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APPENDIX 1

The Percent Penetration of Antituberculous Drugs into the CSF

Drugs	The percent penetration into the CSF	
	in normal	in meningitis
Ethambutol	0 [9]	10-50 % [11] (1-2 mcg/ml) [9]
Isoniazid	20 [11,13,14]	90 % (2 mcg/ml) [8,10,11]
Pyrazinamide	100 [51]	100 % (50 mcg/ml) [8]
Rifampin	0 [11]	10 - 20 % [10]
Streptomycin	< 10 [11,12]	20 % (2-9 mcg/ml) [11,12]

APPENDIX 2

The Cerebrospinal Fluid in Meningitis

Cerebrospinal fluid	Type of Meningitis				
	pyogenic	tuberculous	fungal	viral	parasitic
Pressure	↑	↑	↑	↑ or →	↑ or →
Cells total (per cu mm) differential	>1,000 p+++	< 1,000 L >P	<1,000 L & P	< 1,000 L > P	< 1,000 E
Protein	↑	↑↑	↑	↑	↑
Sugar	↓	↓	↓	→	→

↑ = increased

→ = normal

↓ = decreased

P = Polymorphonuclear leucocytes

L = lymphocytes

E = Eosinophils

APPENDIX 3

Recommended Daily Doses of Antituberculous Drugs

Drugs	Adult	Children
Isoniazid	5 mg/kg or 300 mg	10 - 20 mg/kg (maximum of 500 mg)
Rifampin	600 mg	10 - 20 mg/kg (maximum of 600 mg)
Ethambutol	15 mg/kg	15 - 25 mg/kg/d or 800 - 1600 mg
Streptomycin	15 - 25 mg/kg or 0.75 - 1 g	20 - 40 mg/kg
Pyrazinamide	20 - 35 mg/kg or 1.50 - 2.25 g (maximum of 3 g)	20 - 30 mg/kg
Para - aminosa-licylic acid	200 mg/kg/d or 12 -16 g	200 - 420 mg/kg/d
Cycloserine	10 - 15 mg/kg/d or 0.5 - 1 g	5 - 15 mg/kg
Ethionamide	7 - 15 mg/kg/d or 0.5 - 1 g	10 - 20 mg/kg/ (maximum of 750 mg)
Viomycin	1 - 2 g	NR
Capreomycin	15 mg/kg/d or 1 g	NR
Kanamycin	15 mg/kg/d or 0.5 - 1 g	NR

NR = not recommended

APPENDIX 4

Specific Characteristics of Enterobacter Cloacae in this Study Compared with in "Bergey's Manual of Determinative Bacteriology"

Characteristics	Enterobacter Cloacae	
	in this study	in Bergey's Manual
Gram Strain	gram - negative	gram - negative
Starch Hydrolysis	positive	-
Casein Hydrolysis	negative	-
Gelatin Hydrolysis	negative	positive
Lactic Acid Production	negative	-
Litmus Milk Reaction	6 R	5 R
Nitrate Reduction	positive	positive
Glucose Fermentation	Ⓐ	Ⓐ
Lactose Fermentation	Ⓐ	Ⓐ
Sucrose Fermentation	Ⓐ	A
Indole Test	negative	negative
Voges - Proskauer Test	positive	positive
Methyl Red Test	negative	negative
Hydrogen Sulfide	negative	negative
Detection of Catalase	positive	-

Litmus Milk Code

1 = no change

2 = Alkaline

3 = Alkaline with peptonization

4 = Acid, curd formation

5 = Acid and gas

6 = Acid, no curd

R = Signifies Reduction

Key to fermentation broth results :

A = Acid

Ⓐ = Acid and gas

V = Variable

APPENDIX 5

STANDARD CURVE DETERMINATION

The concentrations of rifampin and streptomycin in the specimens were calculated from their standard curves which were plotted on semilogarithmic paper, using the concentration in mcg per ml. (log) as the ordinate and the diameter in mm. of the inhibition zone as the abcissa.

Example of typical standard curve data for rifampin and streptomycin concentrations estimated using linear regression[1] was shown and plotted as follows :

Standard number	Diameter (mm.)	Conc. (mcg/ml)	Inversely estimated conc[2]	% Theory[3]
1	14.61	10.00	10.06	100.60
2	16.90	20.00	20.02	100.10
3	18.16	30.00	29.23	97.43
4	19.25	40.00	40.55	101.38
5	19.96	50.00	50.20	100.40

