

Nobley, DW PSEBM 60:225-1945 Observations on the antimicrobial  
activity of 2,3-dihydro-1,4-naphthoquinone & its mesal bystanis  
R.

Shive, W. + J. Tharow, JBC 162:451-462 (1946.)  
 Biochemical transformations...  
 I Hypoxanthine.

dl hydroxyaspartic acid is inh. to E coli, reversed by glutamic acid or by aspartic acid. (c.) pantothenic acid raises antibacterial index.

An E coli strain initially non-prototrophic was adapted by serial transfer for use in these expts (!!). (Reisolated?).

Antibact index ca 10-15. index in E coli. In *Sarcospora* 60-100.

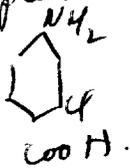
II tried in coli. similar, but index 100-200.

At low levels of I, 1r prot = 10r aspart in reversal. do β-alanine: Hypoxanthineless effluvia. Panto. increases antibact index from 3-20. e.g. other g-t. had no effect.

At higher (I) glut. decreases in activity. α-alanine, valine, succ. + fumaric ineffective. Isoserine had no effect at 1mg/cc!

Interpts off. of panto as indicating shift of limiting nutrient from β-alanine synthetic to another one. Interpts glut. effect as panto-  
 aspect by transamin.

II ~~SA~~ pabr. 463 -  
 also



II reversed completely by methionine.

Series of antib. indices made with addition of different substrates. 1. Methionine 2. adenine 3. . . ?

SA: pabr

3000 nonmeth.  
 10000 meth.  
 20000 panto.

Presumably II is ineffective only at a certain locus of pabr action

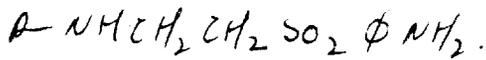
Medinaveitia, J. Biol. Chem. 39:85-91 (1945). Antibacterial substances related to pantothenic acid.

"pantamides". Reference vials. P.T.:  $P-NHCH_2CH_2SO_3Na$ .

L. casei used.

pant-hydroxide was active, but not highly so:  $P-NH_2$ . No other act.

Also, pantoyl - N-2 aminoethyl - (p-aminophenyl) - 1 sulfone.



Not covered by pant; " by pantothen.

Therapeutic activity, in rats & Spyzogones.

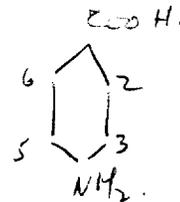
Martin, AR + FL Rose, substances related to pant.

39:91-

1945. Antibacterial sub-

(overlap Wyrstal; Green, Johnson + Pauli).

	2.	3.	5.	6.
1.		Cl		
2.	Cl			15
3.		L		16
4.		Me		17
5.	Me			18
6.		HO		19
7.		MeO		20
8.	MeO			21
9.		EtO		22
10.		NH <sub>2</sub>		23 MeO
11.		COOH		24.
12.		MeS		
13.		EtS		
14.		MeSO <sub>2</sub>		
		EtSO <sub>2</sub>		
		Cl	Cl	
				Cl



2.	3.	5.	6.
	<del>SO<sub>2</sub>Et</del>		<del>Me</del>
	Cl	Cl	<del>Cl</del>
	Cl		Cl
	Cl		NH <sub>2</sub>
	Cl		NHAc
	Bz	Bz	
	Me		Me
	MeO		MeO
		Me	
	MeO		Me.

"S. pyogenes; Wrigley's tooth. + blood.

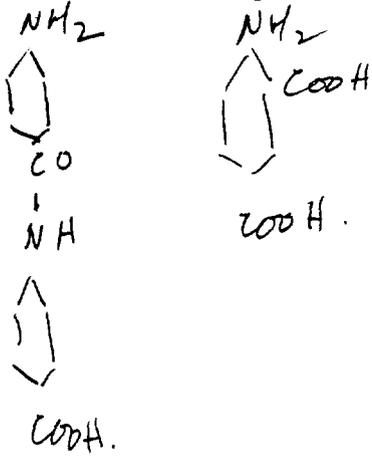
I:  $\frac{1}{27}$  eff. as SA. |  $\frac{2}{5} + \frac{4}{5}$  anti SA.

S. mut.

4-amino isophthalic

4-(4'-amino benzamide) benzoic ac.

& Et. 4-amino benzoate



sl. anti SA activity

McLellan H. Beils. J. 39:329-33 (1945) Biochemical characterization of actions of chemotherapeutic agents. S. lack of gross displacement of pantothenate and pabate from microorganisms by pantooyctaurine & Sulphamida-mide.

