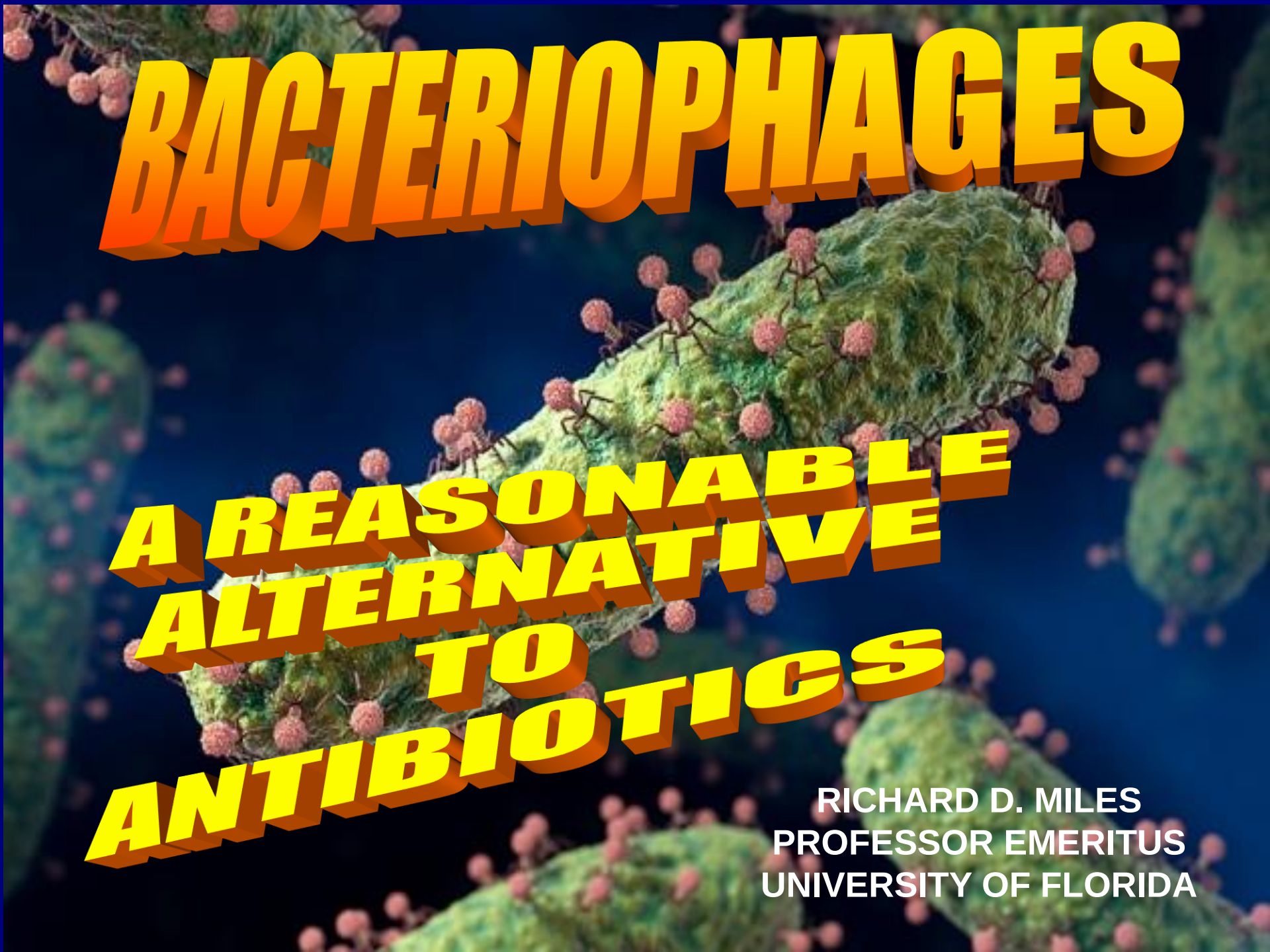
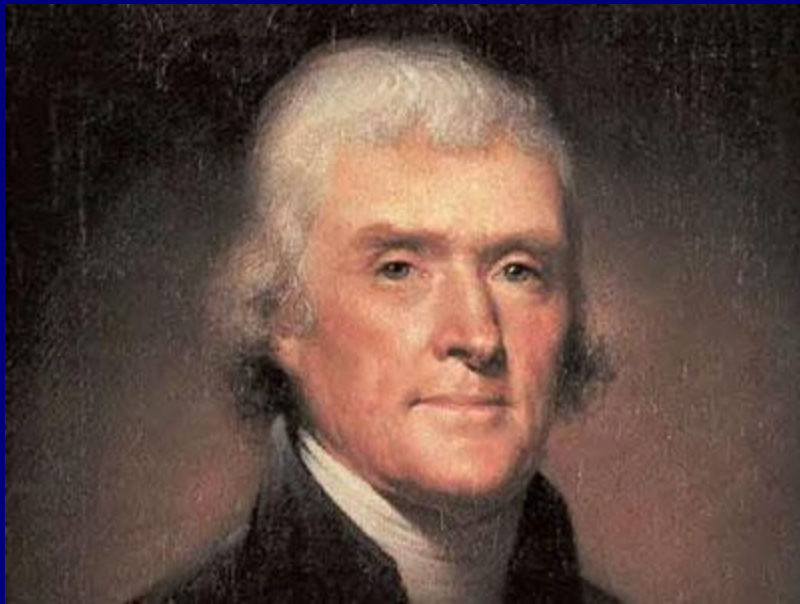


# **BACTERIOPHAGES**



**A REASONABLE  
ALTERNATIVE  
TO  
ANTIBIOTICS**

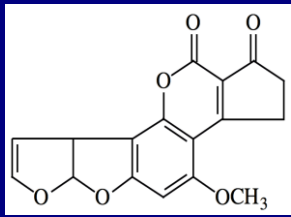
RICHARD D. MILES  
PROFESSOR EMERITUS  
UNIVERSITY OF FLORIDA



# THOMAS JEFFERSON

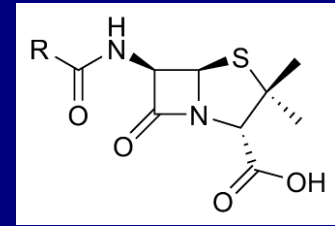
***“WHEN PEOPLE HAVE THE RIGHT INFORMATION  
THEY WILL MAKE THE RIGHT DECISIONS”***





AFLATOXIN B<sub>1</sub>

# MYCOTOXINS



PENICILLIN

**...SIMPLY STATED...**

**THEY ARE TOXIC MOLECULES PRODUCED BY FUNGI  
.....WITH ONLY ONE PURPOSE.....**

# TO KILL

**ANTI-BACTERIAL**

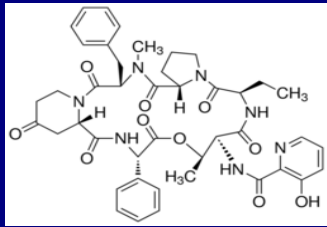
**ANTI-PROTOZOAN**

**ANTI-VIRAL**

**ANTI-INSECT**

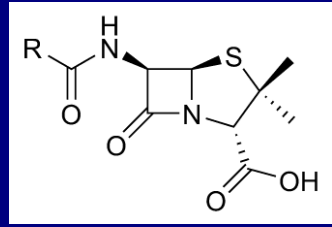
**ANTI- FOOD ANIMAL**

**ANTI-HUMAN**



VIRGINIAMYCIN

# ANTIBIOTICS



PENICILLIN

**...SIMPLY STATED...**

**THEY ARE TOXIC MOLECULES PRODUCED  
.....WITH ONLY ONE PURPOSE.....**

**TO KILL  
BACTERIA**

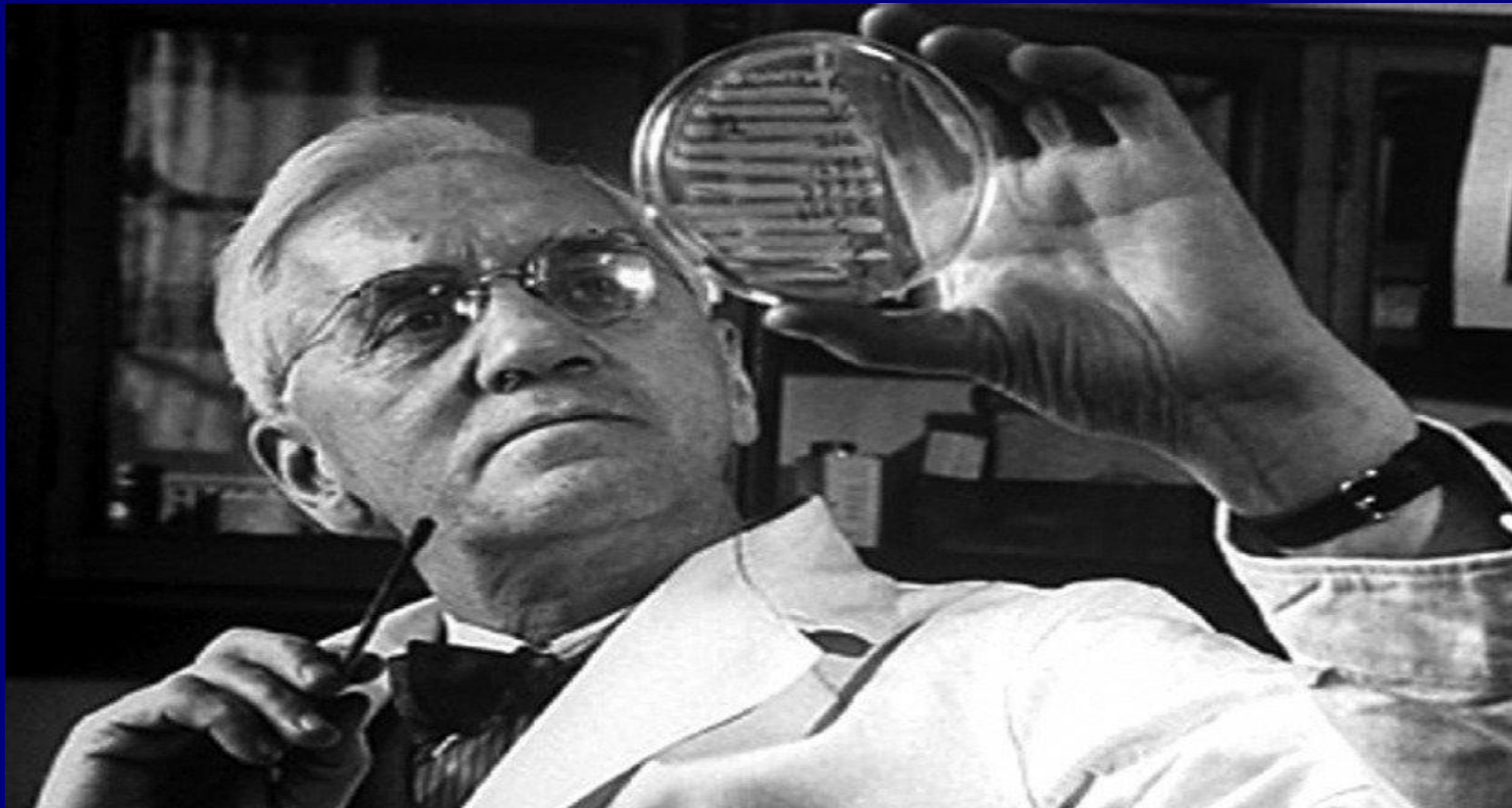


# ANTIBIOTICS

**SIR ALEXANDER FLEMING**

**RECEIVED CREDIT FOR DISCOVERY OF PENICILLIN**

**IN 1928 WHILE AT ST. MARY'S HOSPITAL IN LONDON, ENGLAND**



# ANTIBIOTICS

...GIVING CREDIT WHERE CREDIT IS DUE...



DR. CLODOMIRO PICADO TWIGHT

DOCUMENTED THE DISCOVERY OF PENICILLIN  
IN HIS LABORATORY NOTEBOOKS (1915-1927)  
AND PUBLISHED HIS RESULTS IN 1927

# ANTIBIOTICS



## TWO MAJOR REASONS FOR THE USE OF ANTIBIOTICS IN ANIMALS



### GROWTH ENHANCEMENT/PROMOTION

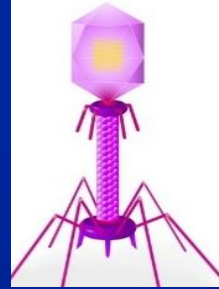
PROVIDED TO HEALTHY ANIMALS AT DIETARY CONCENTRATIONS  
OF BELOW 200 GRAMS PER TON OF FEED FOR MORE THAN 14 DAYS

### THERAPEUTIC AND PROPHYLACTIC USE

PROVIDED TO ANIMALS TO TREAT OR PREVENT INFECTION/DISEASE



# WHEN WERE BACTERIOPHAGES DISCOVERED AND BY WHOM ?



**1896**

**ERNEST HANKIN**

**ENGLISH BACTERIOLOGIST**

**QUESTION**



**GANGES RIVER: CURE FOR CHOLERA**



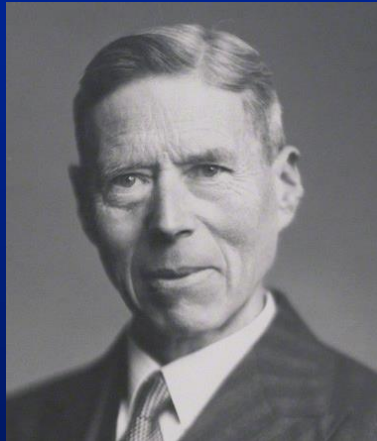
# WHEN WERE BACTERIOPHAGES DISCOVERED AND BY WHOM ?