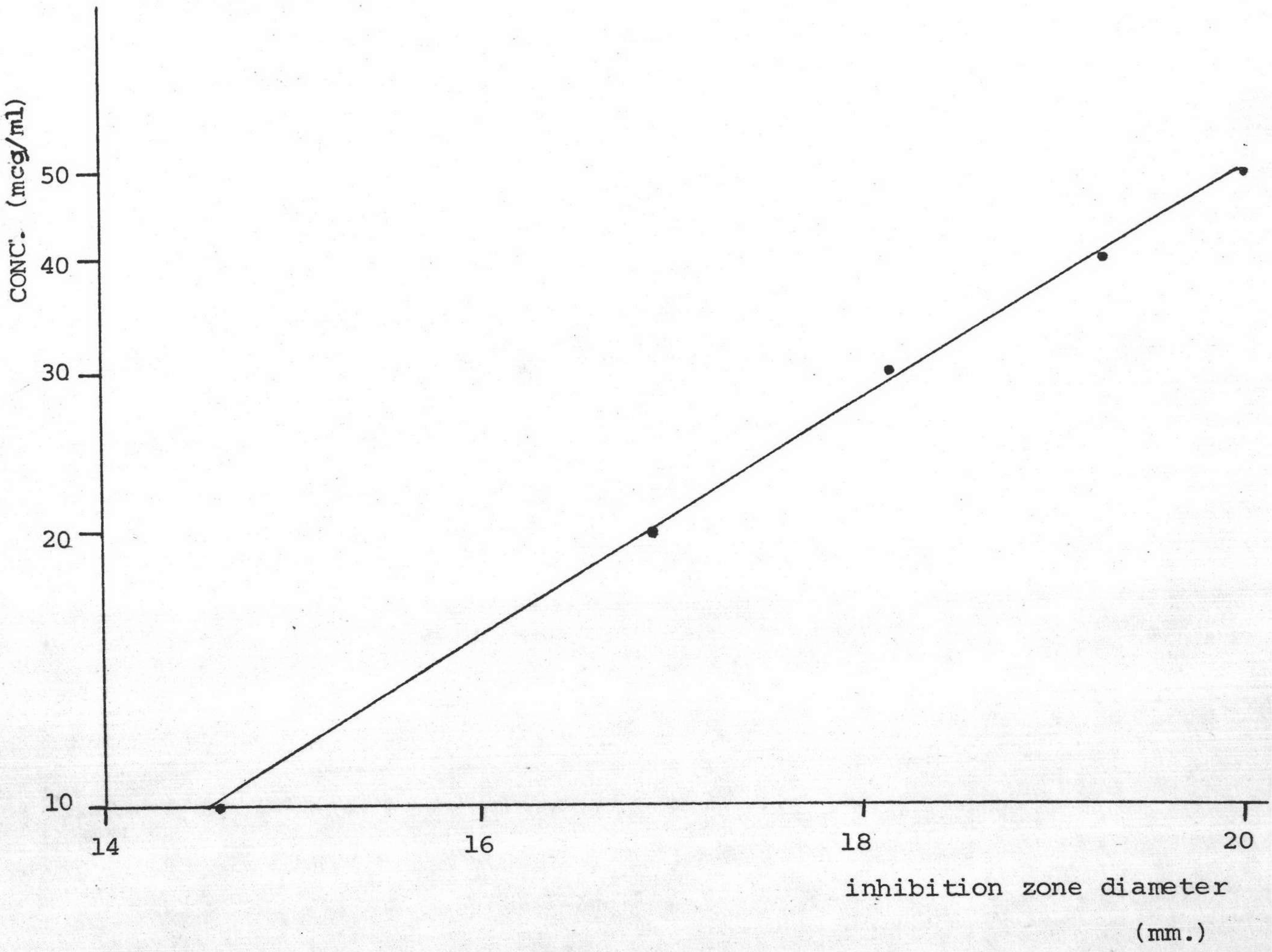
Mean	99.98
S.D.	1.5031
C.V.[4]	1.5034

(1) $R^2 = 0.999$

(2) Inversely estimated conc = -2.3197 + 0.1030 (Diameter)

(3) $\% \text{ Theory} = \frac{\text{Inversely estimated conc.}}{\text{Known conc}} \times 100$

(4) $\text{Coefficient of Variation} = \frac{\text{S.D.}}{\text{Mean}} \times 100$


CONC. (mcg/ml)
50
40
30
20
10
14
16
18
20
inhibition zone diameter
(mm.)

APPENDIX 6

STATISTICAL ANALYSIS

Analysis of Variance (One-way Classification)

Analysis of variance, often referred to as ANOVA, can be used in the comparison of means not only for cases involving two groups but also when three, four, or in fact any of populations are being compared. The null hypotheses we want to test is

$$Ho : \mu_1 = \mu_2 = \ldots\ldots\ldots\ldots\ldots\ldots = \mu_k,$$

where μ_1, μ_2, ... μ_k denote the means of $k \geq 2$ populations. If H_o is rejected, the alternative hypothesis that at least two of the population means are not egual is tenable - that is, $\mu_j \neq \mu_{j'}$, for some pair of means μ_j and $\mu_{j'}$.

The data should be arranged as shown in the Table.

