harold W. Spies,* and Mark H. Lepper

From the Department of Preventive Medicine and Community Health, University of Illinois College of Medicine, the Department of Medicine, Rush-Presbyterian-St. Luke's Medical Center; and the Municipal Contagious Disease Hospital, Chicago, Illinois
1970's: Chloramphenicol indications

Infections caused by anaerobic bacteria
No much fear about adverse events
1970's: Legionnaires' Disease (July 1976)

The New England Journal of Medicine

Description of an Epidemic of Pneumonia

David W. Fraser, M.D., Theodore R. Tsai, M.D., Walter Orenstein, M.D., William E. Parkin, D.V.M., Dr. P.H., H. James Beecham, M.D., Robert G. Sharrar, M.D., John Harris, M.D., George F. Mallison, M.P.H., Stanley M. Martin, M.S., Joseph E. McDade, Ph.D., Charles C. Shepard, M.D., Philip S. Brachman, M.D., and the Field Investigation Team*

The hotel in Philadelphia and the American Legion. Erythromycin works for this entity.
LEGIONNAIRES' DISEASE

Isolation of a Bacterium and Demonstration of Its Role in Other Respiratory Disease

JOSEPH E. MCDADE, PH.D., CHARLES C. SHEPARD, M.D., DAVID W. FRASER, M.D., THEODORE R. TSAI, M.D., MARTHA A. REDUS, WALTER R. DOWDLE, PH.D., AND THE LABORATORY INVESTIGATION TEAM*
1970's: Legionnaires' Disease in Britain

Erythromycin in legionnaire's disease

Sir,—Your leading article on legionnaire's disease (11 November, p 1319) comments that “American enthusiasm for erythromycin was not justified by the British experience.” We saw three patients with a confirmed diagnosis of legionnaire’s disease last summer who were all treated with erythromycin. They all recovered, though one developed renal failure requiring temporary peritoneal dialysis.

A particularly dramatic clinical response to erythromycin was shown in the third case, that of a 34-year-old woman admitted five days after returning from holiday in Spain. She had been unwell for three days with cough, headache, and vomiting with some diarrhoea.

M W McKendrick
A M Geddes

Department of Communicable and Tropical Diseases,
East Birmingham Hospital,
Birmingham


The Disease was present also in Europe and in the rest of the World.

The macrolides resucitation
1970's: Legionnaires' Disease in Spain

Pleural effusion
Pericardial effusion
Cavitary disease
1970's

Coccidioidomycosis and amphotericin B deoxycolate
1970's: My discovery of regional mycoses

Coccidioidal Meningitis
An Analysis of Thirty-one Cases and Review of the Literature

EMILIO BOUZA, M.D., JERROLD S. DREYER, M.D., WILLIAM L. HEWITT, M.D., RICHARD D. MEYER, M.D.
Coccidioides immitis
1970’s: Amphotericin B. The toxicity of drugs

Intrathecal administration of Amphotericin B.
Typhoid fever: other use of Chloramphenicol

1978–84
A disease eradicated with democracy in Spain.

1980's

Brucellosis: an experiment in combination therapy
1980’s: Brucellosis

Combination treatment: Tetra. & Streptomycin

INTERNATIONAL NOTES

Brucellar Meningitis

Emilio Bouza, Manuel García de la Torre, Francisco Parras, Antonio Guerrero, Marta Rodríguez-Créixems, and José Gobernado

From the Infectious Diseases Unit (Microbiology Service) and the Neurology Service, Hospital Ramón y Cajal, Madrid, Spain

Neurobrucellosis develops in less than 5% of cases of systemic brucellosis; however, most patients with neurobrucellosis have meningeal involvement. Seven new cases of brucellar meningitis and 17 cases from the Spanish- and English-language medical literature are analyzed in terms of epidemiologic data, clinical manifestations, laboratory results for cerebrospinal fluid and serum, treatment, and course of the disease. Brucellar meningitis mimics other neurologic and nonneurologic conditions, and its diagnosis is only suggested in the presence of adequate epidemiologic information. Isolation of Brucella from the cerebrospinal fluid is uncommon. Treatment is accomplished with the combination of tetracycline or doxycycline and streptomycin, rifampin, or both. Mean length of therapy in the seven new cases was 6 months. Brucellar meningitis has a better prognosis than other neurodegenerative processes.

