

SLIDE PRESENTATION

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American Society for Microbiology
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"Sterilization And Control – The Role Of The
Independent Consulting Laboratory"

STERILITY TEST PROGRAM

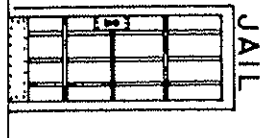
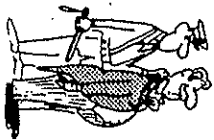
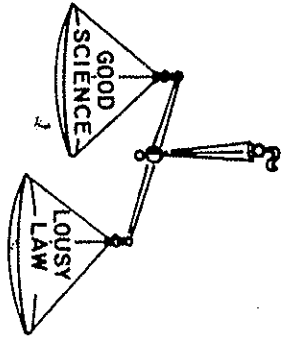
1. NATURE OF PRODUCT AND USE
2. RAW MATERIALS
3. BACKGROUND COUNTS (aerobic & anaerobic)
4. ISOLATION OF ORGANISMS
5. D-VALUE CURVES
6. EXPERIMENTAL STERILIZATION (full or subdose)
7. USP 19 TEST vs USP GUIDELINES
8. INOCULATED PRODUCT - FEASIBLE?
9. FINAL RECOMMENDATION

OFFICIAL USP STERILITY TESTS

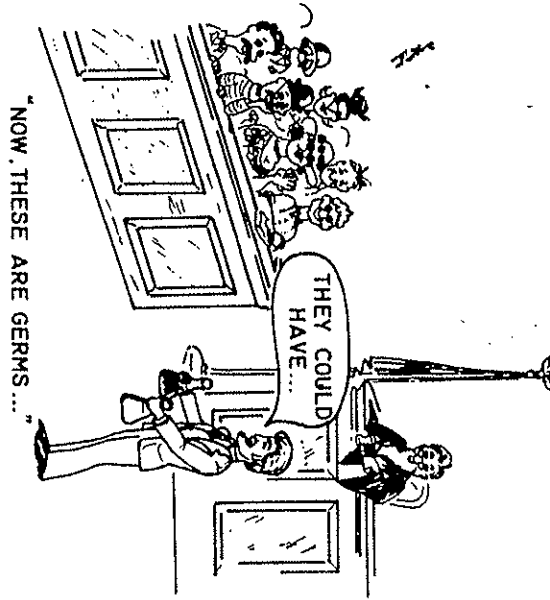
USP	MEDIA	CHAPTERS	SAMPLING
14 (1950)	FTM, SAB (7-15d)	a. Sterility Tests	a. A Sufficient Number*
17 (1965)	FTM, SAB (7-14d)	a. Sterilization b. Sterility Test	a. Nothing b. At Least 20* 14d
18 (1970)	FTM SCD (7-14d)	a. Sterilization (p.830) b. Sterility Tests (p.851)	a. Nothing b. Specific Table p. 855 with Biol. Indicators *
19 (1975)	FTM SCD (7-14d)	a. Sterilization (p.709) b. Sterility Tests (p.592)	a. Specific Table p. 712 with Biol. Indicators b. 20 FTM..... 14d * 20 SCD..... 14d
? (1984)	NONE	a. Sterilization Process b. Air Sampling and Gnotobiosis c. GMP and Disinfection d. Statistics e. Dosimetry f. Background Counts**	NONE ?