**1915**

**FREDERICK WILLIAM TWORT**

**ENGLISH BACTERIOLOGIST**



**DOCUMENTED THE ANTIBACTERIAL  
NATURE OF PHAGES**

**...BUT...**

**DID NOT KNOW  
THE MECHANISM OF  
BACTERIAL DESTRUCTION**



**QUESTION**

**WHO IS CREDITED WITH ISOLATING BACTERIOPHAGES  
AND DISCOVERING THAT BACTERIOPHAGES ARE  
RESPONSIBLE FOR KILLING BACTERIA AND  
PROPOSED “PHAGE THERAPY” AND THE USE OF  
“PHAGE COCKTAILS” TO TREAT DISEASE?**

**1917**

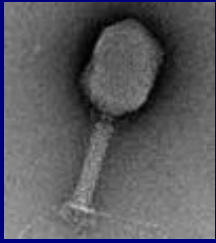


**FELIX d' HERELLE**

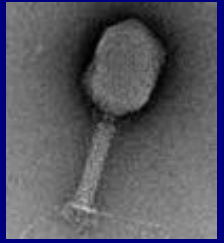
**FRENCH-CANADIAN  
MICROBIOLOGIST**

**DISCOVERS AND CHARACTERIZES  
THE VIRAL NATURE OF PHAGES  
AGAINST BACTERIAL DISEASES**

**QUESTION**



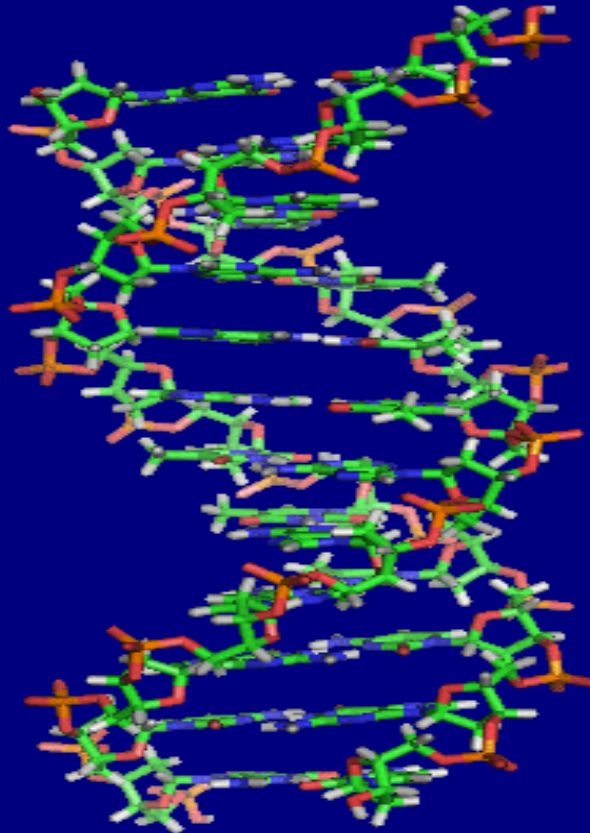
# **BACTERIOPHAGES**



**...FACTS...**

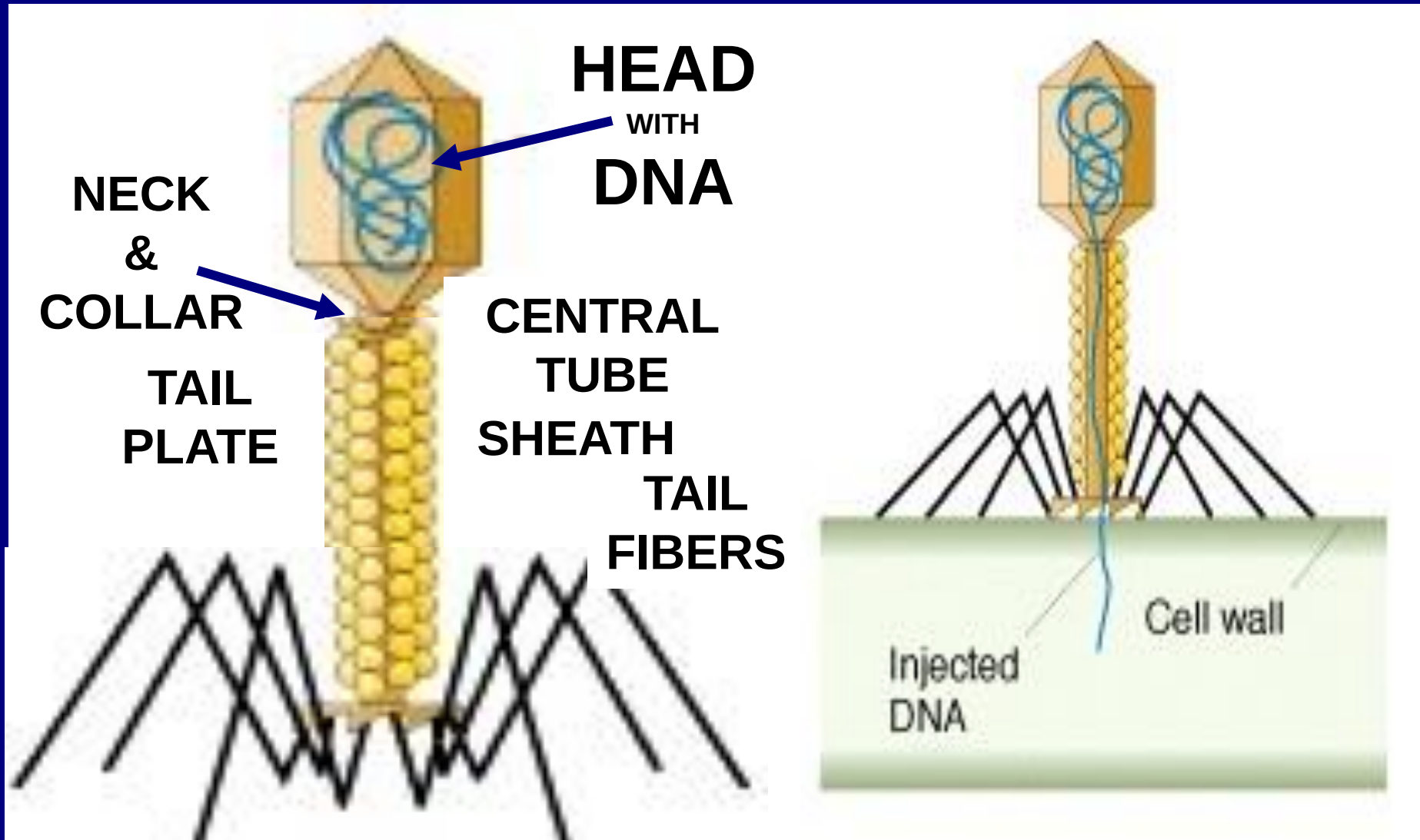
**ARE THE MOST ABUNDANT/DIVERSE**

**FORM OF DNA REPLICATING AGENT ON OUR PLANET**



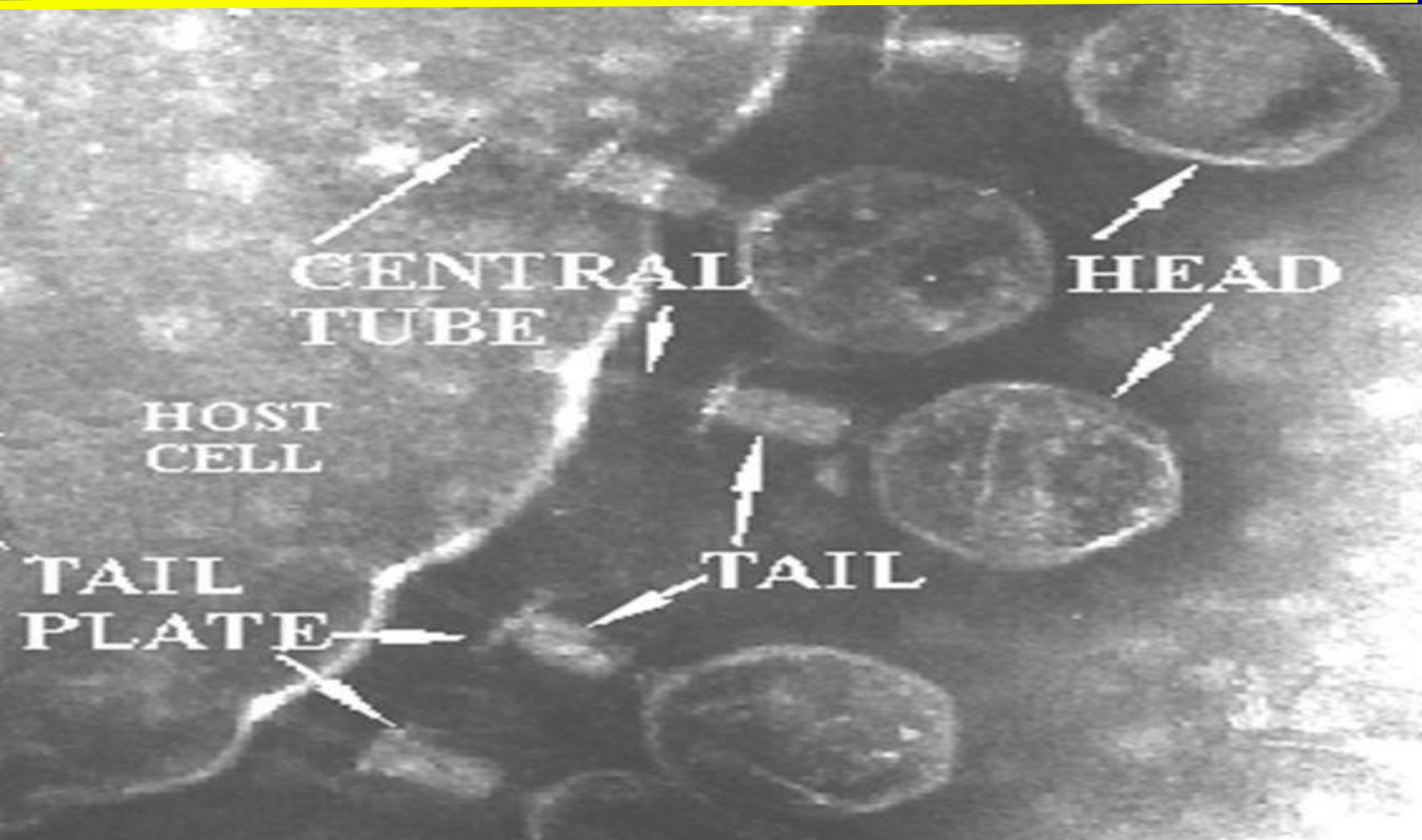


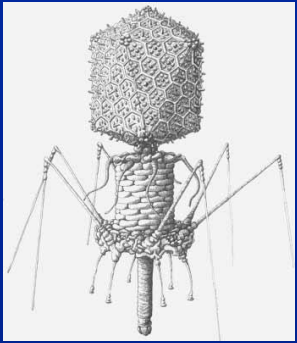
# BACTERIOPHAGE ANATOMY



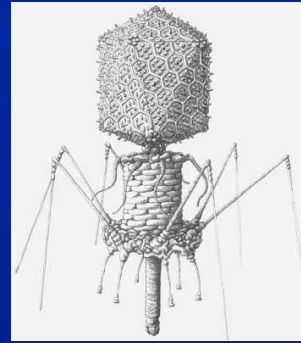


## BINDING TO BACTERIA AND INJECTING DNA





# BACTERIOPHAGES



**...SIMPLY STATED...**

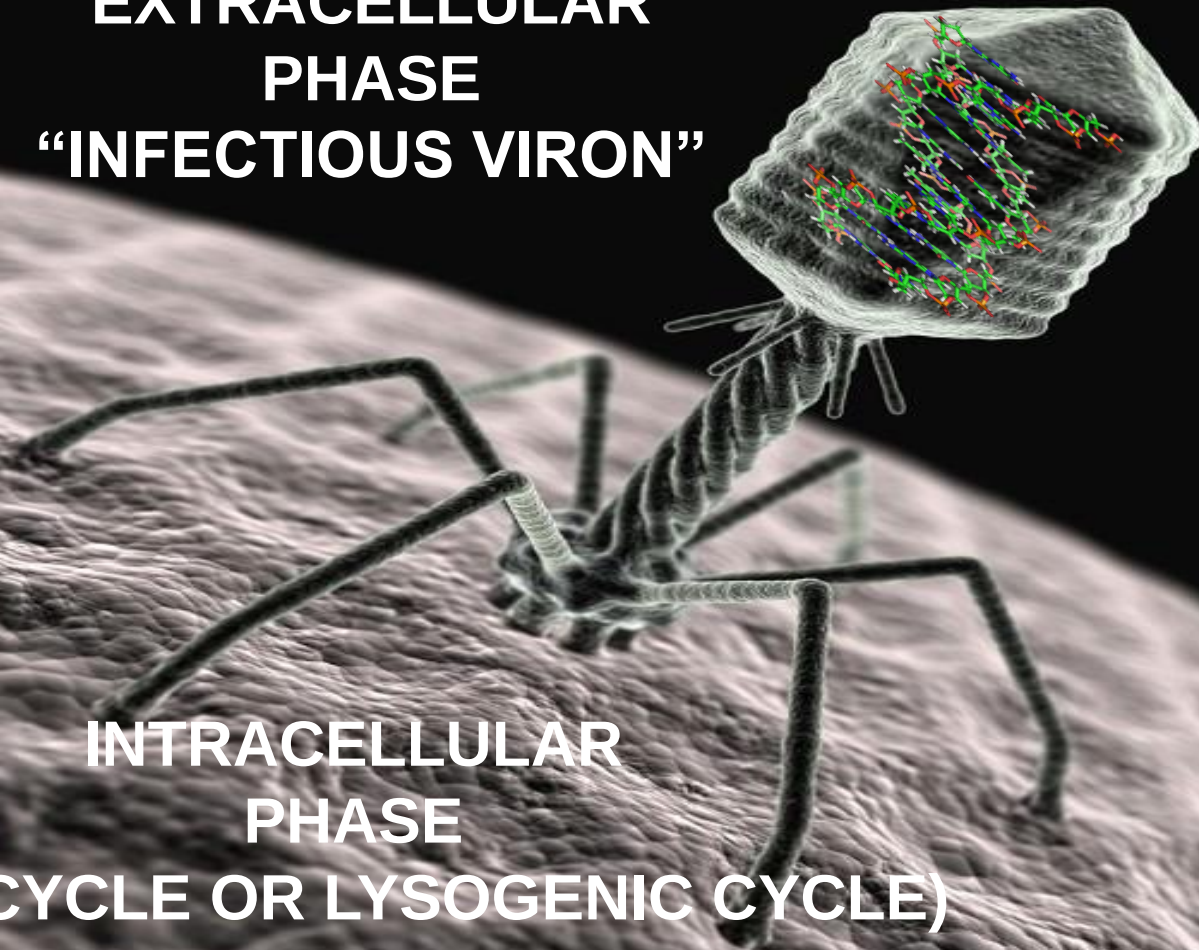
**THEY ARE VIRAL ASSASSINS  
WITH ONLY TWO PURPOSES  
.....FOR THEIR EXISTENCE.....**

**TO KILL BACTERIA  
AND  
REPLICATE**

# BACTERIOPHAGE

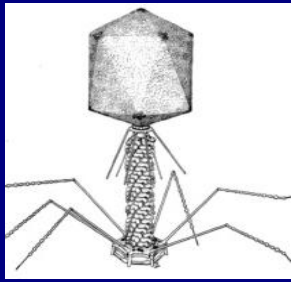
## “LIFE CYCLE”

EXTRACELLULAR  
PHASE  
“INFECTIOUS VIRION”

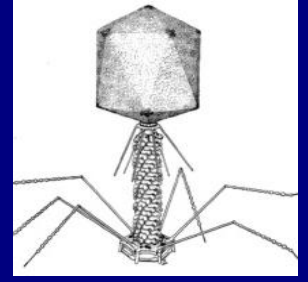


INTRACELLULAR  
PHASE  
(LYTIC CYCLE OR LYSOGENIC CYCLE)





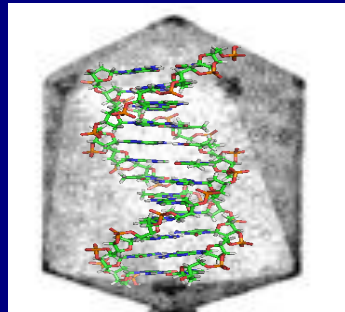
# BACTERIOPHAGE “LIFE CYCLE”