Laboratory-acquired brucellosis: a Spanish national survey


Servicio de Microbiología Clínica-Unidad de Enfermedades Infecciosas-VIH, Hospital General Universitario 'Gregorio Marañón', Universidad Complutense, Madrid, Spain

Received 8 April 2002; accepted 21 February 2005
Brucellosis cases, HGUGM, 25 years
Drug addiction, an unexpected need for antibiotics

1980's

1984 - ......
1980’s: Infections in IV drug abuse

Extrapharyngeal Group A Streptococcal Infections

Syphilis in IV drug abusers

Old penicillin, still the drug of choice
Fleming’s visit to Spain 1948
Fleming’s visit to Spain 1948
1980's

Third generation Cephalosporins and clinical trials.
Comparative Multiple-Dose Pharmacokinetics of Cefotaxime, Moxalactam, and Ceftazidime

RUEDI LÜTHY,1• JÜRG BLASER,1,2 ANTONIO BONETTI,1 HANSPETER SIMMEN,1 RICHARD WISE,3 AND WALTER SIEGENTHALER1

Ceftazidime in patients with pseudomonas infections

Lawrence J. Eron, Choong H. Park, Deborah L. Hixon, Robin I. Goldenberg and Donald M. Poretz

Eron LJ. J.A.C. 1981

Luthy R. A.A.C. 1981
Old Vancomycin back in business
The need for Vancomycin:

1980's: MRSA epidemic in HGUGM.
The AIDS Epidemic: San Francisco and the World
1980’s: AIDS. Viral Diseases

Ocular CMV: The use of Gancyclovir

- 20-40% of AIDS patients
- CD4 < 50 uL
- Eye, GI Tract
- Disseminated...
1980's: AIDS. Viral Diseases

Extensive HSV infections

- SSTI
- Visceral
- Acyclovir Resistance
1980's: AIDS Epidemic. HGUGM

Contribution to *S. aureus* BSI's

<table>
<thead>
<tr>
<th>Year</th>
<th>HIV(-)</th>
<th>HIV(+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1985</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>1986</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>1987</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>1988</td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>1989</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1991</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>1992</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>1993</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

© by author
**1980’s: AIDS Epidemic. HGUGM**

**Contribution to S. pneumoniae BSI’s**

<table>
<thead>
<tr>
<th>Year</th>
<th>VIH (-)</th>
<th>VIH (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>85</td>
<td>41</td>
<td>3</td>
</tr>
<tr>
<td>86</td>
<td>41</td>
<td>1</td>
</tr>
<tr>
<td>87</td>
<td>47</td>
<td>7</td>
</tr>
<tr>
<td>88</td>
<td>45</td>
<td>6</td>
</tr>
<tr>
<td>89</td>
<td>54</td>
<td>10</td>
</tr>
<tr>
<td>90</td>
<td>48</td>
<td>13</td>
</tr>
<tr>
<td>91</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>92</td>
<td>54</td>
<td>13</td>
</tr>
<tr>
<td>93</td>
<td>73</td>
<td>3</td>
</tr>
<tr>
<td>94</td>
<td>85</td>
<td>6</td>
</tr>
<tr>
<td>95</td>
<td>73</td>
<td>7</td>
</tr>
<tr>
<td>96</td>
<td>88</td>
<td>12</td>
</tr>
<tr>
<td>97</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>98</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>99</td>
<td>85</td>
<td>13</td>
</tr>
<tr>
<td>00</td>
<td>48</td>
<td>2</td>
</tr>
<tr>
<td>01</td>
<td>48</td>
<td>2</td>
</tr>
<tr>
<td>02</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>03</td>
<td>27</td>
<td>22</td>
</tr>
<tr>
<td>04</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>05</td>
<td>35</td>
<td>18</td>
</tr>
<tr>
<td>06</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>07</td>
<td>34</td>
<td>18</td>
</tr>
<tr>
<td>08</td>
<td>36</td>
<td>3</td>
</tr>
<tr>
<td>09</td>
<td>36</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>79</td>
<td>13</td>
</tr>
<tr>
<td>11</td>
<td>85</td>
<td>18</td>
</tr>
<tr>
<td>12</td>
<td>85</td>
<td>18</td>
</tr>
<tr>
<td>13</td>
<td>48</td>
<td>2</td>
</tr>
<tr>
<td>14</td>
<td>48</td>
<td>2</td>
</tr>
</tbody>
</table>