Sheep. hemolyticus. limiting pantothenate medium  $\rightarrow$  pantothenate poor cells. No all ex part in heavy part medium growth removed by successive washing.

Suspensions contg 15-60 mg (dry) of cells in 2-5 ml  $^{32}P_4$  part determined by digesting + Proteus growth.

With cells (lg. batches) exposed to SA. No release of anti SA occurred as exposure to buffer, saline or SA.

Pnt. content of bugs grown in initially  $2 \times 10^6$  was

30 mmol/g (dry) Growth for shorter periods - more part, the contemporary level being important. The cells inactivate part.

Cells up to 700 mmol/g were obtained

No part was liberated on exposure to part-taurine of the poor part cells. No did washing. plasma vials. part inactivation.

In part vials cells, part stable at R.T. was released into saline at  $37^\circ$ . The quantity remaining being ca that of part poor. Large inc part-taurine had no effect on quantity removed.

The amt of SA-antigen present is not altered by large amt of SA.

\* It is suggested that although part + part functions in resting bacteria these activities, when the resp. substances are incorporated are not influenced by SA + PT but the reactions involved are the as simulations of the substrates. These are stably bound.

Therefore expect a lag in action for detection of ~~part~~ substrates.

McIlwain, H + DE Hughes, *Biochem. J.* 39:133-139 (1945). 3. Relations  
ships between metabolic and growth inhibition by paralothenate analogues  
: their structural and sp. specificity.

Assay  $\bar{c}$  Proteus.

Several analogues tested for (1) effects on growth, reversed ~~by~~  
by P<sub>th</sub>

Some comp. ind. growth but not P<sub>th</sub> inactivator:  
bis nordeoxy paralothenate. ~~These~~ These were not reversed by  
paralothenate.

All analogues which competed  $\bar{c}$  P<sub>th</sub>, inhibited the  
inactivation of prot.

order of activity of different analogues ~~is~~

& of prot T. in different species is the same for growth &  
prot metabolism.

McIlwain, H., *Biochem. J.* 39:279- (1945) 4. Time-relationships between metabolic and growth inhibition by pantoyltaurine.

1. put + streptococci  $\rightarrow$  slow inactivation of put at uniform rate.
2. not occur at 0°.
3. Inhibited by pantoyltaurine immediately.
4. Growth inhibition has lag ca. 1 hour.; recovery also lags.
5. Reversible on washing & removal of put. occurs very quickly.

$\therefore$  assumes action of ~~put~~ PT is to inhibit the synthesis of a put derivative essential for growth, which can be produced in excess.

Field, J.B., EG Linsen, J. Spero, and KP Feiler, JBC 156: 725-737 (1944)

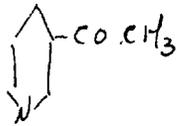
Studies on the ~~hemorrhagic~~ hemorrhagic sweet clover disease.  
XIV. Hypertension induced by methyl xanthines and its  
effect on the action of 3-3'-methylenebis-4-hydroxycoumarin).

Caffeine, theobromine + theophylline stimulate liver production of  
prothrombin + fibrinogen, reversing dicoumarol.

NICOTINIC AC. analogues (Acetylpyridine)

Woolley, D. W. JBC 162:179-80 (1946) Reversal by trypt of the biological effects of 3-acetylpyridine.

Tryptophane was as effective as nic in reversing effect of 3-AP on mice (pellagra!).



Rodriguez.

RIBOFLAVIN, analogues

*L. casei*

Larrett, H.P. JBC 162:87-97 (1946) The effect of riboflavin analogues upon the ~~use~~ utilization of riboflavin and FAD by *L. casei*

Review: isoriboflavin has  $< .5\%$  activity of  $B_6$  for *L. casei*  
inhibits subgrowth at low  $B_6$

Shows: in presence of suboptimal  $B_6$  or FAD, stimulates ac. prod.

Deaminopyrimidine competitively inhibits utilization of  $B_6$ .

Lumiflavin competes  $\bar{c}$  low  $B_6$ , stimulates  $\bar{c}$  high.  
inhibits FAD utilization at lower concn.

*L. casei* is alkali-treated peptone, or Casamino (Tandy + Dickson)

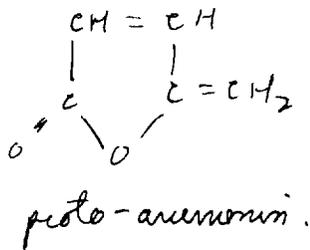
main effects on  $B_6$  enzymes, and not on  $B_6 \rightarrow$  FAD reaction

ANTIBIOTIC: Buttercup Juice

Baer, Harold, M. Holden and BC Seegal, JBC 162(1):65-68 1946

The nature of the antibacterial agent from *Anemone pulsatilla*.