*Progressive
and
Regressive
Quantum
Jumps*

* Official Tests
** Methods Required



JIMMY APPLESEED, ESQ. REPRESENTING SARAH JANE COMATOSE



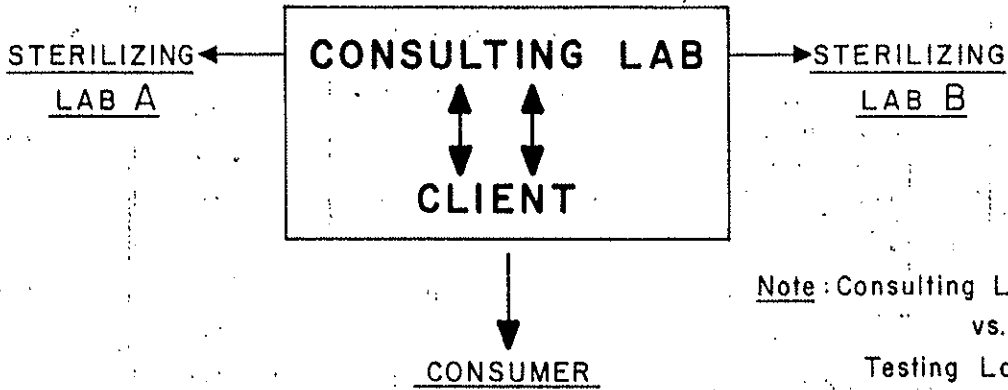
CONSULTING LAB. SUMMARY

1. GMP - KNOWLEDGE OF REGULATIONS
2. STERILIZATION - KNOWLEDGE OF PROCESS
3. STERILITY TEST - "and sleep thee well"