## INTRACELLULAR PHASE

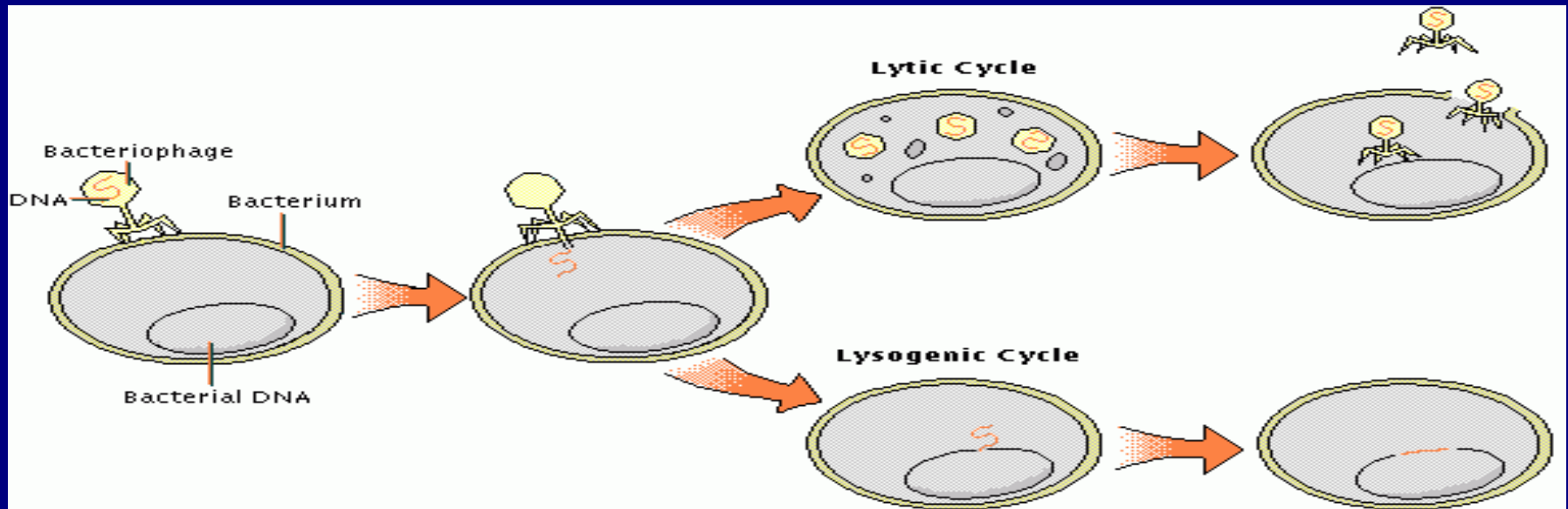
### LYTIC CYCLE

GENETIC MATERIAL  
INJECTED INTO BACTERIA  
REPLICATED IN BACTERIA  
NEW PHAGES FORMED  
BACTERIAL CELL BURSTS (LETHAL)

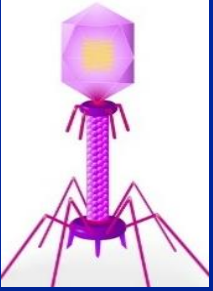


### LYSOGENIC CYCLE

GENETIC MATERIAL  
INJECTED INTO BACTERIA  
STORED IN BACTERIAL DNA  
REMAINS DORMANT (NON-LETHAL)  
(EVENTUALLY RELEASED/LYTIC CYCLE ACTIVATED)



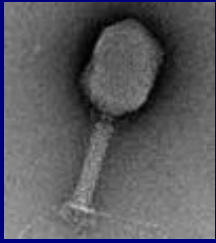
**WHERE CAN BACTERIOPHAGES  
BE FOUND ?**



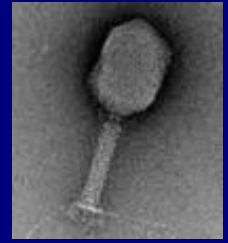
**BACTERIOPHAGES  
ARE  
UBIQUITOUS**

**WHERE YOU FIND BACTERIA  
YOU WILL FIND  
BACTERIOPHAGES**

**QUESTION**



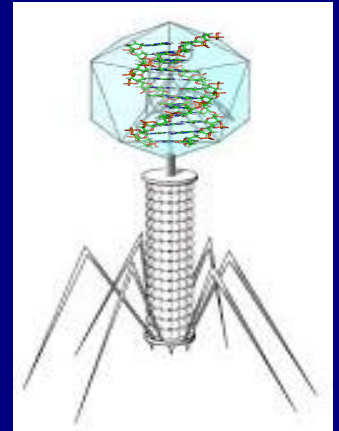
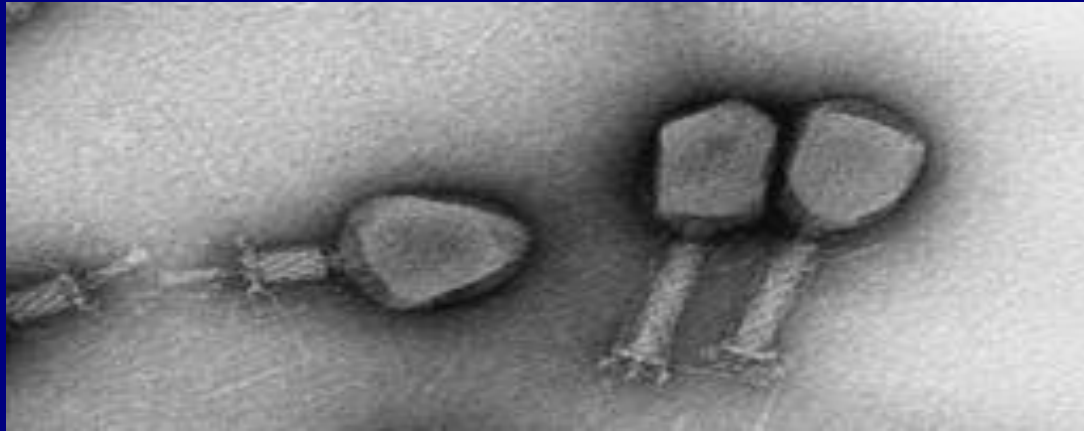
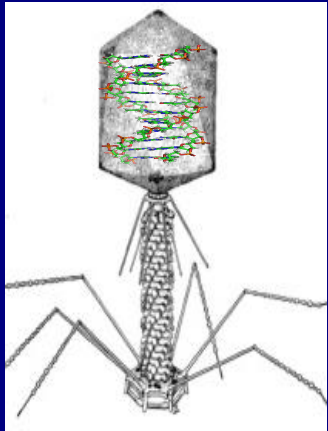
# **BACTERIOPHAGES**



**...FACT...**

**FOUND EVERYWHERE ON EARTH**

**(PROTEINS THAT SURROUND DNA OR RNA GENOME)**

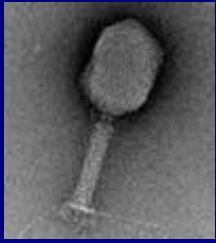


**A VIRUS THAT INFECTS BACTERIA**

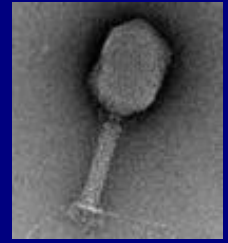
**(BACTERIAL SPECIES SPECIFIC)**

**(NO BACTERIAL RESISTANCE DEVELOPS)**

**(PROVIDE NON-HOST DERIVED IMMUNITY)**



# **BACTERIOPHAGES**



**SEAWATER AND MICROBIAL MATS**

**CONTAIN HIGH NUMBERS OF BACTERIOPHAGES**

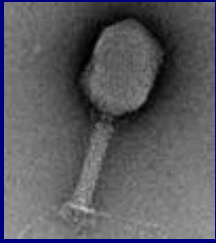
**( $9 \times 10^8$ /ML)**



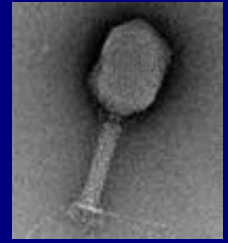
**IT IS ESTIMATED THAT BACTERIOPHAGES DESTROY  
UP TO 40% OF THE BACTERIA IN EARTH'S OCEANS DAILY**







# **BACTERIOPHAGES**



**...FACTS...**

**HAVE BEEN USED FOR OVER 100 YEARS  
AS AN ALTERNATIVE TO ANTIBIOTICS  
IN THE FORMER SOVIET UNION,  
CENTRAL EUROPE AND FRANCE**

**BACTERIOPHAGE BANKS/LIBRARIES EXIST**

**CONTROL BACTERIAL ECOSYSTEMS EVERYWHERE  
(ESPECIALLY IN AN ANIMAL'S DIGESTIVE TRACT)**

---

# GROWTH PROMOTING ANTIBIOTICS

## “OFTEN OVERLOOKED BENEFIT”



FOR OVER 70 YEARS  
THE USE OF GROWTH PROMOTING ANTIBIOTICS  
IN POULTRY HELPED TO MAINTAIN A LEVEL  
OF “*BACTERIAL STABILITY*”  
IN THE BIRD’S DIGESTIVE TRACT

A FACT THAT WAS NOT APPRECIATED  
UNTIL GROWTH PROMOTING ANTIBIOTICS  
WERE PROHIBITED FROM BEING USED



# EARLY “BACTERIAL STABILITY” IS IMPORTANT IN THE BIRD’S DIGESTIVE TRACT



**RAPID  
DIGESTIVE TRACT  
DEVELOPMENT  
IS CRITICAL**



**BACTERIAL INFECTION RISK  
“HIGH”**

**BACTERIAL INFECTION RISK  
“LOW”**

**IMMUNE SYSTEM  
“NOT FULLY DEVELOPED”**

**IMMUNE SYSTEM  
“DEVELOPED”**

# **ANTIBIOTICS**

## **...QUESTION...**

**WHAT “NEW TERM” ORIGINATED AS A RESULT OF THE  
REMOVAL OF GROWTH PROMOTING ANTIBIOTICS IN  
THE EUROPEAN UNION AND IS NOW COMMONLY USED  
BY THE ANIMAL INDUSTRY TO DESCRIBE THE INCREASED  
INCIDENCE OF ENTERITIS IN BROILERS AND  
WET LITTER IN POULTRY HOUSES ?**

***“DYSBACTERIOSIS”***



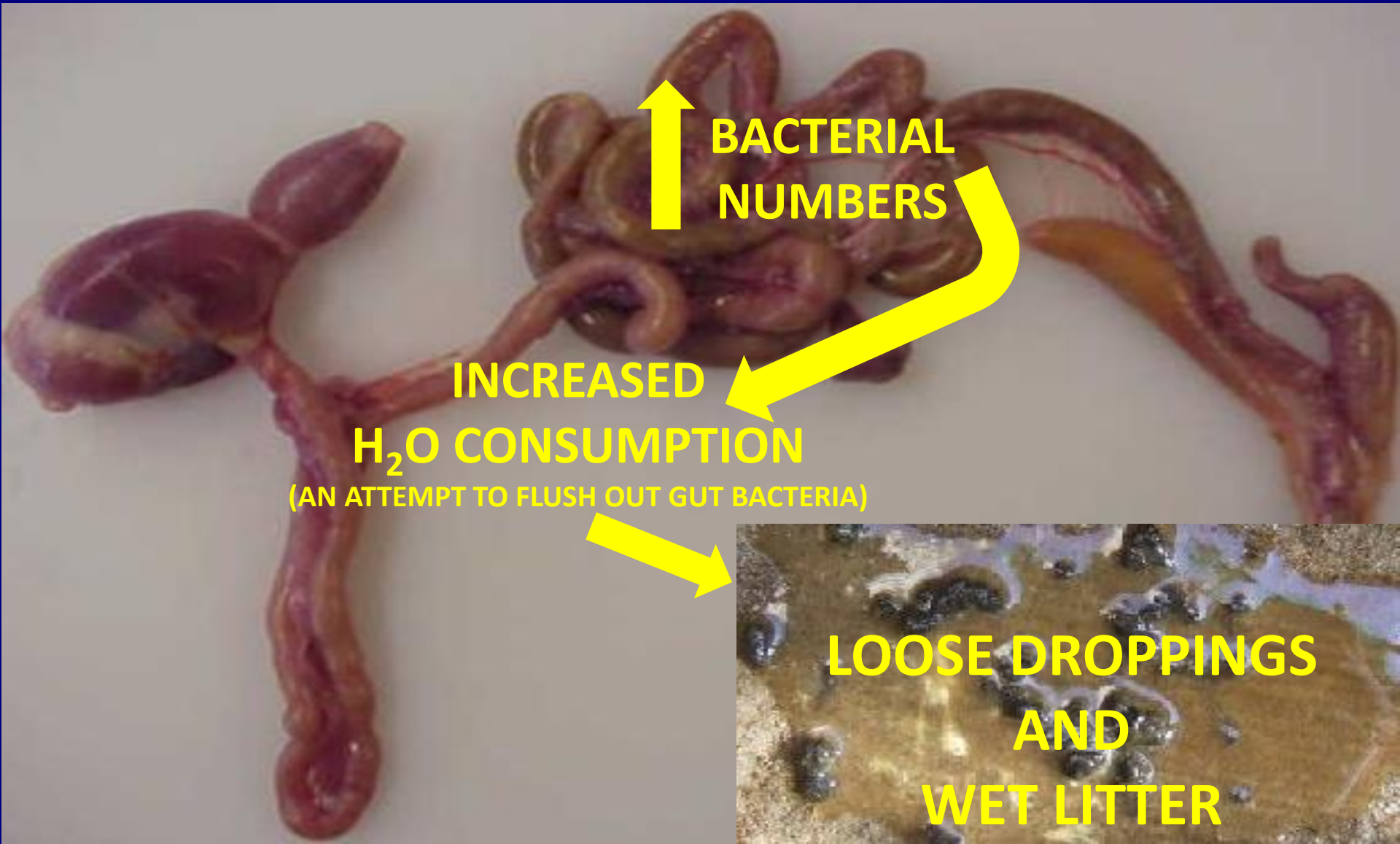
# ***“DYSBACTERIOSIS”***



**DESCRIBES A SITUATION WHERE  
THERE IS A HUGE IMBALANCE IN THE  
BACTERIAL POPULATION IN THE  
BIRD'S INTESTINAL TRACT**

# ***“DYSBACTERIOSIS”***

## **...CONSEQUENCES...**



# WHAT IS A MAJOR WAY THAT BACTERIOPHAGES PROTECT THE ANIMAL'S DIGESTIVE TRACT



## PATHOGENS ENTER THROUGH MUCOSAL SURFACES

MUCUS MAINTAINS A HIGH PHAGE TO BACTERIA RATIO WHICH PROTECTS THE UNDERLYING EPITHELIUM AND PREVENTS INFECTION

THE BACTERIOPHAGE BINDS TO THE MUCIN GLYCOPROTEINS AND ATTACHMENT TO THE MUCIN RESULTS WHICH PROVIDES A "NON-HOST DERIVED IMMUNITY" BY DECREASING BACTERIAL NUMBERS