~~Anemonin~~ ANEMONIN obtained, a polymer of proto-A.



Activity measured against *E. coli*, *Staph.* and *Candida albicans*.

Acetylcyclic ac., nor vinylcyclic had no antibacterial effect.

Kimball, R.F., *Genetics* 24:49-58 (1939). A delayed change of phenotype following a change of genotype in *Paramecium aurelia*.

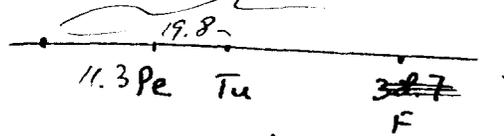
Following endocytosis there is a delay in the expression of change of mating type that may occur.

Frederick, C.C. + G., Genetics 24:1-7 (1939) Non-random crossing over in the 2d chromosome of Neurospora crassa.

See L. '36. Genetics 32: 243-56.

9 chromosomes.  
= 38.7

kuitor lore, peach, tuft + thuffy.



1. Excess of 2 strand exchanges. Deficiency of multiple exchanges.

Jeweries & Tamer, J Bact 49:383- 1945.

The inheritance of environmentally induced characters in bacteria.  
Graded cone.

(Selection favoring wild type in mixed cultures in absence adaptive agent.)

Inoculate mass populations into Agar.

Changes of  
critical  
conc.

NaCl - from 3 to 8%
CuSO <sub>4</sub> - 1:4000 to 1:800
HgCl <sub>2</sub> 1:300,000 to 1:50,000

∴ use 6% salt agar

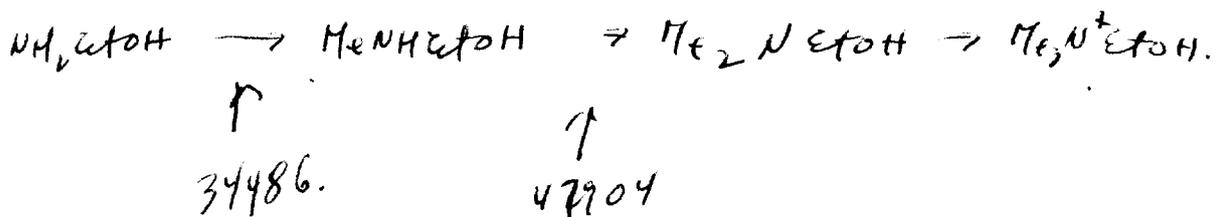
Horowitz, N JBC 162:413 1946.

The isolation & identification of a natural precursor of choline.

$\text{CH}_3\text{-NH-CH}_2\text{CH}_2\text{OH}$  isolated from 47904, active on 34486

Appears only after 7 days. more conc. in mold than medium.

47904 must synthesize type. choline. methylation of diMeEtOH $\text{NH}_2$  also affected.



Fries, Nils. Svensk Botanisk Tidskrift, 39: 270-8 (1945)  
Two X-Ray induced auxo-heterotrophies.

*Ophiostoma* (*Ceratostomella*) *multiaurum*.

wild type requires: B<sub>1</sub> + B<sub>6</sub>. Mutants for Biotin (225) and  
pab (617) obtained by X-Ray. Isolated by special selection technique.

Ark. för Botanik, 32: 1-9 (1945) über Röntgen-induzierte  
physiologische Mutationen bei *Ophiostoma multiaurum*.

50 kv. 2-3 ma. 100 m. Plated irradiated spore suspensions onto minimal  
"Fries agar" + B<sub>1</sub> + B<sub>6</sub>. Mutants "deutlich schlechteres Wachstum abweisen"  
wurden. Von den die auswachsenden Anisomyzelien wurden deshalb  
nur solche isoliert, die sich in dieser ~~Beziehung~~ Beziehung von - des Meistes -  
normalen Myzelien unterscheiden.

1. Temporary radiation effects (back mutations?)
2. Morphologicals.
3. Mutants.

527 isolated. 30 mutants - 6 biochemicals.  
None from ~~the~~ unirradiated material.

- # 225 Biotin
- 358. Reduced S. (parathiotroph - cysteine etc. or 4 valent S. (SO<sub>3</sub><sup>-</sup>)
- 446 Parathiotroph - can use <sup>not</sup> tetravalent S.
- 460 - ~~yes~~ Oracil
- 513 Adenine? low activity
- 617 pab.
- 848 Guanine.

Naturw 30: 44/5 - 1942. Adenine als Wachstumsfaktor  
für *Ophiostoma ulmi* (Bresinans) Kaurf.  
Requires only B<sub>6</sub>.

