“But now I recall all the times when it was so important that I stay inside, a book I had to read or sometimes write, a game I had to watch on TV. I was too busy so many times. So many out-of-town trips, daddy-daughter dinners missed at the school, dance recitals I had to pass up. And then we are out of time”.........

George Cantor; Sept., 1998
Back in the Day....

Infectious Diseases Then and Now:
The Evolution of ID Strategies

G. Blackburn DO, MACOI
ACOI’s 77th Annual Convention and Scientific Sessions
Phoenix
October, 2019
• Disclosures: none

• Comments: my own (only slightly filtered)
Assassination of John F. Kennedy
November 22, 1963
1968
(1955 - 1975)
> 58,000 U.S. deaths
1.5 - 3.6 million total deaths
Assassination of Robert F. Kennedy
June 6, 1968
Assassination of Martin Luther King Jr
March 3, 1969
Stonewall Inn Riots
June 28, 1969
Actress Is Among 5 Slain At Home in Beverly Hills

Sharon Tate, 2d Woman and 3 Men Victims—Suspect Is Seized

By STEVEN V. ROBERTS Special to The New York Times

LOS ANGELES, Aug. 9—Five persons, including the actress Sharon Tate, were found this morning brutally murdered in a home in a secluded area of Beverly Hills.

The home, perched on a wooded hillside overlooking the city of Los Angeles, was being rented by Miss Tate and her husband, Roman Polanski, the movie director, who was in London at the time writing a script for a new movie.

The other victims were identified as Jay Sebring, a men's hair stylist well known in Hollywood social circles; Voytek Frykowski, a Polish film director said to be a close friend of Mr. Polanski; Mr. Frykowski's girl friend, Abigail Folger, a member of the Folger coffee family, and a fifth man who remained unidentified.

The police arrested William Garretson, a 19-year-old caretaker, and charged him with suspected murder. Mr. Garretson was asleep in a small cottage near the main house of the property when the police arrived this morning.

The Los Angeles coroner, Thomas Noguchi, told a news conference that there was no evidence that a party had taken place or that narcotics had been used. He said that no murder weapon had been found. He also said that there was no

Continued on Page 69, Column 1.

August 9, 1969
August 15-18, 1969
CCOM 1969-1973

- My heroes:
  - Ward Perrin DO “WEP”
  - Steve Sokalski DO (Inf Dx)
  - Michael James DO
  - William Peppo DO
  - Paul Benchwick DO
  - Larry Haspel DO
  - Tom Allen DO
  - Don Hollingsworth DO
D.O.H.
1973-74

- My Heroes:
  - Michael Opipari DO
  - Michael Demattia DO
  - James Beck DO
  - Augie Perrotta DO
  - Ronald Blonder DO
Botsford Hospital
1974 - 1976

- the “Susser Group”, including
  - David Susser DO (Cardiology)
  - Michael Biederman DO (GI)
  - Eugene Oliveri DO (GI)
  - Larry Wickless DO (GI)
  - Ray Gadowski DO (Cardiology)
  - Chuck Tenner DO (Endocrine, Pulmonology)
  - Bert Rabinowitz DO (Pulmonology)
  - Joe Kessler DO (Nephrology)
  - Morris Lieberman DO (Oncology)
  - Paul Wenig DO (Rheumatology)
Wayne State University
Infectious Disease Fellowship
1976 - 1978


- My Heroes:
  - Ralph Cushing MD
  - Carl Lauter MD
“You know nothing, G. Blackburn....”
Life before Antibiotics

- War casualties and other trauma
- Intra-abdominal catastrophes
- Bacterial meningitis
- Endocarditis
- Syphilis, gonorrhea
Vaccine Preventable Diseases - Then