**Legend:**
- VIH (-): Green bars
- VIH (+): Red bars

%:
- VIH (-): 7 2 13 12 18 22 24 11 18 22 36 36 36 12 26 22 27 26 23 23 26 28 19 19 25 17 21 26
- VIH (+): 7 2 6 10 13 17 19 16 24 30 32 21 22 21 28 23 22 25 26 34 27 23 27 18 13 17
1980’s: AIDS. Pneumonia

*S. pneumoniae* less mortality than expected

- Unilateral infiltrates (76%)
- More bacteremia
- Low mortality
1980's: AIDS. *S. pneumoniae*

Necrotizing pneumococcal pneumonia
The issue of resistance to penicillin and the proper treatment of meningitis in the 1980's: *Streptococcus pneumoniae*.
Mycobacterium tuberculosis
A total of 67 cases of tuberculosis was diagnosed in the first 100 cases of AIDS, diagnosed according to the former CDC criteria, at a hospital in Madrid, Spain. This is the highest known prevalence of tuberculosis in AIDS patients both within and outside Spain. The clinical manifestations of tuberculosis were very variable and atypical. The rate of isolation of Mycobacterium tuberculosis....
1980's: AIDS. Other manifestations

TUBERCULOUS MENINGITIS IN PATIENTS INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS

Juan Berenguer, M.D., Santiago Moreno, M.D., Fernando Laguna, M.D., Teresa Vicente, M.D., Magdalena Adrados, M.D., Arturo Ortega, M.D., Juan González-LaHoz, M.D., and Emilio Bouza, M.D.

Ocular Tuberculosis

A Prospective Study in a General Hospital

Emilio Bouza, Pilar Merinó, Patricia Muñoz, Carlos Sanchez-Carrillo, Jacobo Yáñez, and Carlos Cortés

Caution with interferences with other drugs
Mycobacterium tuberculosis
1980's: AIDS. Tuberculosis

*Mycobacterium tuberculosis* Visceral Abscesses in the Acquired Immunodeficiency Syndrome (AIDS)


Again combination therapy was the solution
1980's: AIDS. New PCP

More smoldering but still treatable with SXT. The lessons from the neutropenic patients
1980's: AIDS. New Cryptococcosis

An uncommon disease became frequent. Ampho+ 5FC
1980’s: AIDS. New Parasitic infections

Visceral Leishmaniasis in Human Immunodeficiency Virus (HIV)-Infected and Non-HIV-Infected Patients

A Comparative Study

Vicente Pintado, M.D., Pablo Martín-Rabadán, M.D., María Luisa Rivera, M.D., Santiago Moreno, M.D., and Emilio Bouza, M.D.