Nature, No. 3947: 757 (June 23 1945) X-ray induced mutations in the physiology of *Ophiostoma*.

*O. multiauratum*. strains mentioned above.

Parathiotyphs in crosses lost ability to reduce tetravalent S. (#358). Other features identical as 1 gene in crosses.

Needed large quantities of adenine.

Uracil-less used cytidine or cytidylic acid. but not cytosine (lib 129P).

Nature #3847: 105 July 24, 1943.

Vitamin B<sub>1</sub>, Vitamin B<sub>6</sub> + Biotin as growth substances for some *Ascomycetes*.

*Ophiostoma*:

	Needed	Stimulate
<i>O. piceae</i>	Pyr	—
<i>steroceras</i>	P, S, C	Biotin
<i>coeruleum</i>	Pyr	B <sub>6</sub> "
<i>quercus</i>	Pyr	" "
<i>pinus</i>	Pyr, Biotin	B <sub>1</sub>
<i>ulmi</i>	B <sub>6</sub>	Pyr
<i>fagi</i>	B <sub>6</sub>	Biotin
<i>pilliferum</i>	B <sub>6</sub>	Biotin
<i>multiauratum</i>	B <sub>1</sub> + B <sub>6</sub>	—

"Artificial symbiosis" tested + worked. (Heterocaryon?)

Nitrate needs biotin  $\bar{e}$  NH<sub>4</sub> for N; respirable  $\bar{e}$  NO<sub>3</sub> + acid!

Hollander, A. Effect of long uv & short visible radiation on *E. coli*  
J. Bact 46: 531-11 1943.

Saline = NaCl 3g RCl .2g CaCl<sub>2</sub> .2g / 100 ml H<sub>2</sub>O. Protected by hyp barth somewhat.

1. Growth delaying effect before app. lethality (plate counts)
  2. Survival in saline: (incubation).  
control survived quite well 10 hours. (98%).  
irradiated died much more rapidly
- Longer wavelengths much less efficient ( $10^5$  energy eq.).

Wickscham 145

8 ascospores/ascus. after copulation. Relatively anaerobic. Bottom fermentation 3 pellets.

Under slide conditions, hyphae are found. (rel. anaerobic). Nucleus visible in terminal hyphae, ca. 8-10 $\mu$ , particularly anaerobically.

glucose, maltose & sucrose rapidly fermented. Also melibiose.

Not galactose or lactose

Sporulation did not occur from hyphae, or was diminished temporarily.

Trypan blue in agar leads to dark pigm. in aggl. phase (abt. from normal). Growth rapid 30-37°. Colonies develop slowly - 4-6 days. Copulation occurs readily at 20-33°. Ascus ruptures before completing development.

Wickscham, L.S., & Eugénie Duprat.

J. Bact 50: 597- 1945.

A remarkable fermenting yeast, *Pichyosporichia nycos vesatilis*, n.s.,

Lwoff, A. + A. Audenaert, Ann Inst Pasteur - ? 1941.

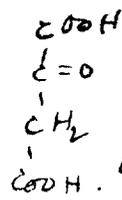
Sur une mutation de *Thiopylla hoeffii* apte a se développer dans les milieux à l'acide succinique.

pp 1-2 missing  
Typical strain will not utilize succinate.  
Rarely mutations appear, influenced by succ. from S- to S+. In presence of EtOH S- outgrows S+. S+ → S- not found. Rate S- to S+  $\approx 10^{-8}$ .

70:51- 1944. *Recherches enzymologiques sur les mutations bactériennes.*

Succinoxidase is present in both strains. *Arabobacteriacae*. is decarbox. spontaneously but not rapidly enough for growth.

Hydroxy fumaric acid studied (evolic form of



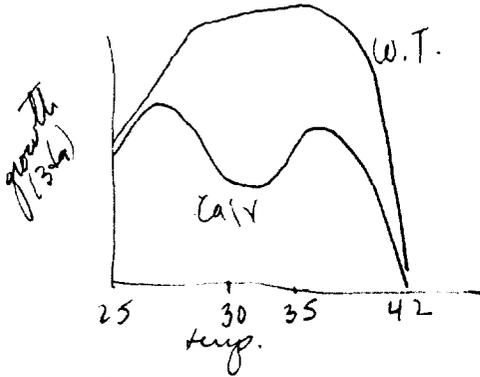
Rate of decarboxylation studied. Rapid at first as ~~by~~ ~~cost~~. S+, but slows down to spont. rate (almost as rapid)

Prove there is an enzyme present? in S-. which is not present in S+?