- measles
- mumps
- rubella
- diphtheria
- pertussis
- tetanus
- polio
- rabies (older version)
- smallpox
<table>
<thead>
<tr>
<th>Vaccine Preventable Diseases - Now</th>
</tr>
</thead>
<tbody>
<tr>
<td>• measles</td>
</tr>
<tr>
<td>• mumps</td>
</tr>
<tr>
<td>• rubella</td>
</tr>
<tr>
<td>• diphtheria</td>
</tr>
<tr>
<td>• dengue</td>
</tr>
<tr>
<td>• pertussis</td>
</tr>
<tr>
<td>• tetanus</td>
</tr>
<tr>
<td>• influenza</td>
</tr>
<tr>
<td>• polio</td>
</tr>
<tr>
<td>• rabies</td>
</tr>
<tr>
<td>• hepatitis A</td>
</tr>
<tr>
<td>• hepatitis B</td>
</tr>
<tr>
<td>• pneumococcus</td>
</tr>
<tr>
<td>• smallpox</td>
</tr>
<tr>
<td>• ebola</td>
</tr>
<tr>
<td>• chlamydia (?)</td>
</tr>
<tr>
<td>• malaria (early)</td>
</tr>
<tr>
<td>• meningococcus /</td>
</tr>
<tr>
<td>• H. influenza</td>
</tr>
<tr>
<td>• H. zoster (chickenpox)</td>
</tr>
<tr>
<td>• H. zoster (shingles)</td>
</tr>
<tr>
<td>• HPV</td>
</tr>
<tr>
<td>• Japanese encephalitis</td>
</tr>
<tr>
<td>• rotavirus</td>
</tr>
<tr>
<td>• typhoid</td>
</tr>
<tr>
<td>• cholera</td>
</tr>
</tbody>
</table>
Rabies

- Early 1900s (U.S.): ~100/yr
  now: < 2/yr
- Worldwide: still 55,000/yr

- Prophylaxis back in the day......
  21 painful intra-abdominal injections
- Now: 4 IM injections
Tetanus

- ~29 cases/yr (U.S.); 2 deaths
- Worldwide: still 59,000 deaths/yr
Vaccine “hesitancy” now listed as one of top ten Global Health Threats for 2019

Unvaccinated boy nearly died from tetanus. The cost of his care was almost $1 million.

6-year-old was infected in 2017 while playing on the family's farm, the first case of tetanus in Oregon in 30 years, according to a CDC report.
Polio ("infantile paralysis") - early 1950s
Measles -

• ~1980: est. 2.6 million deaths/yr (worldwide)

• In the U.S., prior to 1963
  • 2 - 4 million cases of measles
  • 48,000 hospitalizations
  • 4000 cases of encephalitis, 1/4 of which suffered life-long disabilities
  • 100 - 400 cases of SSPE
  • 400 - 500 deaths (~1 in 10,000)(other references cite 1 - 2 in 1000)
Measles

• Worldwide, still kills over 90 - 120,000 (mostly) children/yr; 400 deaths/day in 2013

• Mortality may be as high as 1 in 10 in countries where severe malnutrition is rampant

• Infrequently seen in the U.S. and other advanced countries until recently (1,182 cases as of 8/08/19)

• Nearly 100% preventable

• Estimated 21,000,000 deaths prevented since 2000 by vaccination (Paules et al NEJM June 6, 2019)
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>U.S. deaths/yr</th>
<th>Deaths worldwide/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>&lt; 2000</td>
<td>1,000,000</td>
</tr>
<tr>
<td>H. influenza</td>
<td>&lt; 5</td>
<td>199,000</td>
</tr>
<tr>
<td>Menningococcus</td>
<td>120</td>
<td>50,000</td>
</tr>
<tr>
<td>Measles</td>
<td>&lt; 1</td>
<td>&gt; 90,000</td>
</tr>
<tr>
<td>Pertussis</td>
<td>&lt; 20</td>
<td>160,000</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>&lt; 22,000</td>
<td>826,000</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>&lt; 10</td>
<td>215,000</td>
</tr>
<tr>
<td>Chickenpox</td>
<td>&lt; 20</td>
<td>&gt; 4200</td>
</tr>
<tr>
<td>Polio</td>
<td>0</td>
<td>? (but few)</td>
</tr>
<tr>
<td>Smallpox</td>
<td>0</td>
<td>0 (1967 - 5,000,000)</td>
</tr>
</tbody>
</table>
Newly Described or Newly Emerged Infectious Diseases Since the Late ‘70s