	Treatment					
	1	2	3	....	k	
	X_{11}	X_{12}	X_{13}	....	X_{1k}	
	X_{21}	X_{22}	X_{23}	....	X_{2k}	
	X_{31}	X_{32}	X_{33}	....	X_{3k}	
	⋮	⋮	⋮	⋮		
	$Xn_1 1$	$Xn_2 2$	$Xn_3 3$	....	$Xn_k.k$	
Total	T.1	T.2	T.3	....	T.k	T..
mean	$\bar{X}.1$	$\bar{X}.2$	$\bar{X}.3$	....	$\bar{X}.k$	$\bar{X}..$

ij = any one observation (i) for the j^{th} factor level

i = 1, 2, ..., n_j ; j = 1, 2, ..., k

$$T._j = \sum_{i=1}^{n_j} X_{ij}$$

In analysis of variance, parts of this formula are calculated separately and brought together in the "Summary table".

1. Correction term or C = $\frac{T..^2}{N}$

2. Sum of squares (SS)

   2.1 The total sum of square (SS_{total}) = $\sum_{j=1}^{k} \sum_{i=1}^{n_j} X_{ij}^2 - C$

   2.2 The within treatment (or error) sum of square

$$(SS_{within}) = \sum_{j=1}^{k} \sum_{i=1}^{n_j} X_{ij}^2 - \sum_{j=1}^{k} \frac{(T.j)^2}{n_j}$$

   2.3 The between treatment sum of square ($SS_{between}$)

$$= \sum_{j=i}^{k} \frac{(T.j)^2}{n_j} - C$$

$$SS_{total} = SS_{between} + SS_{within}$$

Source of Variation	SS	df	MS	F^*
Between treatment	$SS_{between}$	k-1	$\frac{SS_{between}}{k-1}$	$\frac{MS_{between}}{MS_{error}}$
Error	SS_{error}	N-k	$\frac{SS_{error}}{N-k}$	
Total	SS_{total}	N-1		

if $F^* \leq F\ (1-\alpha\ ;\ k-1,\ N-k)$ accept H_o

$F^* > F\ (1-\alpha\ ;\ k-1,\ N-k)$ reject H_o

Mann-Whitney U Test

This test is one of non-parametric statistics. It is used to test whether the two population distributions are identical. It assumes the populations are continuous and random samples have been drawn from each group. The test statistics is based on the ranks of observations rather than on their numerical values.

Data summary table :

					Sample sizes
Group 1	x_1	x_2	x_3	.... x_{n1}	n_1
Group 2	y_1	y_2	y_3	.... y_{n2}	n_2

x_i and y_i are rankable observations

n_1 is the number of observations in group 1

n_2 is the number of observations in group 2

Procedure described here can be used when both sample sizes are 20 or less

a. rank all the observations in single array from 1 to $n_1 + n_2$

b. Find the sum of ranks in two groups (R)

$$R_1 = a_1 + a_2 + \ldots\ldots\ldots\ldots + a_i$$

$$R_2 = b_1 + b_2 + \ldots\ldots\ldots\ldots + b_j$$

c. Calculate U_1, U_2

$$U_1 = n_1 n_2 + \frac{n_1 (n_1 + 1)}{2} - R_1$$

$$U_2 = n_1 n_2 + \frac{n_2 (n_2 + 1)}{2} - R_2$$

where n_1 = size of the first sample

n_2 = size of the second sample

R_1 = sum of the ranks of the first group

R_2 = sum of the ranks of the second group

As a check on your calculations, $U_1 + U_2$ should equal $(n_1) \times (n_2)$

d $U_\alpha = \text{Min}(U_a, U_b)$, $U_{1-\alpha} = \text{Max}(U_a, U_b)$

The value of U_α must be equal to or smaller than the value in the table to be significant.

<u>Pearson's Correlation Coefficient</u> (r)

The correlation coefficient is appropriate for describing the relationship between two quantitative variables that are linearly related. The definitional formula for Pearson's r is

$$r = \frac{\Sigma(X_i-\bar{X})(Y_i-\bar{Y})}{\sqrt{\left[\frac{\Sigma(X_i-\bar{X})^2}{n}\right]\left[\frac{\Sigma(Y_i-\bar{Y})^2}{n}\right]}}$$

where r is a measure of correlation whose value lies between -1 and +1. Value of r near to 0.0 indicate a low degree of correlation. Positive values of r indicate that high values of X are associated with high values of Y and vice versa. Negative values of r indicate that low values of X are associated with high values of Y.

Testing the significance of r

It is frequently desired to test between :

H_o : $\rho = 0$

H_1 : $\rho \neq 0$

The reason for interest in this test is that in the case where Y_1 and Y_2 are jointly normally distributed, $\rho = 0$ implies that Y_1 and Y_2 are independent.

The statistics for testing can be expressed directly in term of r :

$$t^* = \frac{r\sqrt{n-2}}{\sqrt{1-r^2}}$$

If $|t^*| \leq t\ (1-\alpha/2\ ;\ n-2)$, accept H_o

$|t^*| > t\ (1-\alpha/2\ ;\ n-2)$, reject H_o

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