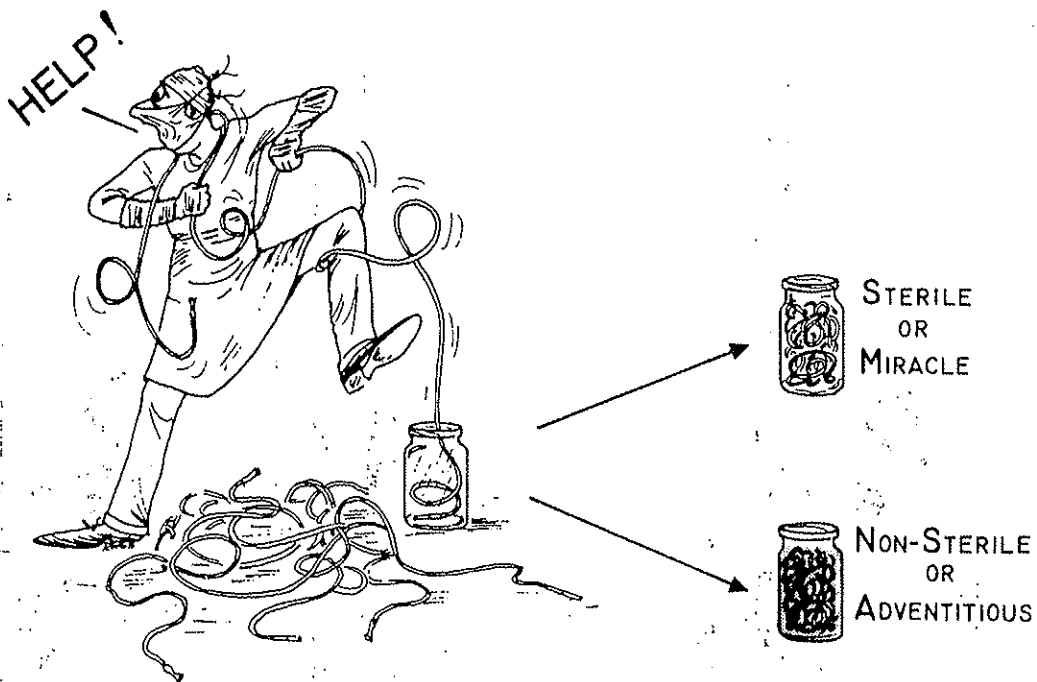


PROTECT YOUR PRODUCT
PROTECT THE CONSUMER
PROTECT YOURSELF

FDA

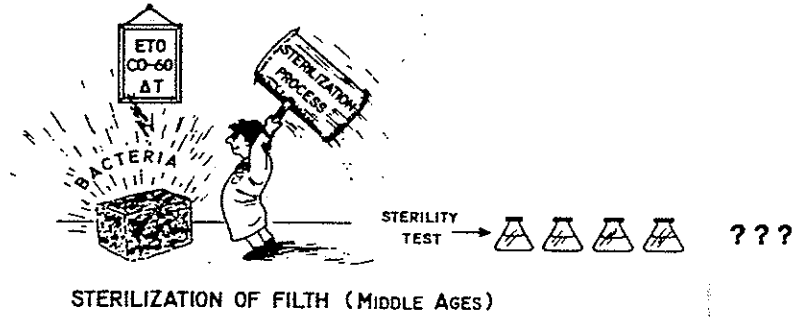


TECHNICAL PROBLEMS

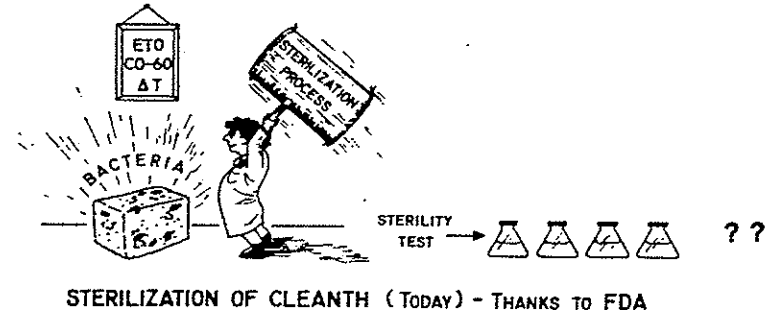


THE MONSTER DEVICE - DIRECT STERILITY TEST

VALUE OF STERILITY TEST



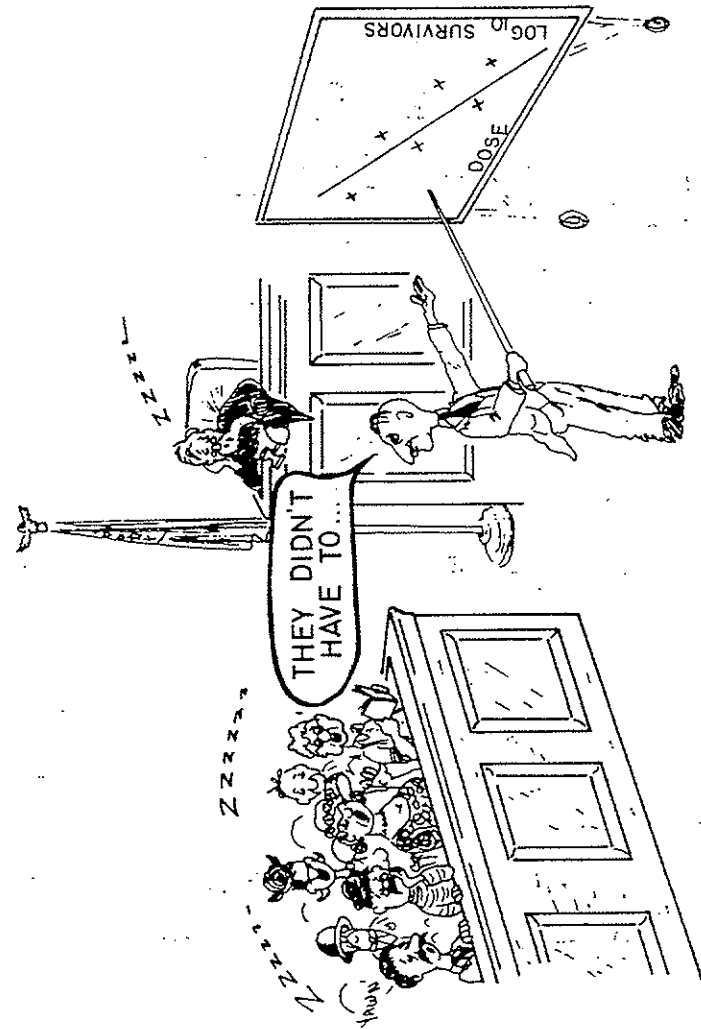
STERILIZATION OF FILTH (MIDDLE AGES)