<table>
<thead>
<tr>
<th>Category</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Flaccid Myelitis</td>
<td>Antibiotic-resistant gonorrhea</td>
</tr>
<tr>
<td>Anaplasmosis</td>
<td>Hanta virus</td>
</tr>
<tr>
<td>Agents of Bioterrorism</td>
<td>HIV</td>
</tr>
<tr>
<td>Chikungunya</td>
<td>Legionnaire’s dx</td>
</tr>
<tr>
<td>Candida auris</td>
<td>Lyme dx</td>
</tr>
<tr>
<td>C. difficile</td>
<td>MDR GNRS</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>MERS</td>
</tr>
<tr>
<td>“Flesh-eating” Grp A strep</td>
<td>Erlichiosis</td>
</tr>
<tr>
<td>MRSA, including “CA” MRSA</td>
<td>SARS</td>
</tr>
<tr>
<td>TSS</td>
<td>VRE</td>
</tr>
<tr>
<td>West Nile</td>
<td>XDR, MDR TB</td>
</tr>
<tr>
<td>Zika</td>
<td></td>
</tr>
</tbody>
</table>
Newly Described or Newly Emerged Infectious Diseases Since the Late ‘70s

- Hepatitis C
- Delta hepatitis
- Hepatitis E
- Hepatitis G (?)
- Marburg virus
- Lassa fever
- Ebola
- Prion dx
- Grp B strep infections in adults
- Whipples
- H. pylori
- Post-splenectomy sepsis
- Anaerobic microbiology
- Pneumocystis
- Microsporidiosis
- Acanthameba
- Naegleria
- Babesiosis
- Cryptosporidium
- Cyclospora
TO: ALL DISTRICT MANAGERS IN THE SOUTHERN REGION

FROM: SAM G. BROCK

SUBJECT: EASY PREY FOR TERRAMYCIN.

Computations from the latest Market Research Report reveal that the leading tetracycline product has advanced 4% during July and August over May and June. During this same period, Terramycin sales dropped 1/2 percentage point. This gain of tetracycline was picked up from a loss in Aureomycin sales. In other words, Aureomycin continues to account for a sizeable portion of the over-all market.

Competition is switching Aureomycin users directly to tetracycline. This is understandable since competition is deliberately selling Aureomycin down the river.

What do we do? We will help them to reduce the sale of Aureomycin by switching these doctors directly to Terramycin. Your men have a vast knowledge and experience in the ways and means to combat Aureomycin with a good solid Terramycin detail. Let's pick up the trail of all physicians who are using Aureomycin and concentrate on switching them to our side of the fence. Your representatives should know which doctors are using Aureomycin, which is the first step in the program.

On the more encouraging side, we continue to enjoy the leading position in private hospital purchasers with Terramycin; however, tetracycline is showing some inroads into the business. The next few weeks will be a very critical period, and may form the pattern for many months to come. It is imperative that you keep abreast of every situation in your district and waste no time in lending your full support to the troubled areas.

Your men should be impressed fully with the importance of their whole-hearted and best efforts. There is no reason whatsoever why Terramycin biotics.

SGB: no

cc: Mr. T. G. Bradley
    Mr. George Dugas
    Mr. C. H. Barwick
    Mr. H. R. Stewart

October 8, 1954
Clostridium difficile

• Back in the day (1973-74)…..