The problems with glucanthime.
The role of Ampho B
The use of Myltefosine
1990's

The AIDS Epidemic points to a solution: Combination antimicrobial therapy
The Vancouver Conference.
Three drugs do much more than two

One World, One Hope
1990's

The transplantation boom: The need to care for interactions with antibiotics
1990's: Infections in SOT

Old and new microorganisms. Drug interactions

Tuberculosis in Heart Transplant Recipients

P. Muñoz, J. Palomo, R. Muñoz, M. Rodríguez-Creixéms, T. Pelaez, and E. Bouza

From the Divisions of Microbiology-Infectious Diseases and Cardiology, Hospital Universitario “Gregorio Marañón,” Madrid, Spain

Pneumocystis carinii Infection in Heart Transplant Recipients

Efficacy of a Weekend Prophylaxis Schedule

Patricia Muñoz, Rosa María Muñoz, Jesús Palomo, Marta Rodríguez-Creixéms, Roberto Muñoz, and Emilio Bouza
1990’s: Infections in SOT

Old and new microorganisms. Drug interactions

Munoz P. RHODOCOCCUS EQUI INFECTION IN TRANSPLANT RECIPIENTS.
Transplantation 1998.
1990's: Infections in SOT

Kaposi Sarcoma caused by Herpes Virus

Incidence and Clinical Characteristics of Kaposi Sarcoma After Solid Organ Transplantation in Spain

Importance of Seroconversion Against HHV-8

PATRICIA MUÑOZ, PATRICIA ALVAREZ, FERNANDO DE ORY, FRANCISCO POZO, MARISA RIVERA, AND EMILIO BOUZA

Medicine (Baltimore) 2002
The growing need for Vascular Catheters: Antibiotic locks
1990's: IV catheters
1990’s: IV catheters
1990's: Antibiotic lock-therapy

Randomized, Double-Blind Trial of an Antibiotic-Lock Technique for Prevention of Gram-Positive Central Venous Catheter-Related Infection in Neutropenic Patients with Cancer

JORDI CARRATALÀ, JORDI NIUBÓ, ALBERTO FERNÁNDEZ SEVILLA, EULALIA JUVÉ, XAVIER CASTELLSAGUÉ, JUAN BERLANGA, JOSEFINA LINARES, AND FRANCESC GUDIOL

Stability of Antibiotics Used for Antibiotic-Lock Treatment of Infections of Implantable Venous Devices (Ports)

THIELE UMALI ANTHONY AND LORRY G. RUBIN
Ethanol lock therapy in the prevention of catheter-related bloodstream infections after major heart surgery

M.J. Pérez, J.M. Barrio*, C. Rincón, J. Hortal, P. Martín-Rabadán, S. Pernia, E. Bouza (Madrid, ES)

Prospective randomized, clinical trial
Intensive Care Unit post Major Heart Surgery
Prevention of CR-BSI, Tolerance

Ethanol Locks every 3 days

Pérez-Granda M. ECCMID 2012
2000’s: Antimicrobial therapy is more complex
2000's

New and promising anti-Gram positive drugs
2000's

IV Antibiotics at home
Some consequences of antimicrobial abuse: ESKAPE microorganisms
ESKAPE microorganisms

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>E</th>
<th>S</th>
<th>K</th>
<th>C</th>
<th>A</th>
<th>P</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nosocomial acquisition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmissible</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Universal distribution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High burden</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficult to treat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Some consequences of antimicrobial use: Clostridium difficile
CDI: England and Wales

CDI: Incidence in Europe

< 1/10,000
1-2/10,000
2-5/10,000
5-10/10,000
>10/10,000

Bauer M. Lancet. 2011

4.1/10,000 days
0.0 -19.1/10,000
Resistance to Metronidazole?

Reassessment of *Clostridium difficile* Susceptibility to Metronidazole and Vancomycin

T. Peláez, L. Alcalá, R. Alonso,* M. Rodríguez-Créixems, J. M. García-Lechuz, and E. Bouza

Microbiology and Infectious Diseases Service, Hospital General Universitario “Gregorio Marañón,” Madrid, Spain

Received 10 August 2001/Returned for modification 1 November 2001/Accepted 10 February 2002

In Vitro Activity of Ramoplanin against *Clostridium difficile*, Including Strains with Reduced Susceptibility to Vancomycin or with Resistance to Metronidazole

T. Peláez,* L. Alcalá, R. Alonso, A. Martín-López, V. García-Arias, M. Marín, and E. Bouza

Department of Clinical Microbiology and Infectious Diseases, Hospital General Universitario “Gregorio Marañón,” Madrid, Spain
New drugs?