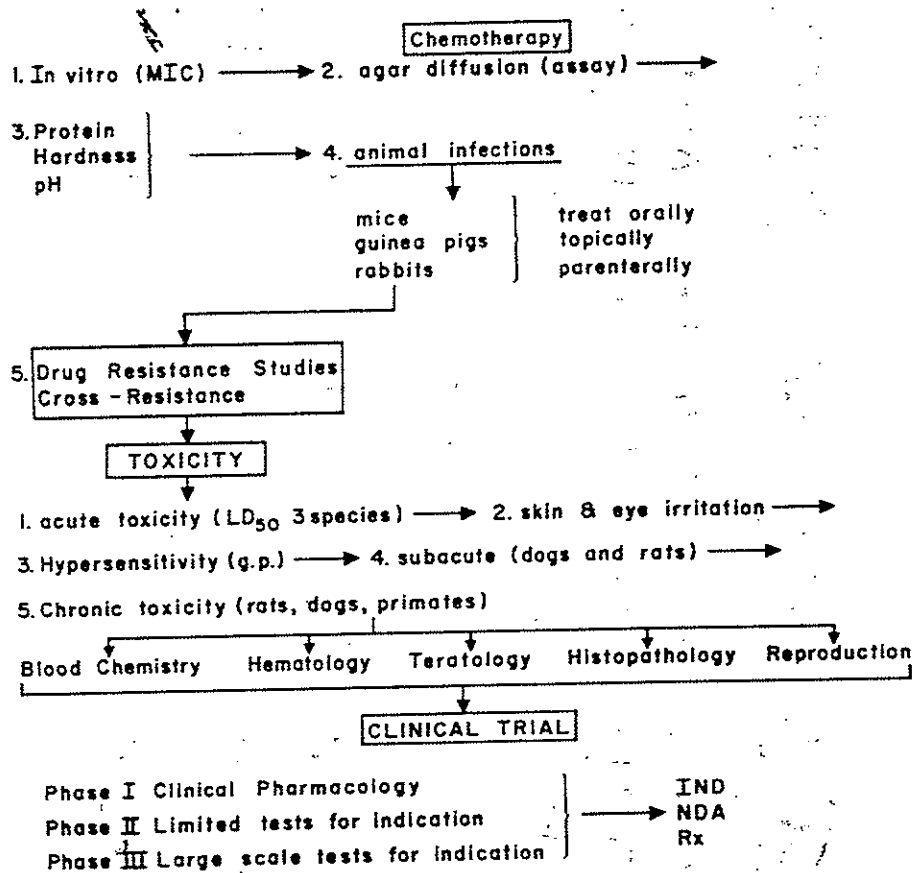
STERILIZATION OF CLEANTH (TODAY) - THANKS TO FDA



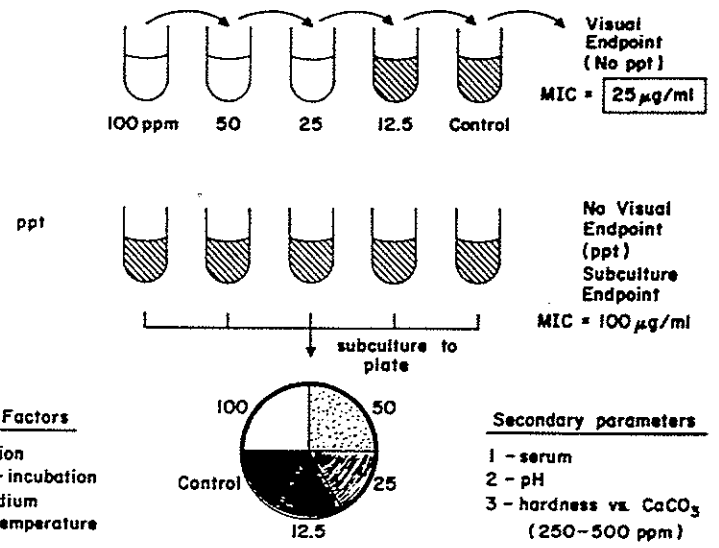
STERILIZATION OF SUPER CLEANTH (TOMORROW) - SUPER GMP



L.
DRUGS - R & D ROUTE



C.