# QUESTION

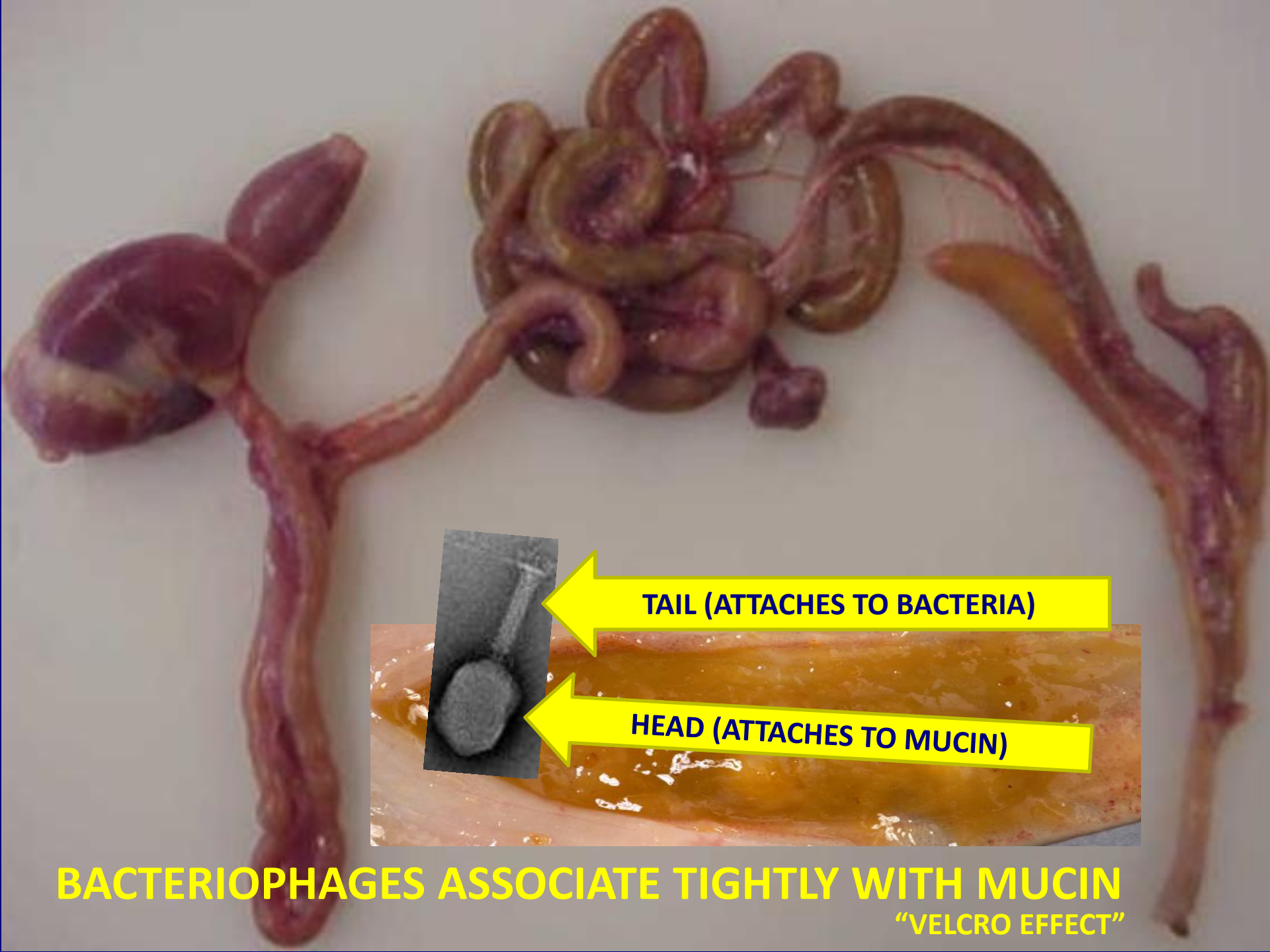


**BACTERIOPHAGES ASSOCIATE TIGHTLY WITH MUCIN**  
"VELCRO EFFECT"





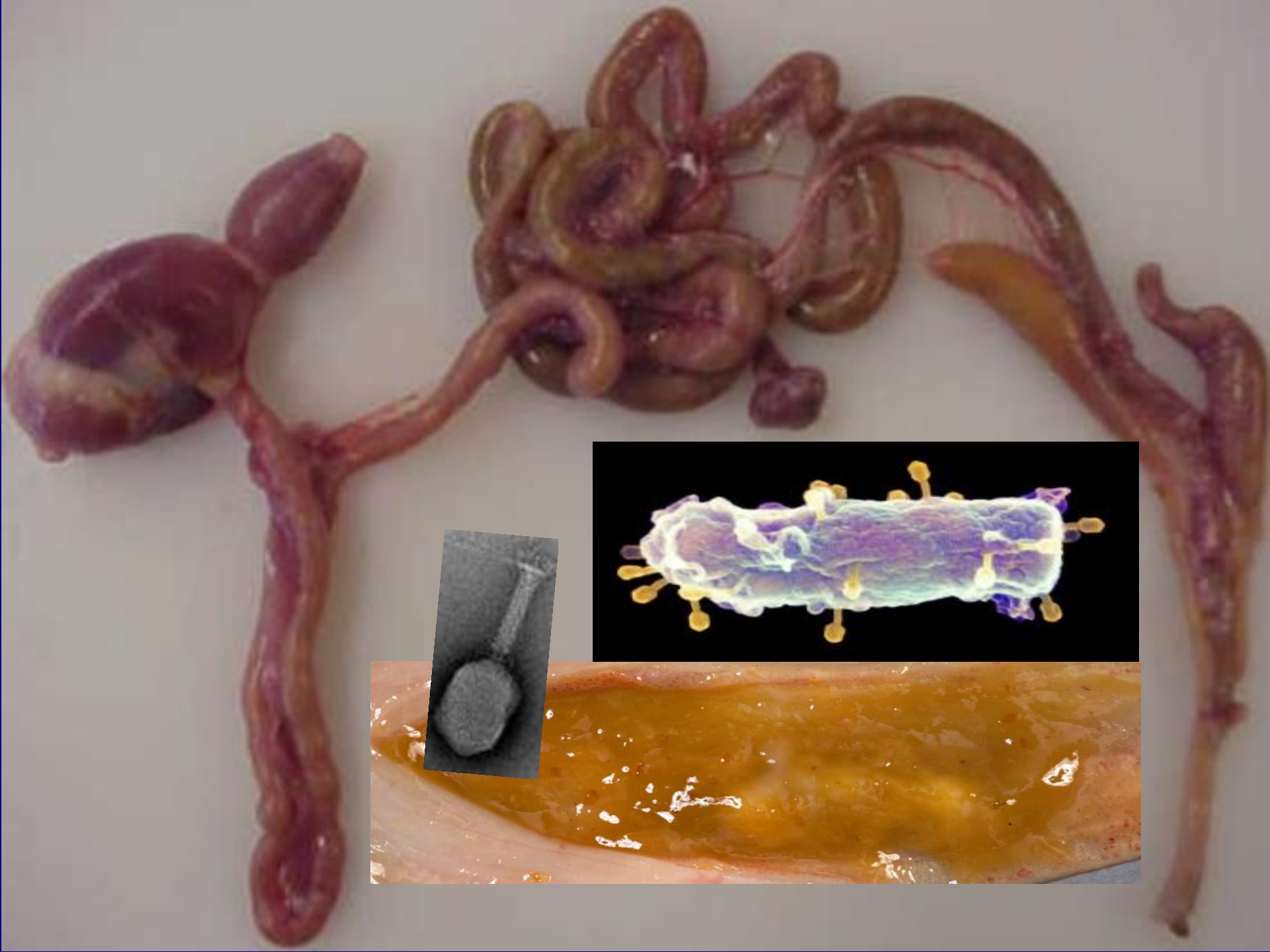
**BACTERIOPHAGES ASSOCIATE TIGHTLY WITH MUCIN**  
“VELCRO EFFECT”



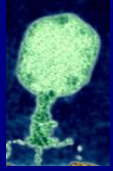
**TAIL (ATTACHES TO BACTERIA)**

**HEAD (ATTACHES TO MUCIN)**

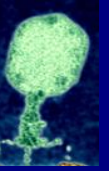
**BACTERIOPHAGES ASSOCIATE TIGHTLY WITH MUCIN**  
“VELCRO EFFECT”







# BACTERIOPHAGES

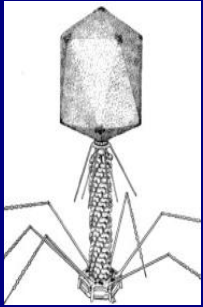


PROMOTE  
HEALTH OF THE DIGESTIVE TRACT AND  
A STABLE MICROBIAL POPULATION

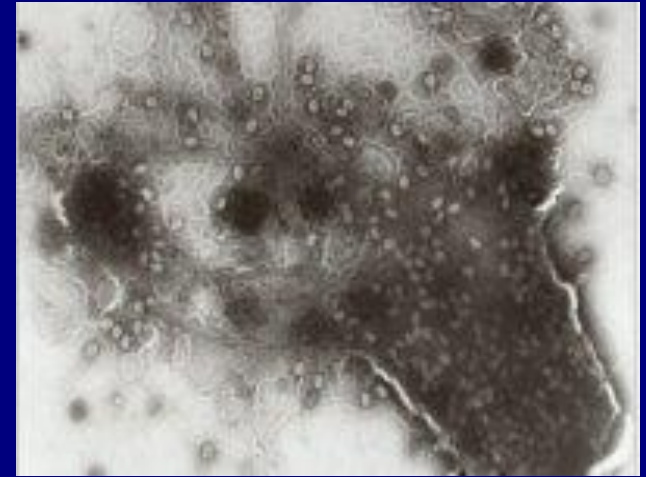
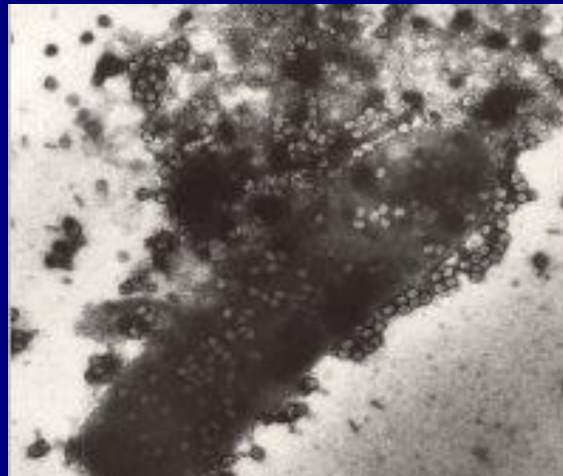
**“PHAGEBIOTIC”**



**WHEN ONE BACTERIOPHAGE INJECTS ITS DNA INTO A BACTERIAL CELL AND CELL LYSIS OCCURS HOW MANY NEW BACTERIOPHAGES CAN BE FORMED ?**



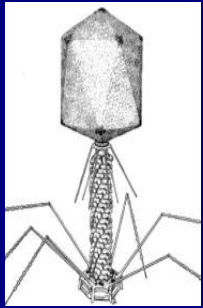
**THE NUMBER CAN VARY  
BUT FROM 50-100(200) IS COMMON**



**QUESTION**

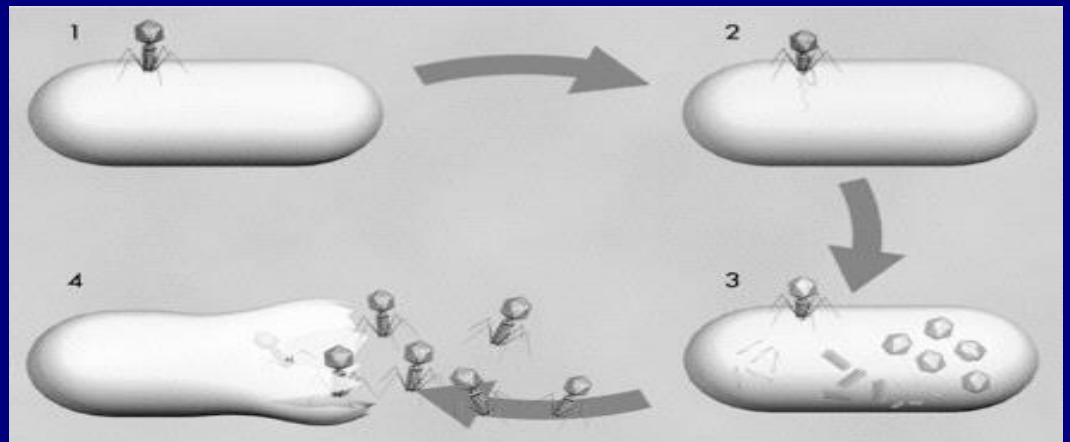
**BACTERIAL CELL LYSIS**

# WHAT LIMITS THE NUMBER OF NEW BACTERIOPHAGES ? WHY NOT MORE, LET'S SAY 200, 300, 400, +

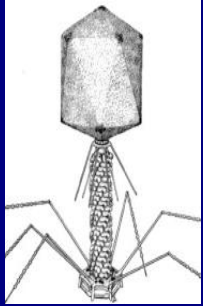


THE DNA OF THE BACTERIOPHAGE COMMANDS THE BACTERIAL CELL'S METABOLIC MACHINERY TO PRODUCE BACTERIOPHAGES AND EVENTUALLY THE **"BUILDING MATERIAL"** WITHIN THE BACTERIA REQUIRED FOR CONSTRUCTING BACTERIOPHAGES **IS DEPLETED**