• Tedesco F. - *Clindamycin-Associated Colitis*
  
  • 200 pts:
    
    • 21% with diarrhea
    
    • 10% pseudomembranous colitis

• 1978 - C. difficile identified as culprit

C. difficile

- Est. 453,000 cases (2011 data for U.S.)
- Est. 29,000 deaths
- Still problems with diagnostic testing
- Rx continues to evolve, including stool transplant
• 1960s-70s
  
  • “Infectious” hepatitis (“A”)
    
    • short incubation
    
    • fecal - oral transmission
    
    • highly contagious
    
    • usually self-limited; no chronicity
    
    • vaccine introduced (in U.S.) 1995
• 1960s-70s

• “Serum” hepatitis (“B”)
  • discovered in 1965; vaccine available in 1981
  • longer incubation
  • parenteral or serum transmission
  • less contagious
  • chronic infection
  • Hmmmmmm…. once testing became available, screening decreased post-transfusion hepatitis by only 25 - 50%
Hepatitis C

• “Non A - Non B” hepatitis
  • recognized as a major cause of post-transfusion hepatitis
  • chronic hepatitis in 75% of cases, with progression to cirrhosis and liver cancer
  • early attempts at treatment ~ 1984
  • finally isolated and described in 1989 -> “Hepatitis C”
  • testing developed to remove from blood supply ~ 1990-1992
from Pawlotsky J-M, *From non-A, non-B hepatitis to hepatitis C virus cure.*
• 1882:
  - Robert Koch described the etiologic agent of TB
  - 1/3 of all infant deaths due to TB
  - 1/2 of all deaths between the ages of 15-45 due to TB
Back in the Day….

- TB was extremely common; in the early 1900s:
  - ~80% of U.S. population infected by age 30
  - Responsible for 1 of every 7 deaths in U. S.
  - Note: PPD introduced ~ 1907 w/ multiple refinements since then; BCG introduced in 1906
- 70,000 deaths/yr (U.S.) in the 1930s; 547 in 2009
As a health care worker, if your PPD is 10mm in induration, you are a candidate for prophylaxis for latent tuberculosis.

If 9 mm, you are not. Why not? What’s the difference?
Back in the Day….

• Treatment limited and often ineffective before the mid-1950s

• 1948 - Dr. Neal Browne, Minister of Health, Ireland:
  • No physical activity; absolute bed rest
  • Nutritious food; fresh air
  • 2 pints of Guiness daily

• 1954 - INH (resistance now an issue, including MDR, XDR, prophylaxis)
Back in the Day……..

- Mass screening
  - Mobile neighborhood Xray units
  - Widespread use of Tine skin testing
- Surgical approaches to treatment
  - Rib resection - “collapse” therapy
  - Induced pneumothorax; plombage
  - Lung resection
- Isolation - often for months or years
- Rx of 18 months or greater (even after 1954)
% of pts treated w/ "collapse therapy" (Canada)
Currently:

- 1/4 of the world’s population is infected w/ M. tuberculosis (2,000,000,000+)
- 10 million persons newly infected each year
- 1.6 million die/yr from tuberculosis (300,000 HIV+)
- The #1 infectious cause of death; 25% of all preventable deaths
- ~ 641 kids children die/DAY of tuberculosis
Closer to home…

- 9,105 cases of active TB reported in U.S. (2017)
- 547 deaths from TB in U.S. (2009)
- Foreign born persons have 15 times greater likelihood of developing active TB*
  - Asians greatest, but also
  - American Indians/Alaska Natives
  - Black/African American
  - Native Hawaiians/other Pacific Islanders
- Socioeconomic and genetic factors

Source: CDC June, 2019
Herpes Encephalitis

- Back in the day .......... (~mid seventies and later)
  - Hemorrhagic CSF (non-traumatic)
  - Diagnosis: Brain biopsy (CSF culture negative)
  - Treatment: Vidarabine (1976)
Herpes Encephalitis

• Currently…..

  • Non-hemorrhagic CSF (especially when obtained early) does not r/o this dx

  • Diagnosis: PCR for HSV 1

  • Treatment: Acyclovir
Sepsis

- Nebacumab (Centoxin ®): FDA approval denied - 1992

- Drotrecogin alfa (Xigris ®): withdrawn from marketplace - 2011

- Recombinant Human Soluble Thrombomodulin (the SCARLET trial) JAMA (May 28, 2019)
Somewhere between 1902 - 1932
a deadly virus silently enters the human population
June 5, 1981 MMWR:

Pneumocystis Pneumonia - Los Angeles

“In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed P. carinii pneumonia at 3 different hospitals in Los Angeles, CA. Two of the patients died. All 5 patients had laboratory confirmed previous or current CMV infection and candida mucosal infection.”
What was causing this disease (almost exclusively w/in the gay community in the U.S.)?