Primary Factors
concentration
organism + incubation
time + medium
solvent + temperature

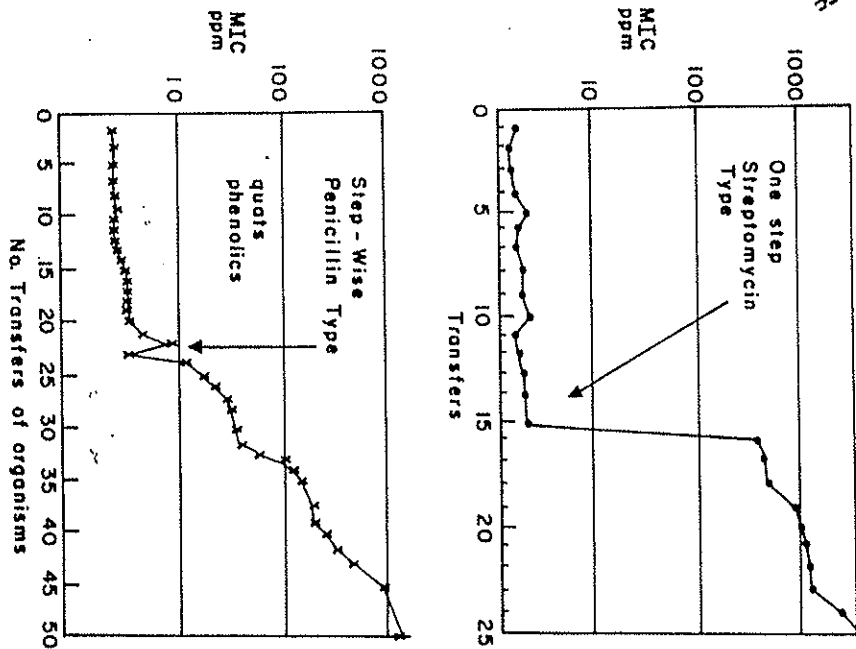
Secondary parameters
1 - serum
2 - pH
3 - hardness vs. CaCO₃
(250-500 ppm)