## QUESTION

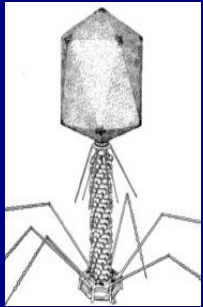


**IN COMPARISON TO BACTERIA  
HOW BIG ARE BACTERIOPHAGES ?**

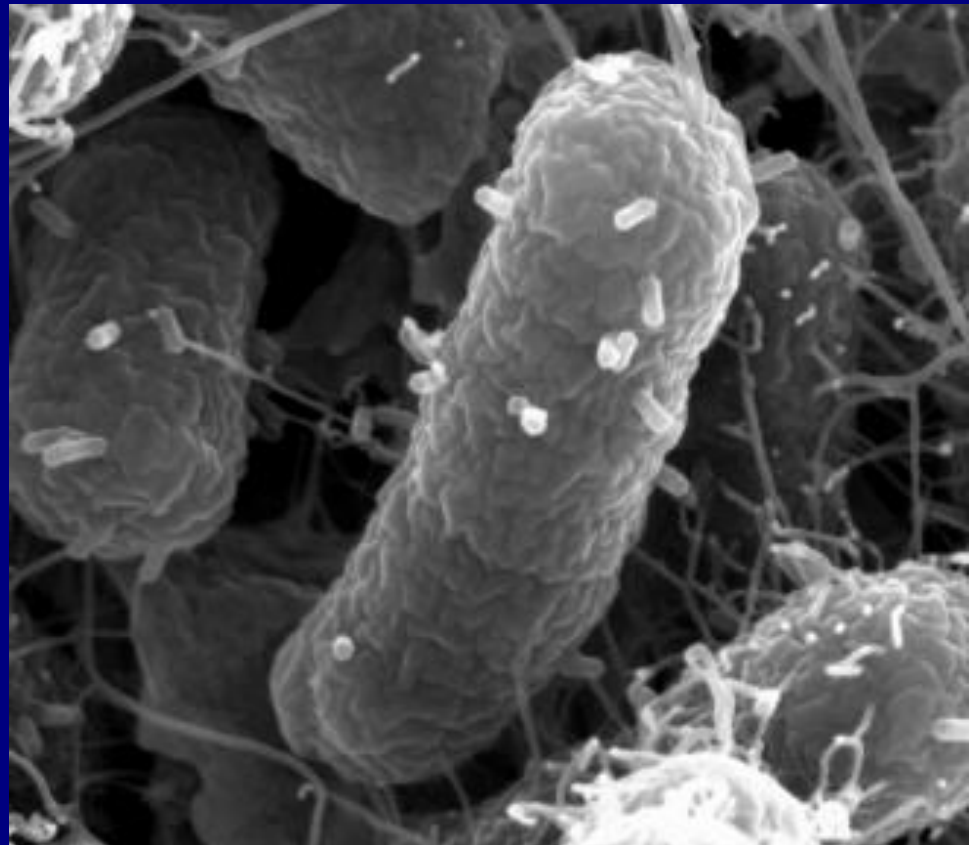


**QUESTION**

# IN COMPARISON TO BACTERIA HOW BIG ARE BACTERIOPHAGES ?



**BACTERIOPHAGES ARE NORMALLY  
ABOUT 100 TIMES SMALLER THAN BACTERIA**

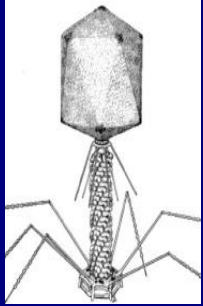


**QUESTION**

**ESTIMATED NUMBER ON EARTH  $10^{31}$**

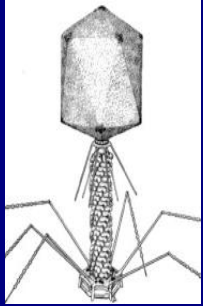


**WHAT HAPPENS TO THE BACTERIOPHAGE IN THE ENVIRONMENT AFTER ITS DNA HAS BEEN INJECTED INTO THE BACTERIA ?**

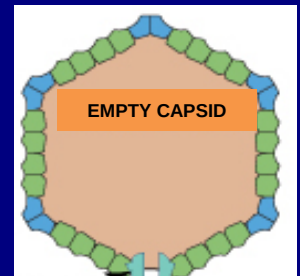
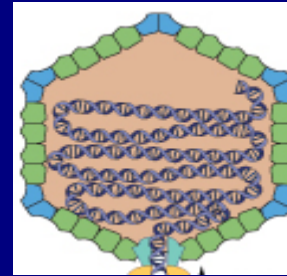
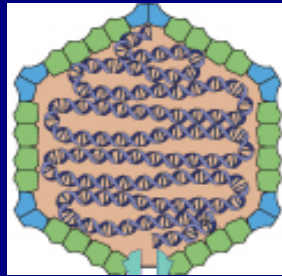


**QUESTION**

# WHAT HAPPENS TO THE BACTERIOPHAGE IN THE ENVIRONMENT AFTER ITS DNA HAS BEEN INJECTED INTO THE BACTERIA ?



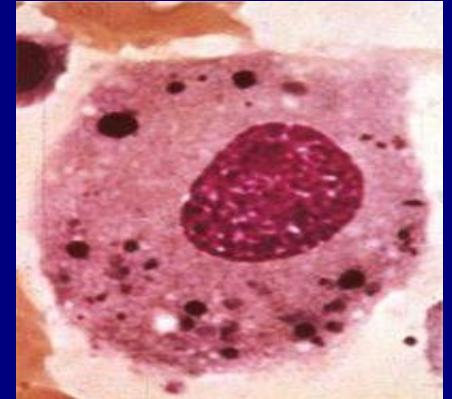
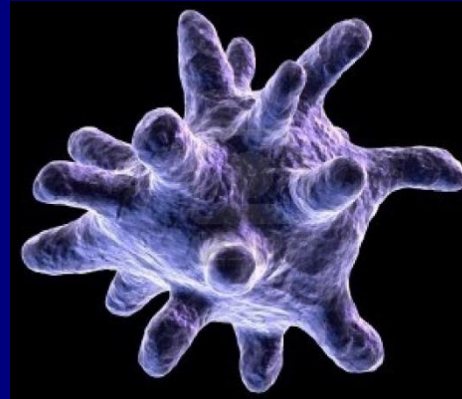
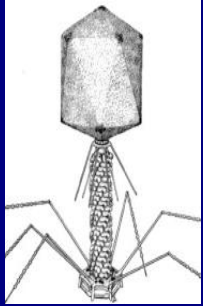
**THE BACTERIOPHAGE  
IS THEN NOTHING BUT  
AN EMPTY PROTEIN SHELL  
WHICH WILL EVENTUALLY DECAY**



**QUESTION**



# WHAT HAPPENS TO THE BACTERIOPHAGE IN THE ANIMAL AFTER ITS DNA HAS BEEN INJECTED INTO THE BACTERIA ?



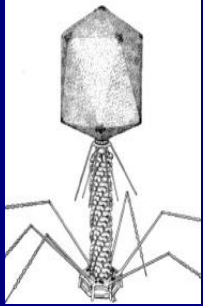
**RETICULOENDOTHELIAL SYSTEM  
“MACROPHAGE SYSTEM”**

**IN THE ANIMAL**

**THE MACROPHAGES  
CONSUME THE EMPTY SHELL  
OF THE BACTERIOPHAGES**

**QUESTION**

# DO BACTERIOPHAGE RESISTANT BACTERIA EVER DEVELOP ?



# YES

## ...HOWEVER...

THE RESISTANT BACTERIA ARE A MINORITY  
AND THE BACTERIOPHAGES ARE CONSTANTLY  
CO-EVOLVING AND WILL EVENTUALLY  
DESTROY THE BACTERIA

**3.5 BILLION YEARS WITHOUT  
TOTAL RESISTANCE DEVELOPING**

# QUESTION



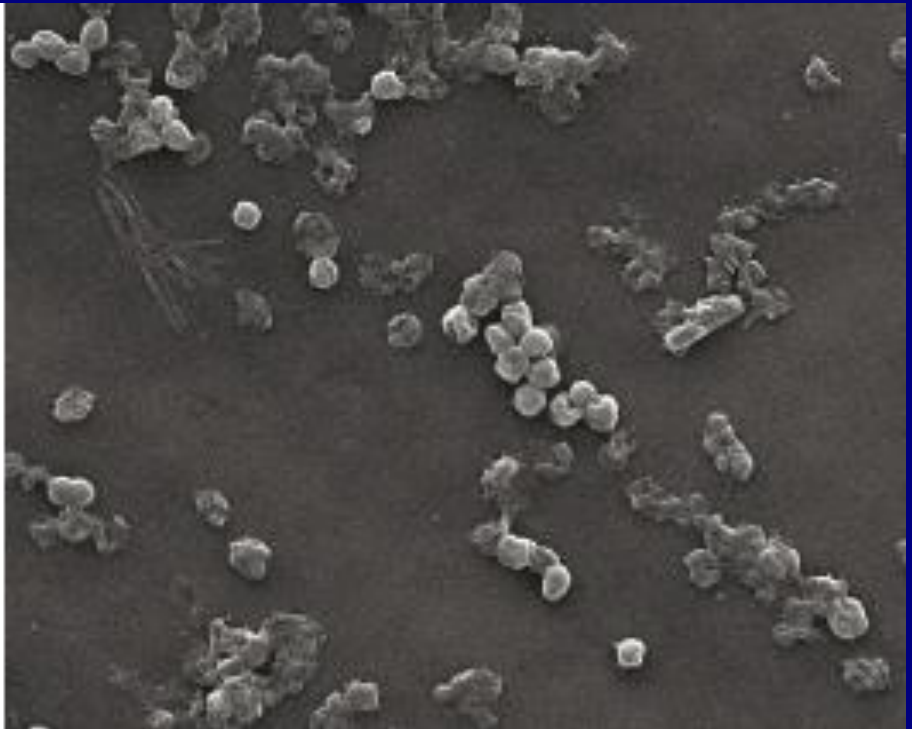
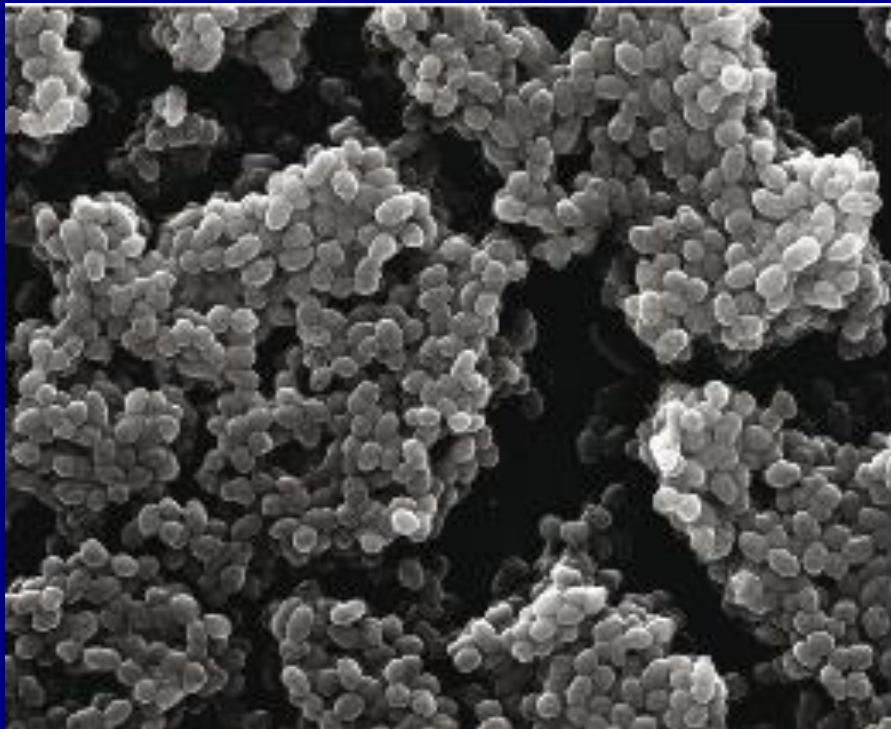


# BACTERIOPHAGE



**“MAJOR ADVANTAGE”**

**THEY HAVE ENZYMES THAT ALLOW  
FOR PENETRATION OF  
COMPLEX BIOFILM ENVIRONMENTS**



# AVERAGE EXPECTED PERFORMANCE RESPONSE FROM GROWTH PROMOTING ANTIBIOTICS USED IN THE DIET OF VARIOUS ANIMALS

|            |                                                                                               | IMPROVEMENT            |                |
|------------|-----------------------------------------------------------------------------------------------|------------------------|----------------|
|            |                                                                                               | <u>WEIGHT GAIN (%)</u> | <u>FCR (%)</u> |
| BROILER    |              | + 3.6                  | - 3.4          |
| LAYING HEN |              | + 2.8                  | - 2.7          |
| TURKEY     |              | + 3.1                  | - 2.2          |
| PIG        | STARTING    | + 15.7                 | - 8.6          |
|            | GROWING    | + 8.1                  | - 4.8          |
|            | FINISHING  | + 3.2                  | - 2.0          |

# MAJOR FACTORS KNOWN TO INFLUENCE THE MAGNITUDE OF RESPONSE TO GROWTH PROMOTING ANTIBIOTICS IN VARIOUS SPECIES OF ANIMALS

---

## FACTOR

GERM FREE ENVIRONMENT (NO MICROBES)

FARM HYGIENE (CLEAN VS DIRTY)

AGE OF ANIMAL (YOUNG VS OLD)

FARM MANAGEMENT (STRESS LEVEL)



# MAJOR FACTORS KNOWN TO INFLUENCE THE MAGNITUDE OF RESPONSE TO GROWTH PROMOTING ANTIBIOTICS IN VARIOUS SPECIES OF ANIMALS

---

## FACTOR

GERM FREE ENVIRONMENT (NO MICROBES)

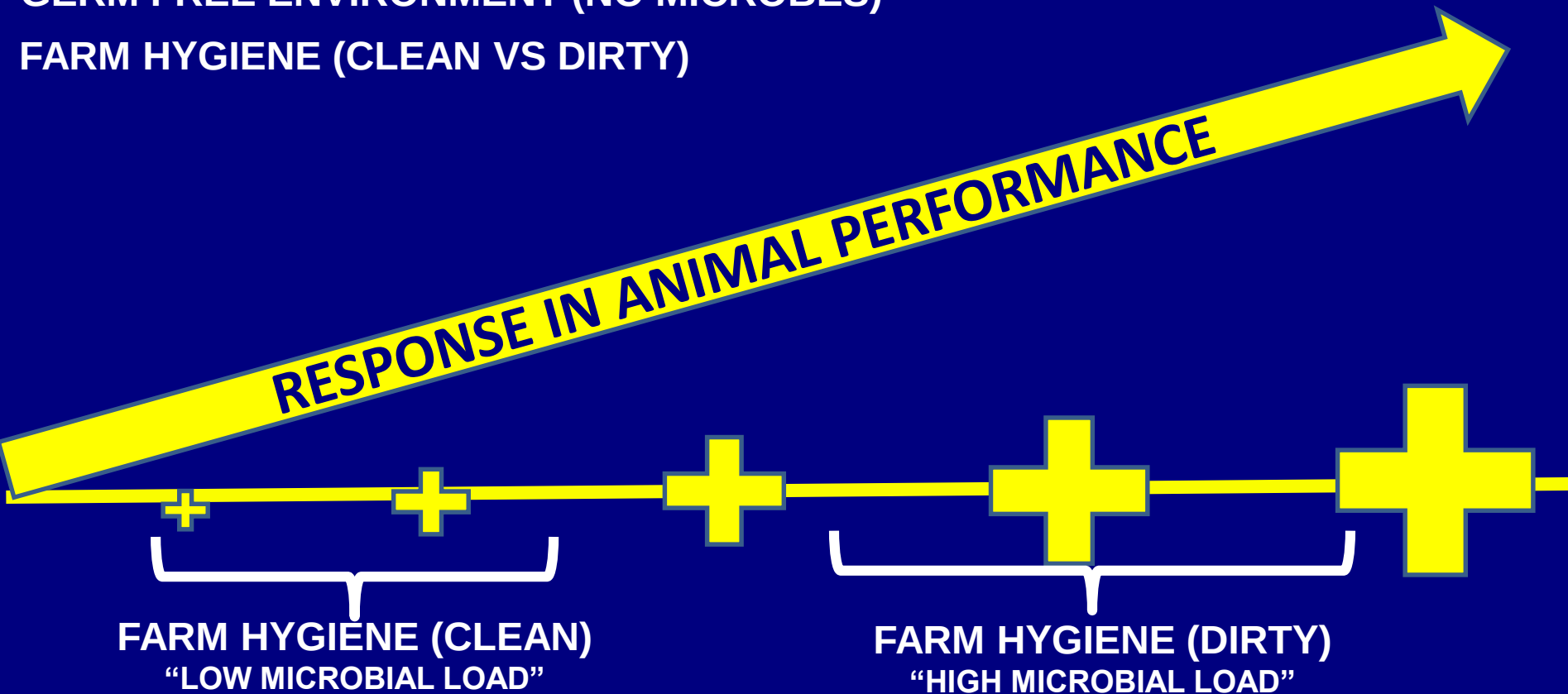


# MAJOR FACTORS KNOWN TO INFLUENCE THE MAGNITUDE OF RESPONSE TO GROWTH PROMOTING ANTIBIOTICS IN VARIOUS SPECIES OF ANIMALS