Mitchell, H.K. and M.B. Houlahan, ASB 33:31- 1946.

*Neurospora* CV. A temperature sensitive *Neurospora* mutant.

51602. At 31° or above, requires riboflavin absolutely.  
S-shaped response curve .1-2.5  $\mu$ g. At high B<sub>2</sub>, growth curves  
like wild, at low levels, bimodal temperature response.



Grows on 20 ml

at higher temperatures,  $\bar{c}$  a small B<sub>2</sub> supplement,  
(ca. 3 r) full wt. can eventually be obtained (200 hours =  
8 days.) containing full B<sub>2</sub> content by L. casei.

For B<sub>2</sub> determ., autoclave cultures in medium & analyze filtrate. F. is up

ca 6-9 r/100 mg. Mutant grows intermittently, coming up + syn-  
thesizing vitamins. Not tested as *Neurospora*.

Inhibited by leucichrome; reversed by B<sub>2</sub>. R<sub>50</sub> = 1.2-2.5.

Some unlabeled in tissue extracts.

*Neurospora* may contain a doubly functioning set of genes for different temperatures.

Abb 4A x 21a.

Tatum, E. L. + T. T. Bell.

A. J. B. 33(18): 15-21 (1946)

Neurospora<sup>44</sup>. Biosynthesis of thiamin.

		Distance from center
1090 (sitophila).	45 asci	23
9185	24 "	8.3
18558	8 "	0
17084.	33 "	35

No interspecific heterozygosis.

3 day growth, some / 125 ml flask.

18558 requires thiazole  
9185 intact thiamine

When grown on limiting thiamin, accumulators of pyrimidine was established by 18558 (Keston 17084, + Phycomyces) Analogues of thiazole had activity very similar to Phycomyces, except that 5th ethyl may have ca. 1% activity of B<sub>1</sub> for 18558.

2-methyl derivative was also app. active

Factor S did not influence 9185 response.

17084, 1090 (and 56501), require both pyr and thz. Mixture has same activity as thiamin. Filtrates have a 9185 active component, which loses activity on sulfite treatment. It is also active for 18558 and Phycomyces. Not active for 17084.

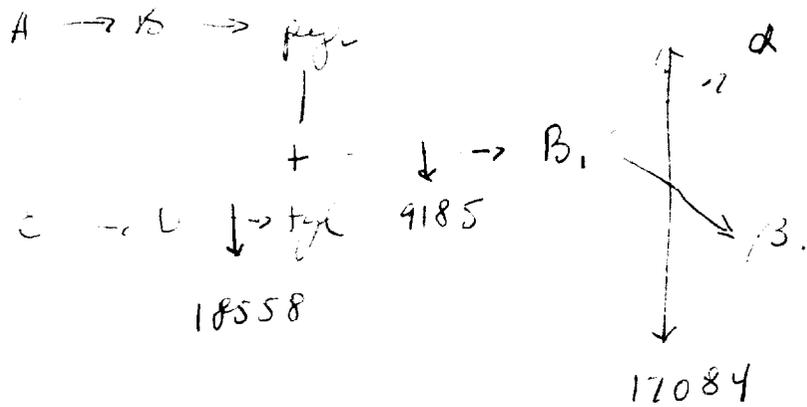
299 as low B<sub>6</sub> responds only to B<sub>1</sub> or pyr + thz.

Wodley's conclusions on pyritiamin not confirmed. 17084 and 1090 cannot pyritiamin for pyrimidine.

A thiamin metabolism error may exist in 1090 + 10084.

These strains have a higher requirement.

i.e.



Carrel, A. *Pr. Am. Phil. Soc.* 68: 129-32 (1929) The nutritional properties of malignant cells.

Neurology

Kellogg, W.N., et al S 103:49. 1946.  
LogS.

Special conditioning in

## RADIATION: Cathode

Wychoff, RWS + T.M. Rivers, ~~JEM~~ JEM 51: 921- 1930.

The effect of cathode rays upon certain bacteria.

$1.5 \times 10^5$  volts

The absorption of a single electron will kill a cell.

Concluded that only .008 of the incident electrons are absorbed from phantom expts.

" Only 85% of the single hits were effective, but when death occurred, a single hit sufficed ..

(data from dose response curve, and calculated absorption by the bacteria.)

[How can this be compared to the production of rays by radioactive P, etc?]

RADIATION: u-v

Hollaender, A + RM Duggar, J. Biol 36:17 1938

The effects of sublethal doses of monochromatic u-v radiation on the growth properties of bacteria.

2653A

Reles, N.H., *Genetics* 28: 398- 1943. Comparative studies of the cytogenetical effects of neutrons and X-Rays.