(MIC)- Minimum Inhibitory Concentration Test - Broth Culture

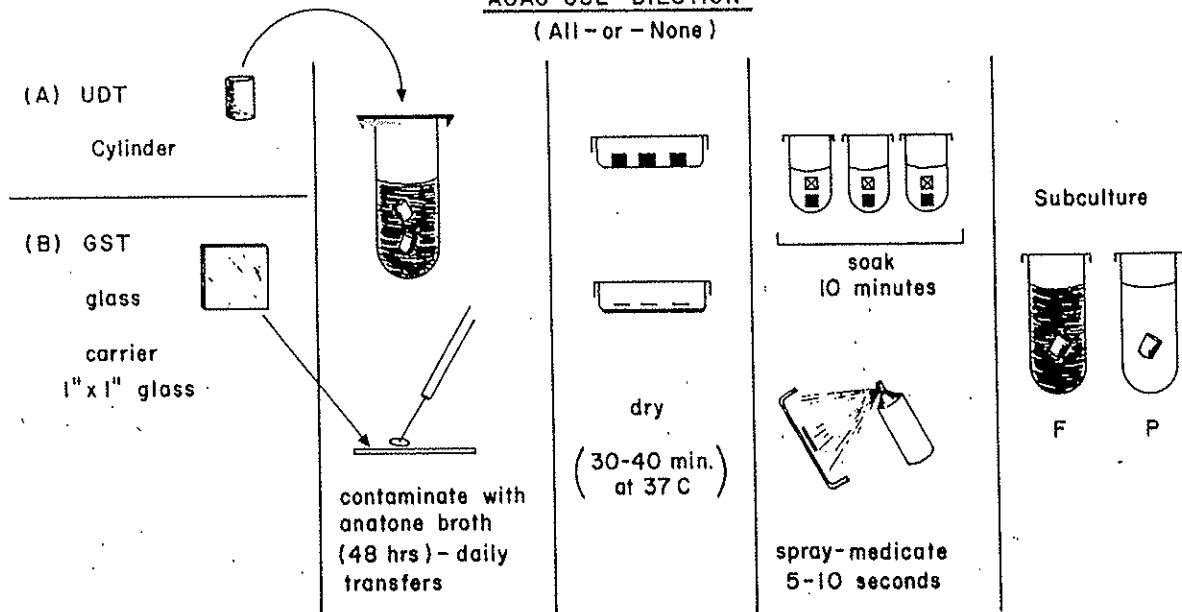
Extrapolations and Interpretations

Primary screen (MIC vs. E. coli)		Weber & Black AOAC 30 sec. killing study in water	Interpretation
Agent	ppm	25 ppm vs. E. coli	
W	250	very active - 6 log reduction	protein effect
X	12.5	inactive -	metabolic inhibition
Y	12.5	inactive -	hard water effect
Z	12.5	active - 5 log reduction	contact kill

H-1
DRUG RESISTANCE



E.
AOAC USE-DILUTION
 (All-or-None)



- Organisms : *Salmonella cholerasuis* ATCC-10708
Staphylococcus aureus ATCC-6538
Pseudomonas aeruginosa ATCC-15442
Trichophyton interdigitale ATCC-640
Mycobacterium tuberculosis (BCG)
 Ether-sensitive and ether-resistant viruses
 (Herpes) (Coxsackie)

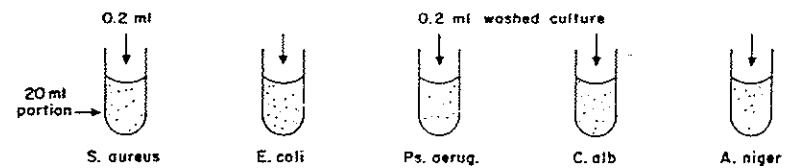
F.

USP PRESERVATIVE EFFICACY

(Parenterals)



Bacteriostatic water etc.