- Drugs?
- A transmissible agent?

- Over next few years, found to be due to a virus initially labeled HTLV-III

- Brutal stigma from this diagnosis; also a death sentence - median survival w/ dx of AIDS: 12 - 24 months

[see Frey J. You Have No Idea. JAMA 2011;306(5):469-470]
David Kirby's mother, Kay, holds a photograph of her son -- taken by Ohio photographer Art Smith -- before AIDS took its toll.

Therese Frare
Bill Kirby tries to comfort his dying son, David, 1990.
Therese Frare
Gay is not a choice
Milestones:

- **1985** - Ab testing available for screening U.S. blood supply
- **Late 1980’s/early 1990’s** - single drug rx; however, very toxic, very inconvenient, with benefits lasting only a short time
- **1996** - recognition that triple drug “cocktails” were reasonably effective at controlling progression of disease while limiting rapid development of resistance

Downside: very high pill burden, many serious side effects
The Bad News:

- 1.1 million HIV + in U.S.; (36.9 million worldwide)
- 1 in 7 unaware of their HIV +; many others in denial
- < 1/3 completely virally suppressed.
- 37,600 newly infected each year in U.S.; over 1/2 MSM - responsible for up to 30% of transmission!
- 38,000 newly diagnosed each year will present with advanced disease (16,000 will die)
The Good News:

- Extremely effective treatment w/ very minimal side effects w/ a single pill/day!
- Post-exposure prophylaxis (PEP) effective!
- Pre-exposure prophylaxis (PrEP) effective!
- U = U !!!!
On Being a (good) Doctor

- Curiosity

- Learn the name of that dog

- The only lasting “legacy” you will leave behind is what you have taught your students and have done by example
Someday, you, and all those you care about, will be a patient

How comfortable will you be if YOUR doctor turns out to be someone you trained?
On Being a D.O.

- Back in the day……
- Perhaps as a result, we worked harder
- Perhaps also as a result, we are all bothers and sisters - members of the same tribe…..
- We were different - are we still?
The Future

- Vaccines will continue to play a very important role in the prevention of potentially deadly diseases (someday... a “universal” flu vaccine?)

- Antibiotic and antiviral options will, in some cases, be limited, while in other cases be completely ineffective - there will be a greater role for alternative/supplemental approaches to infection e.g. phage therapy, manipulation of the microbiome (see below)

- The human microbiome will prove to be an amazing area of science yet to be explored and understood

- But... only half of I.D. Fellowships fill
“So….Blackburn….What’s going to kill us (and for which we are not prepared)?”

- Short of a global disaster, if you are otherwise reasonably healthy, it’s the common bugs that will kill most of us - staph, strep, E. coli, pneumococcus, influenza

- Nuclear war

- At the population level, an influenza-like virus with a high mortality - pandemic “Disease X” (think SARS)
“When the Next Big One arrives........it will be signaled first by quiet, puzzling reports from faraway places - reports to which disease scientists and public health officials, but few of the rest of us, pay close attention.”  
- D. Quammen. NYT 5/9/13

(Think “Reston” strain of Ebola, SARS MERS, pandemic H1N1)
“So….Blackburn….What’s going to kill us (and for which we are not prepared)?”

- Bioterrorist event - planned or unplanned

- Climate change, other environmental factors - change in range of many organisms (e.g. Vibrio, Naegleria, C. auris), vectors (Chaga’s dx, Zika), zoonoses

“….climate change is the greatest public health emergency of our time and is particularly harmful to fetuses, infants, children and adolescents”

Salas R.N. et al. NEJM May 30, 2019
Thank you