## FACTOR

GERM FREE ENVIRONMENT (NO MICROBES)

FARM HYGIENE (CLEAN VS DIRTY)



***THIS SHOULD ALSO BE TRUE WHEN USING BACTERIOPHAGES***



# MAJOR FACTORS KNOWN TO INFLUENCE THE MAGNITUDE OF RESPONSE TO GROWTH PROMOTING ANTIBIOTICS IN VARIOUS SPECIES OF ANIMALS

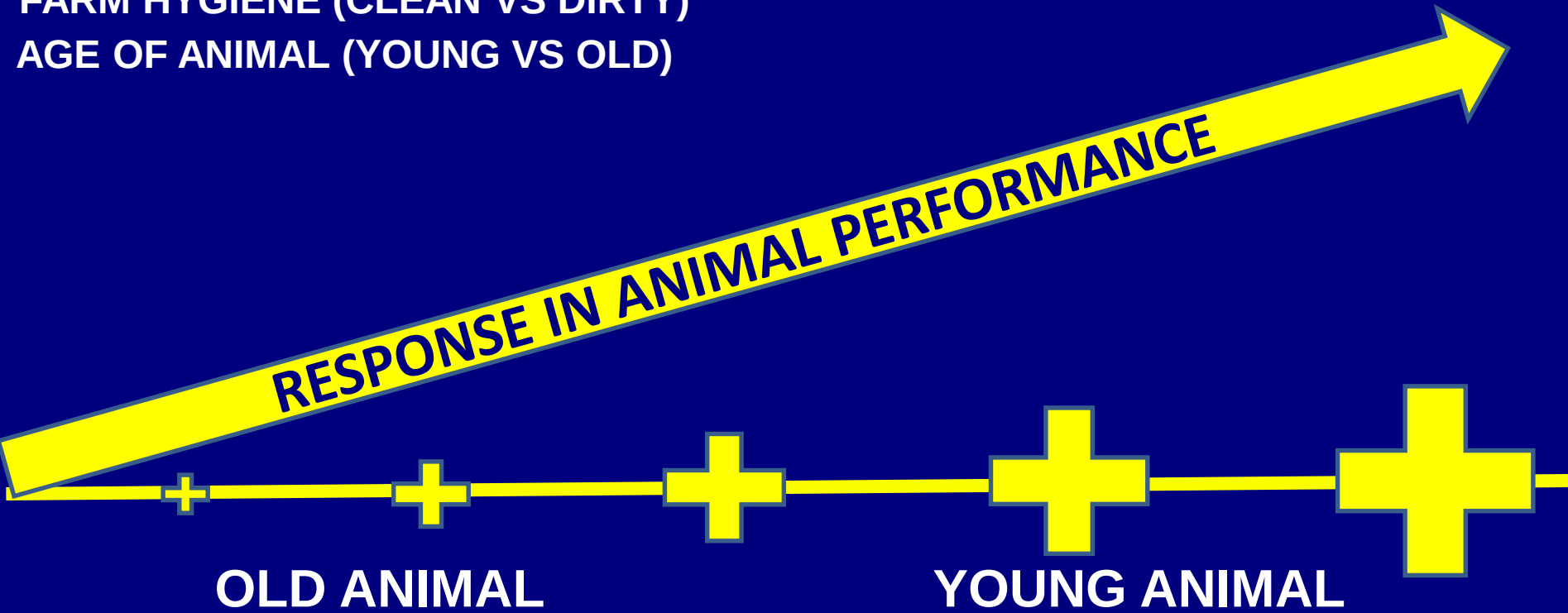
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## FACTOR

GERM FREE ENVIRONMENT (NO MICROBES)

FARM HYGIENE (CLEAN VS DIRTY)

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*THIS SHOULD ALSO BE TRUE WHEN USING BACTERIOPHAGES*

# MAJOR FACTORS KNOWN TO INFLUENCE THE MAGNITUDE OF RESPONSE TO GROWTH PROMOTING ANTIBIOTICS IN VARIOUS SPECIES OF ANIMALS

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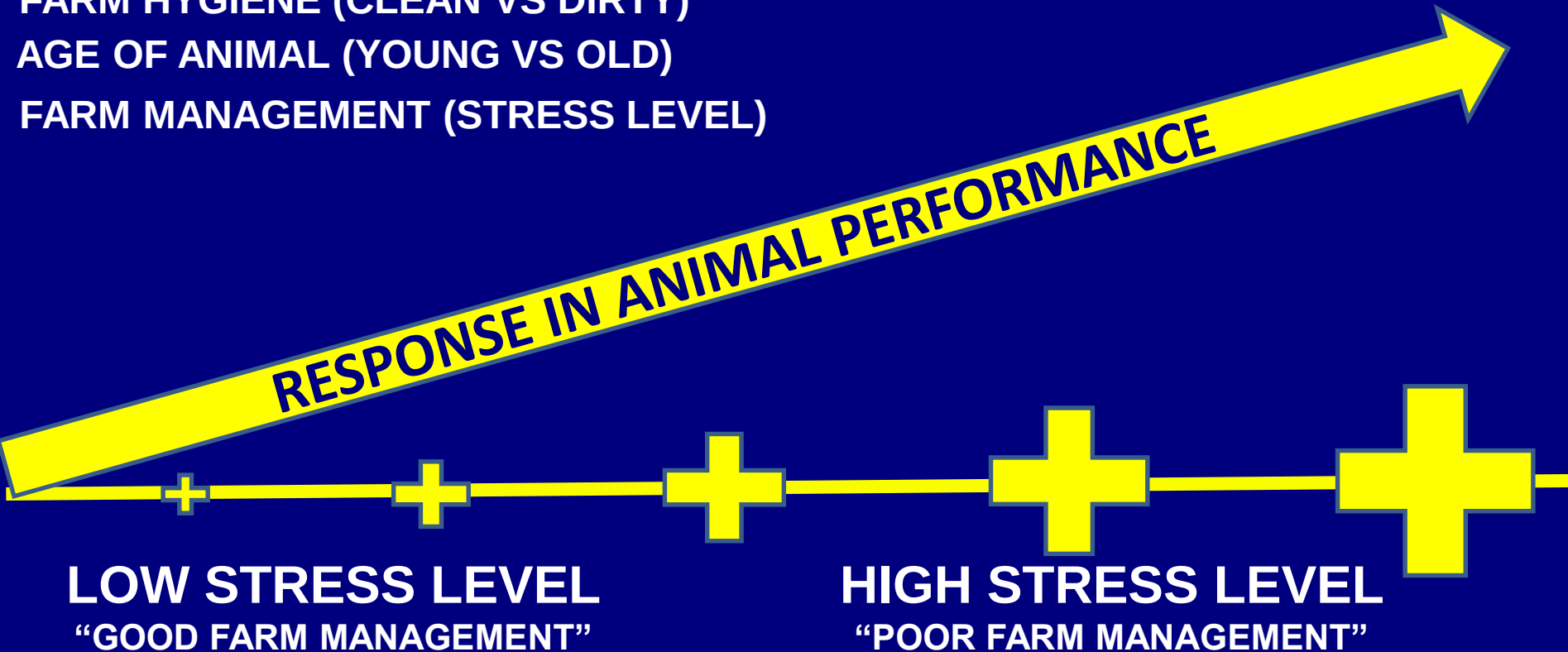
## FACTOR

GERM FREE ENVIRONMENT (NO MICROBES)

FARM HYGIENE (CLEAN VS DIRTY)

AGE OF ANIMAL (YOUNG VS OLD)

FARM MANAGEMENT (STRESS LEVEL)



***THIS SHOULD ALSO BE TRUE WHEN USING BACTERIOPHAGES***

**BROILER UNIFORMITY  
IS OF EXTREME IMPORTANCE  
AND IS INCREASED BY FEEDING  
GROWTH PROMOTING ANTIBIOTICS**





**...QUESTION...**

**DO ALL BIRDS IN A FLOCK  
HAVE SIMILAR PERFORMANCE ?**

**...IF THE ANSWER IS NO...THEN  
IN RESEARCH IS IT POSSIBLE TO IDENTIFY  
WHICH BIRDS ARE RESPONDING BETTER  
TO GROWTH PROMOTING ANTIBIOTICS ?**

**...YES...**

**RESEARCH HAS SHOWN THAT FEEDING  
GROWTH PROMOTING ANTIBIOTICS BENEFITS  
SOME BIRDS MORE THAN OTHERS**



# **ANTIBIOTICS**

**...SO...**

**IF GROWTH PROMOTING ANTIBIOTICS  
ARE BENEFITTING SOME BIRDS IN  
A FLOCK MORE THAN OTHERS ?**

**...THEN...**

**BETTER FLOCK UNIFORMITY WOULD BE EXPECTED**



# BETTER UNIFORMITY USUALLY OCCURS (EXAMPLE)

## The Effect of Withdrawing Growth Promoting Antibiotics from Broiler Chickens: A Long-Term Commercial Industry Study

H. M. Engster,<sup>2</sup> D. Marvil, B. Stewart-Brown

*Perdue Farms, Inc., 31083 Old Ocean City Rd., Salisbury, Maryland 21804*

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**Primary Audience:** Nutritionists, Veterinarians, Researchers, Broiler Producers

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### SUMMARY

A comprehensive study with close to 7 million growing broilers spanning 3 yr and 158 paired-houses was conducted in two different geographic locations under industry conditions. A limited number of farms, most having tunnel-ventilated, dark-out facilities and all having similar equipment were selected to enhance repeatability over time. Equal numbers of birds from different breeder flocks were placed in the trial and control houses. The control treatment used the current field feed coccidiostat, roxarsone, and growth-promoting antibiotics (GPA) program, and the trial was identical to the control treatment with no GPA. The average age of all flocks in the entire trial was 52 d of age. Removal of GPA from the feed resulted in an average reduction in livability of 0.2% on the Delmarva Peninsula (DMV) and 0.14% in North Carolina (NC), an average decrease in body weight of 0.03 lb on DMV and 0.04 lb in NC, and an average increase in feed conversion ratio of 0.016 on DMV and 0.012 in NC. Skin color scores and field condemnations were not significantly negatively impacted by removing GPA. Both male and female body weights were less uniform without GPA. Placing new litter on farms resulted in only temporary improvement in field performance of birds given no GPA. The pattern of difference for feed conversion between trial and control over time was different between geographic locations. This study clearly shows that making a decision to withdraw GPA should not be made with only limited data conducted in one location or over a short time.

**Key words:** broiler, growth-promoting antibiotic, paired-house field trial, live performance

2002 J. Appl. Poult. Res. 11:431-436

# AN EXAMPLE OF BETTER UNIFORMITY & ISOLATING THE PERFORMANCE RESPONSE

## Virginiamycin and Laying Hen Performance<sup>1,2</sup>

R. D. MILES, D. M. JANKY, and R. H. HARMS

*Poultry Science Department, University of Florida, Gainesville, Florida 32611*

(Received for publication December 6, 1983)

**ABSTRACT** Two experiments were conducted for five 28-day periods each. In Experiments 1 and 2, Hyline W-36 hens, 36 and 26 weeks of age, respectively, were used. Experiment 1 was designed to measure the effect of virginiamycin on hen performance and egg characteristics when supplementing a diet having low pigmentation potential. In Experiment 2, the diet contained 3% added fat with 0, 10, and 20 ppm virginiamycin.

In Experiment 1, virginiamycin-supplemented hens showed increased ( $P \leq .05$ ) egg production, body weight, and improved feed efficiency. When egg production and feed efficiency were ranked by quartiles within the control and virginiamycin-supplemented groups, virginiamycin was shown to benefit only the poorer producing hens. In Experiment 2, added fat improved feed efficiency; however, the response to virginiamycin, as observed in Experiment 1, did not occur.