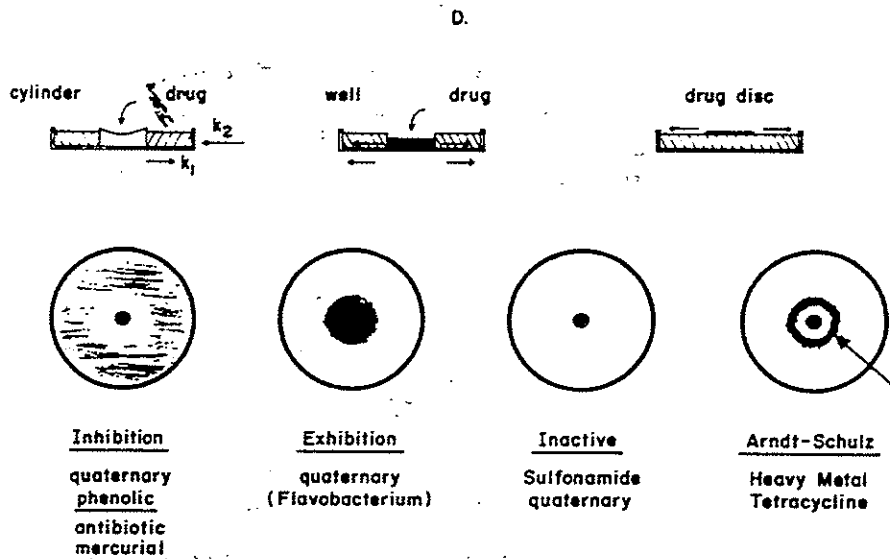
Total count
per ml

Zero T = 10^5 /ml

1 day	10^2	10^4	10^5	10^5	10^5
7 days	10^1	10^3	10^4	10^5	10^5
21 days	<10	10^2	10^3	10^4	10^5
28 days	<10	10^1	10^2	10^4	10^5
Δ log reduction	5	4	3	1	0
% kill	99.999	99.99	99.9	90	0
Result	P	P	P	P	P

Standardization

1. strains and propagation
2. volume of parenteral tested
3. % reduction (B = 99.9% F = stasis)
4. length of test



(ZI) ZONE OF INHIBITION TEST-AGAR DIFFUSION

(A) k_1 = rate at which substance diffuses from well (Solubility)

(B) k_2 = rate at which organism multiply (growth of bio-mass)

$ZI = \frac{(A) \text{ Solubility}}{(B) \text{ Growth}} \quad A/B = a \text{ constant} \quad \therefore \quad ZI = k \frac{\text{Solubility}}{\text{Growth}}$

solubility as grams % (Broth) or mm^3 per hour (agar)

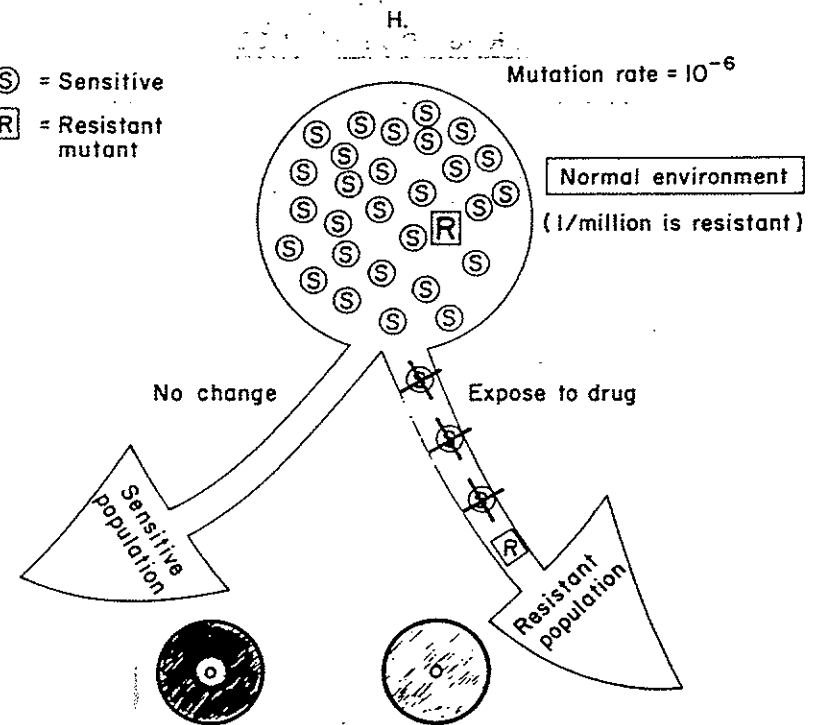
growth as generation time at temperature, pH and O_2 = g

g (*E. coli*) (Nutrient broth) = 30-40 minutes

g (*Pseudomonas stutzeri*) (in powder) = 84 hours (pigment D&C No. 7)

⊙ = Sensitive

⊠ = Resistant mutant



NATURAL SELECTION (Darwinian)

(Lwoff, Lederberg, Hershey)

Resistance to drugs occurs naturally independent of presence of drug - Presence of drug exerts pressure toward population wherein resistance has survival value.