Fidaxomicin versus Vancomycin for Clostridium difficile Infection

Phase 3 Clinical Trial. Adults with CD

Fidaxomicin 200 mg bid p.o.

Vancomycin 125 qid p.o.

2000's

Influenza again:
2000’s: Influenza H1N1

Better knowledge of antiviral agents. New drugs
2000’s: Influenza H1N1

Better knowledge of antiviral agents. New drugs

Clinical Experience in Adults and Children Treated with Intravenous Peramivir for 2009 Influenza A (H1N1) Under an Emergency IND Program in the United States

Jaime E. Hernandez,1 Raghavendra Adiga,4 Robert Armstrong,5 Jose Bazan,7 Hector Bonilla,8 John Bradley,6 Robin Dretler,9 Michael G. Ison,10 Julie E. Mangino,7 Stacene Maroushek,11 Avinash K. Shetty,2 Anna Wald,12 Christine Ziebold,13 Jenna Elder,3 Alan S. Hollister,1 and William Sheridan,1 on behalf of the eIND Peramivir Investigators

Hernández J. C.I.D. 2011
2000's

The fungus problems and antifungal therapy
2000’s: The fungus problems

Candins everywhere

Demolition of a hospital building by controlled explosion: the impact on filamentous fungal load in internal and external air

E. Bouza, T. Peláez, J. Perez-Molina, M. Marín, L. Alcalá, B. Padilla, P. Muñoz and the Aspergillus Study Team*
2000’s: The fungus problems

Common and uncommon fungal pathogens are still very difficult to treat

Risk Factors of Invasive Aspergillosis after Heart Transplantation: Protective Role of Oral Itraconazole Prophylaxis

Patricia Muñoz, Claudia Rodriguez, Emilio Bouza, Jesús Palomo, Juan F. Yanez, María Jesús Domínguez and Manuel Desco

Opportunistic Mycelial Fungal Infections in Organ Transplant Recipients: Emerging Importance of Non-Aspergillus Mycelial Fungi

Shahid Husain, Barbara D. Alexander, Patricia Muñoz, Robin K. Avery, Sally Houston, Timothy Pruett, Richard Jacobs, Edward A. Domínguez, Jan G. Tollemer, Katherine Baumgarten, Chen M. Yu, Marilyn M. Wagen, Peter Linden, Shimon Kusne, and Nina Singh
Combination of Voriconazole and Caspofungin as Primary Therapy for Invasive Aspergillosis in Solid Organ Transplant Recipients: A Prospective, Multicenter, Observational Study

Nina Singh, Ajit P. Limaye, Graeme Forrest, Nasia Safdar, Patricia Muñoz, Kenneth Pursell, Sally Houston, Fernando Rosso, Jose G. Montoya, Pamela Patton, Ramon del Busto, Jose M. Aguado, Robert A. Fisher, Goran B. Klintalm, Rachel Miller, Marilyn M. Wagener, Russell E. Lewis, Dimitrios P. Kontoyiannis, and Shahid Husain
The need to return to old drugs and old practices?
Efficacy and safety of high-dose ampicillin/sulbactam vs. colistin as monotherapy for the treatment of multidrug resistant Acinetobacter baumannii ventilator-associated pneumonia

Alex P. Betrosian, Frantzeska Frantzeskaki, Anna Xanthaki, Emmanuel E. Douzinis

Betrosian AP. J. Infections 2008
Sugar for the local treatment of infected wounds

2000’s: Old methods still usefull
The 2010’s: The Future

"It is difficult to make predictions, especially about the future"

Niels Bohr

Prevention is going to be the main issue in the field of I. D.
The 2010’s: The Future of young teams
2010’s: The future of antimicrobials
Thank you