(Key words: virginiamycin, laying hen, performance, egg characteristics)



# AN EXAMPLE OF ISOLATING THE PERFORMANCE RESPONSE

TABLE 3. *Pen performance of hens by quartile when ranked by egg production and feed efficiency (Experiment 1)*

**NOTICE THE HIGHER OVERALL EGG PRODUCTION AND BETTER FEED CONVERSION WITH VIRGINIAMYCIN**  
**NOTICE THE BEST PRODUCING HENS DID NOT RESPOND TO VIRGINIAMYCIN EXCEPT IN FEED CONVERSION**  
**NOTICE THE HENS THAT PRODUCED LESS RESPONDED GREATLY TO VIRGINIAMYCIN (THEY NEEDED HELP)**

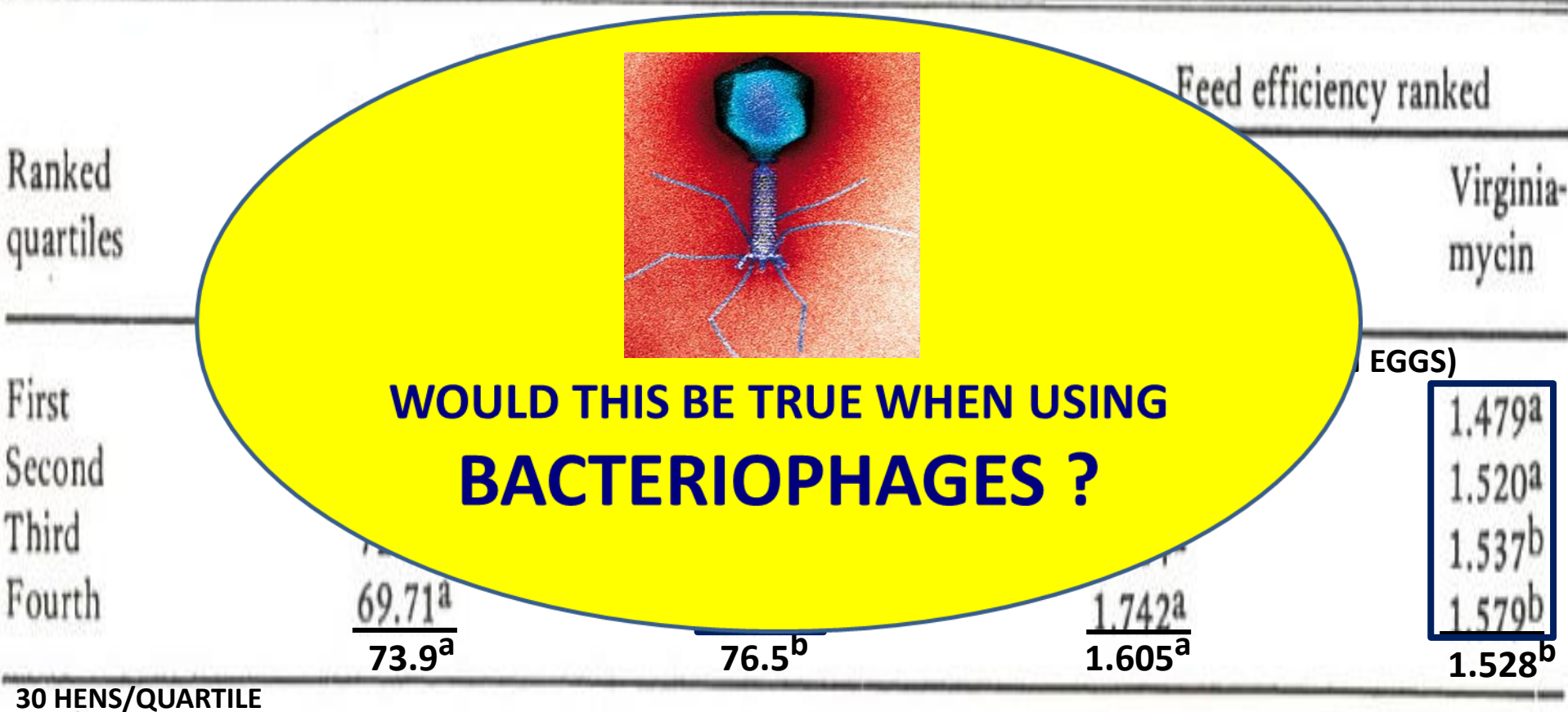
| Ranked quartiles | Control            | Virginia-mycin     | Control            | Virginia-mycin     |
|------------------|--------------------|--------------------|--------------------|--------------------|
|                  | (% EGG PRODUCTION) |                    | (KG/DOZEN EGGS)    |                    |
| First            | 78.04 <sup>a</sup> | 76.83 <sup>a</sup> | 1.495 <sup>a</sup> | 1.479 <sup>a</sup> |
| Second           | 75.38 <sup>a</sup> | 76.79 <sup>a</sup> | 1.552 <sup>a</sup> | 1.520 <sup>a</sup> |
| Third            | 72.65 <sup>a</sup> | 76.69 <sup>b</sup> | 1.604 <sup>a</sup> | 1.537 <sup>b</sup> |
| Fourth           | 69.71 <sup>a</sup> | 75.49 <sup>b</sup> | 1.742 <sup>a</sup> | 1.579 <sup>b</sup> |
|                  | 73.9 <sup>a</sup>  | 76.5 <sup>b</sup>  | 1.605 <sup>a</sup> | 1.528 <sup>b</sup> |

30 HENS/QUARTILE

<sup>a,b</sup> Means with different superscripts within a row are significantly different ( $P \leq .05$ ).

# AN EXAMPLE OF ISOLATING THE PERFORMANCE RESPONSE

WHEN COMPARED TO CONTROL BIRDS NOTICE THE BETTER  
UNIFORMITY IN PERFORMANCE WITH THE VIRGINIAMYCIN BIRDS ?



<sup>a,b</sup> Means with different superscripts within a row are significantly different ( $P \leq .05$ ).

# **ANTIBIOTICS**

## **"CURRENT POSITION"**

**CONSUMER DEMAND  
HAS ALWAYS BEEN THE MAJOR DRIVING  
FORCE IN THE POULTRY INDUSTRY**

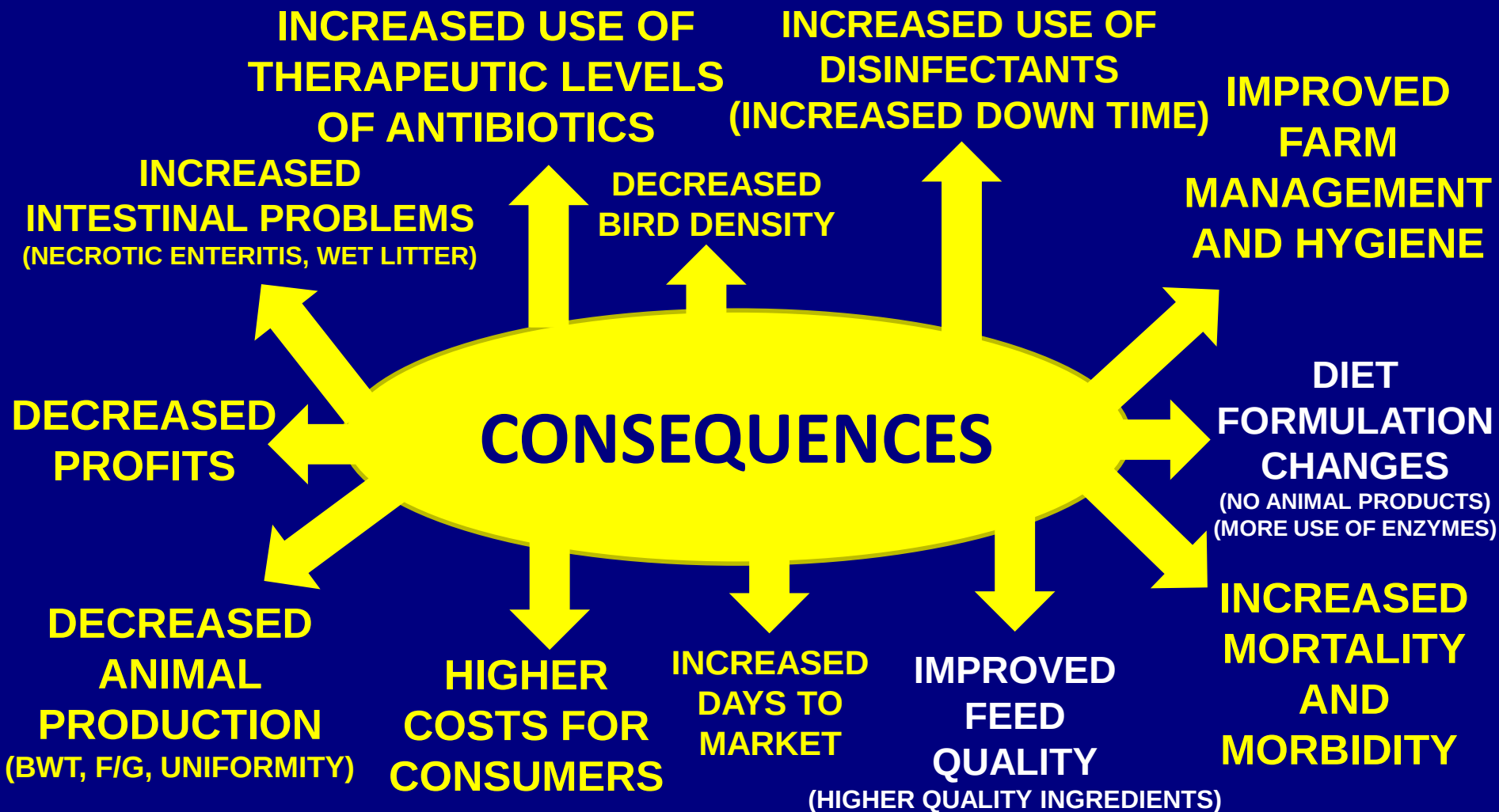
**...AND NOW...**

**CONSUMERS ARE DEMANDING  
ALL ANIMAL PRODUCTS BE PRODUCED  
WITHOUT THE USE OF ANTIBIOTICS**



# CONSEQUENCES OF BANNING GROWTH PROMOTING ANTIBIOTICS IN THE EUROPEAN UNION

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# **ANTIBIOTICS**

**...FACT...**



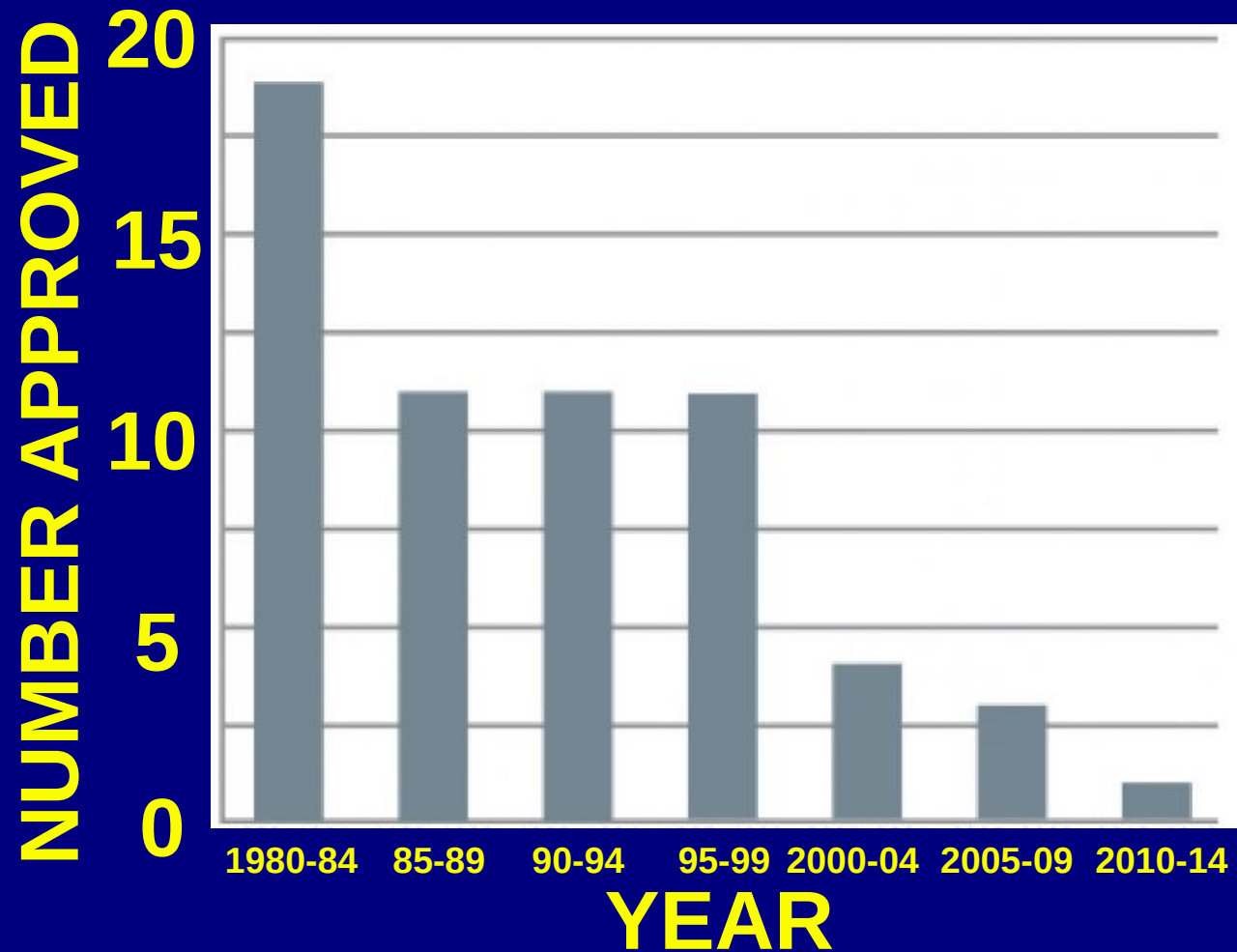
**IT IS VERY UNLIKELY THAT ANY NEW  
GROWTH PROMOTING ANTIBIOTICS  
WILL BE DEVELOPED AND APPROVED  
IN THE NEAR FUTURE FOR USE  
IN THE ANIMAL INDUSTRY**

---

**THE COST OF DEVELOPMENT AND TESTING ANTIBIOTICS  
IS BECOMING COST PROHIBITIVE  
AND**

**THE FUTURE TREND SEEMS TO BE NOT TO APPROVE  
AS MANY NEW ANTIBIOTICS AS IN THE PAST**

# NUMBER OF “SYSTEMIC” ANTIBACTERIAL NEW DRUG APPLICATION APPROVALS TO THE FDA SINCE 1980



# **POSSIBLE ALTERNATIVE REPLACEMENTS FOR GROWTH PROMOTING ANTIBIOTICS**

---

**ANTIBACTERIAL  
VACCINES**

**MICROBIAL  
COMMUNICATION  
DISRUPTORS**

**HOST IMMUNE  
STIMULATORS**

**PROBIOTICS  
PREBIOTICS  
SYNBIOTICS**

**BACTERIOPHAGES**

**PLANT EXTRACTS  
PLANT OILS  
MICROBIAL BINDERS**

**ANTIMICROBIAL  
PEPTIDES**

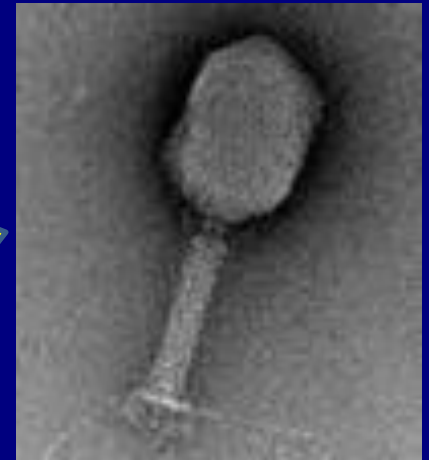
**FEED ENZYMES  
ORGANIC ACIDS**

**NUMEROUS  
OTHERS**

# **“IDEAL CHARACTERISTICS” OF GROWTH PROMOTING ANTIBIOTIC ALTERNATIVES**

- 1) NON-TOXIC AND HAVE NO SIDE EFFECTS
- 2) EASY TO ELIMINATE FROM THE BODY
- 3) NO ENVIRONMENTAL RESIDUES
- 4) NO BACTERIAL RESISTANCE
- 5) STABLE IN FEED
- 6) STABLE IN STORAGE
- 7) PROMOTE GROWTH
- 8) PROMOTE ANIMAL'S RESISTANCE TO DISEASE

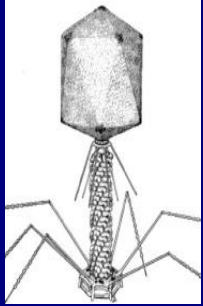
**BACTERIOPHAGES**  
POSSESS ALL OF THESE  
IDEAL CHARACTERISTICS



- 9) PROMOTE GROWTH OF BENEFICIAL BACTERIA
- 10) PROMOTE ANIMAL'S RESISTANCE TO DISEASE
- 11) PROMOTE GROWTH AND IMPROVE FEED EFFICIENCY
- 12) PROVIDE A POSITIVE CONSISTENT PERFORMANCE RESPONSE



# CAN BACTERIOPHAGES BE USED WITH ANTIBIOTICS ?



# YES

## VERY SUCCESSFULLY

**...IMPORTANT FACTS TO REMEMBER...**

### ANTIBIOTICS

**ARE NOT SPECIFIC FOR A CERTAIN BACTERIAL SPECIES  
AND EVEN LESS SPECIFIC AGAINST CERTAIN STRAINS  
OF BACTERIA WITHIN A SPECIES**

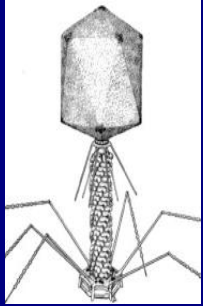
**(USUALLY KILL BACTERIA UNDERGOING A RAPID GROWTH PHASE)**

### BACTERIOPHAGES

**ARE VERY SPECIFIC FOR ONLY ONE BACTERIAL SPECIES  
AND SPECIFIC FOR CERTAIN STRAINS WITHIN A SPECIES  
(KILL BACTERIA INDEPENDENTLY OF THE GROWTH PHASE)**

## QUESTION

# HOW SAFE ARE BACTERIOPHAGES ? ? ? ?



## VERY SAFE

**APPROVED BY  
USDA, FDA & FSIS  
FOR USE ON MANY FOOD ITEMS  
(SUCH AS CARCASSES AND READY TO EAT MEAT PRODUCTS)**



**QUESTION**

# ...BACTERIOPHAGES...

FAVORABLE EXPECTED CONSEQUENCES  
OF THEIR USE IN ANIMAL DIETS

GROWTH ENHANCEMENT

IMPROVED FEED CONVERSION

IMPROVED FLOCK UNIFORMITY

LESS SUBCLINICAL DISEASE

BETTER INTESTINAL “BACTERIAL STABILITY”

(PREVENT DYSBACTERIOSIS)

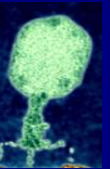
REDUCED IMMUNE STIMULATION

IMPROVED PRODUCT SAFETY & QUALITY

...AND...

# OTHERS

# USING BACTERIOPHAGES



“SOMETHING TO THINK ABOUT”

## BROILER BREEDER FEED

**IF BACTERIOPHAGES ARE USED  
WILL BROILER BREEDER FEED  
CONTINUE TO BE PELLETTED ?**



# USING BACTERIOPHAGES



**“SOMETHING TO THINK ABOUT”**

## BROILER/BROILER BREEDER FEED



**MEAT MEAL**



**FISH MEAL**



**POULTRY MEAL**

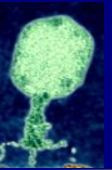
**IF BACTERIOPHAGES ARE USED  
WILL MORE ANIMAL BY-PRODUCT  
FEED INGREDIENTS BE IN THE DIET ?**



# USING BACTERIOPHAGES



“SOMETHING TO THINK ABOUT”



## BROILER/BROILER BREEDER FEED

**Iron Availability Increases the Pathogenic Potential of *Salmonella Typhimurium* and Other Enteric Pathogens at the Intestinal Epithelial Interface**

Guus A. M. Kortman, Annemarie Boleij, Dorine W. Swinkels, and Harold Tjalsma\*  
Stefan Bereswill, Editor

[Author information](#) ► [Article notes](#) ► [Copyright and License information](#) ►  
This article has been [cited by](#) other articles in PMC.

**IF BACTERIOPHAGES ARE USED  
WILL MORE BLOOD MEAL FIND ITS  
WAY INTO POULTRY DIETS ?**

# USING BACTERIOPHAGES



**“SOMETHING TO THINK ABOUT”**

***IN OVO* NUTRITION/FEEDING**  
**(HUMAN INTERVENTION AT DAY 17-18)**

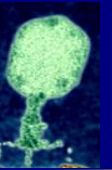


**IF BACTERIOPHAGES ARE USED  
ALONG WITH *IN OVO* PROCEDURES WHAT  
BENEFITS WILL RESULT AFTER HATCH ?**

# USING BACTERIOPHAGES



**“SOMETHING TO THINK ABOUT”**



**USE WITH VERY STRESSFUL SITUATIONS  
WITH COMERCIAL EGG-TYPE LAYING HENS**



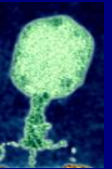
**IF BACTERIOPHAGES ARE USED  
WITH MOLTING PROGRAMS WILL THE  
SALMONELLA THREAT BE LESS ?**



# USING BACTERIOPHAGES



“SOMETHING TO THINK ABOUT”



WHEAT  
(ARABINOXYLANS)



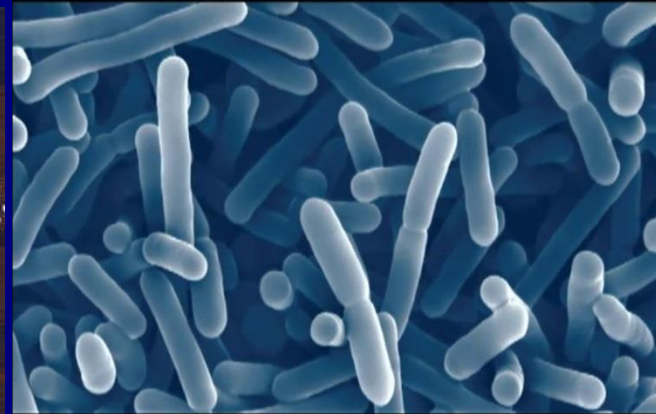
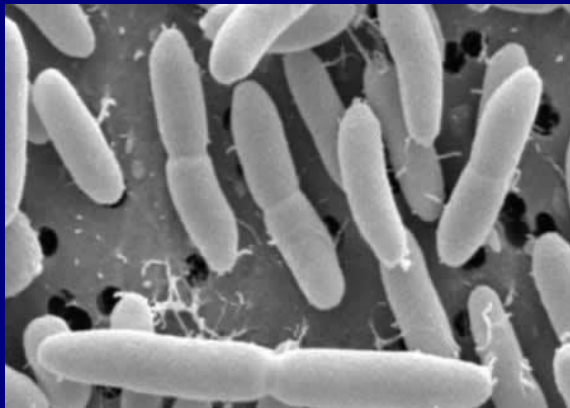
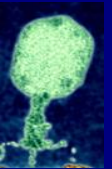
BARLEY  
(BETA-GLUCANS)

IF BACTERIOPHAGES ARE USED  
WITH DIETS CONTAINING HIGHLY VISCOUS  
NSP'S WHAT WILL BE THE RESULT ?

# USING BACTERIOPHAGES



**“SOMETHING TO THINK ABOUT”**



**IF BACTERIOPHAGES ARE USED  
WITH PROBIOTICS, PREBIOTICS AND  
SYNBIOTICS ALONE OR AS A COCKTAIL  
WILL POSITIVE THINGS HAPPEN ?**



# USING BACTERIOPHAGES



**“SOMETHING TO THINK ABOUT”**



**IF BACTERIOPHAGES ARE USED  
IN HYDRATED NUTRIENT SOURCES  
IN CHICK BOXES AND DURING BROODING  
WHAT WILL BE THE EFFECT ?**

# THIS HEADLINE SUMS UP EVERYTHING ABOUT THE FUTURE USE OF ANTIBIOTICS USED FOR GROWTH PROMOTION

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**ScienceNews**  
MAGAZINE OF THE SOCIETY FOR SCIENCE & THE PUBLIC

## Science & the Public

Humans & Society, Nutrition, Earth & Environment, Biomedicine, Agriculture

### **Growth-promoting antibiotics: On the way out?**

*Court instructs FDA to resume efforts aimed at banning use of low-dose antibiotics in livestock feed*

By Janet Raloff 1:30pm, March 23, 2012

# **BACTERIOPHAGES**

**...FACT...**

**RECENT RESEARCH INTEREST IN THE USE  
OF BACTERIOPHAGES IN ANIMAL DIETS IS  
INCREASING AT A VERY RAPID RATE  
AND**

**INTEREST WILL CONTINUE TO INCREASE AS WE  
DISCOVER MORE ABOUT THERE BENEFITS  
IN PROMOTING ANIMAL PERFORMANCE**



# ...IN THE PAST AND PRESENTLY...

## MOST BACTERIOPHAGE RESEARCH IS RELATED TO HUMANS (PHAGE THERAPY)

### Bacteriophage adhering to mucus provide a non–host-derived immunity

Jeremy J. Barr<sup>a,1</sup>, Rita Auro<sup>a</sup>, Mike Furlan<sup>a</sup>, Katrine L. Whiteson<sup>a</sup>, Marcella L. Erb<sup>b</sup>, Joe Pogliano<sup>b</sup>, Aleksandr Stotland<sup>a</sup>, Roland Wolkowicz<sup>a</sup>, Andrew S. Cutting<sup>a</sup>, Kelly S. Doran<sup>a</sup>, Peter Salamon<sup>c</sup>, Merry Youle<sup>d</sup>, and Forest Rohwer<sup>a</sup>

<sup>a</sup>Department of Biology, San Diego State University, San Diego, CA 92182; <sup>b</sup>Division of Biological Sciences, University of California, San Diego, CA 92093;

<sup>c</sup>Department of Mathematics and Statistics, San Diego State University, San Diego, CA 92182; and <sup>d</sup>Rainbow Rock, Ocean View, HI 96737

Edited by Richard E. Lenski, Michigan State University, East Lansing, MI, and approved April 18, 2013 (received for review March 28, 2013)

Mucosal surfaces are a main entry point for pathogens and the principal sites of defense against infection. Both bacteria and phage are associated with this mucus. Here we show that phage-to-bacteria ratios were increased, relative to the adjacent environment, on all mucosal surfaces sampled, ranging from cnidarians to humans. In vitro studies of tissue culture cells with and without surface mucus demonstrated that this increase in phage abun-

epithelium may respond by increased production of antimicrobial agents, hypersecretion of mucin, or alteration of mucin glycosylation patterns to subvert microbial attachment (29–31).

Also present in the mucus environment are bacteriophage (phage), the most common and diverse biological entities. As specific bacterial predators, they increase microbial diversity through Red Queen/kill-the-winner dynamics (32, 33). Many





# PUBLISHED RESEARCH

## Effects of Dietary Supplementation of Bacteriophage on Productive Performance and Egg Quality in Laying Hens after Forced-molting

G. P. Han, J. E. Shin, J. H. Kim, and D. Y. Kil

*Department of Animal Science and Technology, Chung-Ang University, Anseong-si, Republic of Korea*



### British Poultry Science

Publication details, including instructions for authors and subscription information:  
<http://www.tandfonline.com/loi/cbps20>

### Effect of dietary supplementation of bacteriophage on performance, egg quality and caecal bacterial populations in laying hens

J.H. Kim<sup>a</sup>, J.W. Kim<sup>a</sup>, H.S. Shin<sup>a</sup>, M.C. Kim<sup>a</sup>, J.H. Lee<sup>b</sup>, G.-B. Kim<sup>a</sup> & D.Y. Kil<sup>a</sup>

<sup>a</sup> Department of Animal Science and Technology, Chung-Ang University, Anseong-si, Gyeonggi-do, Republic of Korea

<sup>b</sup> CTCBio Inc., Seoul, Republic of Korea

Accepted author version posted online: 04 Dec 2014. Published online: 13 Jan 2015.

# PUBLISHED RESEARCH



**Asian-Aust. J. Anim. Sci.**  
**Vol. 25, No. 7 : 1015 - 1020**  
**July 2012**

[www.ajas.info](http://www.ajas.info)  
<http://dx.doi.org/10.5713/ajas.2012.12026>

## **Effects of Bacteriophage Supplementation on Egg Performance, Egg Quality, Excreta Microflora, and Moisture Content in Laying Hens**

**P. Y. Zhao, H. Y. Baek and I. H. Kim\***

Department of Animal Resource and Science, Dankook University, Cheonan, Choongnam, 330-714, Korea



**Asian-Aust. J. Anim. Sci.**  
**Vol. 26, No. 4 : 573-578 April 2013**  
<http://dx.doi.org/10.5713/ajas.2012.12544>

[www.ajas.info](http://www.ajas.info)  
pISSN 1011-2367 eISSN 1976-5517

## **Evaluation of Bacteriophage Supplementation on Growth Performance, Blood Characteristics, Relative Organ Weight, Breast Muscle Characteristics and Excreta Microbial Shedding in Broilers**

**J. P. Wang, L. Yan, J. H. Lee<sup>1</sup> and I. H. Kim\***

Department of Animal Resource and Science, Dankook University, Cheonan, Choongnam, 330-714, Korea

# PUBLISHED RESEARCH



- Effect of dietary supplementation of bacteriophage on performance, egg quality and caecal bacterial populations in laying hens. British Poultry Science, 2015



- Effect of dietary supplementation of bacteriophage on growth performance and cecal bacterial populations in broiler chickens raised in different housing systems. Livestock Science, 2014



- Bacteriophage and probiotics both enhance the performance of growing pigs but bacteriophage are more effective. Anim. Feed Sci. Technol., 2014



- Evaluation of bacteriophage supplementation on growth performance, blood characteristics, and excreta microbial shedding in broilers. AJAS, 2013



- Effect of bacteriophage supplementation on the growth performance, nutrient digestibility, blood characteristic, and fecal microbial shedding in growing pigs. AJAS, 2012



- Effectiveness of bacteriophage supplementation on egg performance, egg quality, excreta microflora, and moisture content in laying hens. AJAS, 2012

# PUBLISHED RESEARCH



- Bacteriophage based nature friendly control technology for prevention and treatment of bacterial infection commonly encountered in flounder *Paralichthys olivaceus* culture. 5th Int. Symposium Cage Aquaculture. Asia, 2015



- Protective effects of bacteriophage against *S. Typhimurium* infection on weaning pigs. 6th APVS, 2013



- Protective effect of bacteriophage against enterotoxigenic *E. coli* K88 infection on weaned pigs. KOSVES, 2013



- Effect of dietary supplementation of bacteriophage on laying performance, egg quality, and cecal microbial population in laying hens. WCAP, 2013





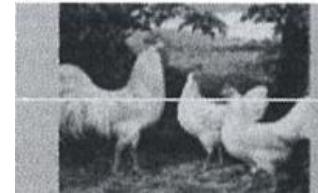
# Effect of dietary bacteriophage supplementation on internal organs, fecal excretion, and ileal immune response in laying hens challenged by *Salmonella* Enteritidis



P. A. Adhikari, D. E. Cosby, N. A. Cox, J. H. Lee, W. K. Kim ✉

Poult Sci pex109. DOI: <https://doi.org/10.3382/ps/pex109>

**Published:** 26 April 2017 **Article history** ▼



Journal of Applied Poultry Research

# **BACTERIOPHAGES**

**AND**

**...FINALLY...**

**HOW DO I FEEL ABOUT THE FUTURE  
WITHOUT GROWTH PROMOTING ANTIBIOTICS**





**MUCHAS  
GRACIAS**