24-1930

potash - gro.

K_2CO_3

manuf. of, 9928[2]

purification of, 4361[1]

KCl

soly. in EtOH in presence of other salts,

5576[2]

K_2SO_4

manuf. of, 4593[7]

15 - 1921 KCl

152. Potassium chloride from furnace dust. C. Anderson and F. S. Moon, Jr. U.S. 1,354,642, Oct 5. Furnace dust containing K_2SO_4 and KCl is leached with a soln. containing sufficient $CaCl_2$ to convert the alkali metal sulfates into chlorides and KCl is recovered from the soln. thus obtained.

<u>K_2CO_3</u>

$KHCO_3$, manuf. of, p 994.

<u>KCl</u>

from bitterns, p 3176

from cement-kiln dust, p 999.

<u>K_2SO_4</u> - zero

16 — 1922 K_2CO_3

994. Potassium carbonate. J. F. Harlow. U.S. 1,400,542, Dec. 20. Alk. brittle such as U.S. alk. plains brine is mixed with $MgCO_3 \cdot 3H_2O$ and the mixt. is treated with CO_2 at a temp. of about 20° to ppt. KHMg carbonate which is then sepd. and heated to form sol. $MgCO_3$ and $KHCO_3$ in soln.

16 - 1922 KCl

2176". Potassium chloride from bittern. J. F. Harlow. U.S. 1,422,571, July 11. A bittern contg. K_2CO_3 and Na salts concd. to approx. satn. is treated with $CaCl_2$ in proportion chem. equiv. to the K present and heated to 95° to ppt. $CaCO_3$ and leave the K in soln. as KCl. The soln. is then concd. to 0.75 its former vol. to affect crystn. of Na salts while the soln. was still hot and after the sepn. of these salts the soln. is cooled to about 20° to obtain KCl.

C O

KCl

16-1922

999. Potassium chloride from cement-kiln dust. F. S. Taylor. U.S. 1,402,173, Jan. 3. Cement kiln flue dust is agitated in H_2O to dissolve Na and K salts and the soln is treated with sufficient CaCl$_2$ to convert Na and K sulfates into chlorides. KCl is obtained from the soln by fractional cryst.

C O

17 - 1923

K_2CO_3 - zero.

KCl - zero.

K_2SO_4

amount of, p 15362

C O

17 – 1923 K_2SO_4

1536. Potassium sulfate. C. Hoest. 21.8. 1,446, 185, Feb. 20. $CaSO_4$, suspended in an aqueous soln. of KOH is reacted on by CO_2 to form a satd. soln. of K_2SO_4 and the latter is sepd. from the soln. on cooling.

17 – 1924

K_2CO_3

$KHCO_3$, manuf. by electrolysis of KCl soln., P. 512'.

K_2CO_3, soly. of alc. in aq. soln. of, vii 437.

KCl – no.

K_2SO_4 – no.

C O

18-1924 K_2CO_3

512. Potassium bicarbonate by electrolysis of potassium chloride solutions. R. Lucky. U.S. 1,499,086, Dec. 1. A KCl soln. is electrolyzed and the KOH formed in the catholyte is reacted upon with $KHCO_3$ to form K_2CO_3. Fresh KCl is added to replace that consumed by the electrolysis and $KHCO_3$ is ppd. from the end-liquor conty. K_2CO_3 by introducing CO_2.

18-1924 K_2CO_3

2493. Water solubility in homologous series. H. Fühner. Ber. 57B, 510-5 (1924); cf. CA. 17, 106, and earlier papers — [on the following members of interest] — the only (mols. per l.) of Me, Et, Pr, and Bu alcs. in 50 cc. solns. contg. 20 g. K_2CO_3 are 10.00, 1.54, 0.24, and 0.039 resp.; with less K_2CO_3 (5.0 and 3.5 g. per 50 cc. solns.), the ratios of the solys. of 1 alc. to that of its next higher homolog are of the same order of magnitude (about 4.) as that of the higher alcs. in H_2O alone.

C O

19 - 1925

K_2CO_3 - zero.

KCl - zero.

K_2SO_4

compared with H_3PO_4, 2178'

177 (melting 178°). Constitution of phosphoric acid. I. Fröhlich. Rad. Acad. Sci. Zagreb 228, 16-37 (1923). — [Only the following is of interest] — When K_2SO_4 is dissolved in conc. H_3PO_4 and the soln. poured into alc., a cryst. precipitate, $2K_2SO_4 \cdot H_3PO_4$ is formed. If hot H_3PO_4 is satd. with K_2SO_4 until crystals appear on cooling, and then satd with alc, crystals with the composition $K_2SO_4 \cdot H_3PO_4$ sep.

4/16/50

20 - 1926

6/16/59
JW

K_2CO_3 - zero.

KCl - zero.

K_2SO_4 - zero.

21-1927

K_2CO_3 - мало.

KCl - мало.

K_2SO_4 - мало.

22-4927

6/6/50

Potash

– as sugar industry by-product, 1867'.

– K_2CO_3 – [illegible]

KCl – [illegible].

K_2SO_4 –

[illegible] from $K_4Fe(CN)_6$ by [illegible], ~1840.

C a

22 - 1928 potash

1868. Certain by-products of the sugar industry. Their production and use in South Africa. W. C. Dymond. Planter sugar mfr. 79, 3 (1927).— a review discussing the production of motor fuel, glycol, potash, NH_3, amines, cyanides, etc.

22 - 1928 K₂SO₄

2640. separation of potassium sulfate from crude potassium ferricyanide by crystallization. V. P. Il'inskii and N. P. Lépin. Trans. state Inst. applied chem. (Moscow) 1927, no. 5, 8-17. — K_2SO_4 is the principal impurity of technical $K_4Fe(CN)_6$ obtained by the calcination of animal matter with K_2CO_3 and Fe. Technical $K_4Fe(CN)_6$ sometimes contains up to 10% of this impurity, which is due to the oxidation of the S of organic matter, and also contains a little chloride and carbonate. The only practical method of purifying this $K_4Fe(CN)_6$ is by crystn. from H_2O. The dividing system $K_4Fe(CN)_6$ - K_2SO_4 is found to be remarkable in this respect that the line of separation of crystn. fields is almost a st. line parallel to

22-1923 K_2CO_3

2640. the aid of alcohol; this circumstance is particularly favorable to the sepn. of the two salts. Tables of solubilities of mixts. of $K_4Fe(CN)_6$ and K_2SO_4 at 25°, at 40°, at 55° and at the b.p. temp. are shown. If the admixt. of K_2SO_4 is small, the recommendation is to sep. it by cooling the satd. soln. of the 2 salts at high temp. If the proportion of K_2SO_4 is large, it is necessary to allow it first to cool moderately, then sep. the part of K_2SO_4 which crystallizes and finally cool the satd. soln. for the sepn. of $K_4Fe(CN)_6$.

C d

23 - 1929

6/6/50

potash - zero

K_2CO_3 -

septum : K_2SO_4 - 44.0 — 1.4676

KCl - zero

K_2SO_4 - zero

m. w. i.

24 - 1930 K_2CO_3

928. Manufacture of potassium carbonate. Société anonyme alcalina. Belg. 360,705, June 29, 1929. K_2CO_3 is obtained by decompn. of an acid double salt of Mg and K which is itself obtained by the reaction of a concd. soln. of a K salt satd. with CO_2 on nascent $MgCO_3$. The latter is produced by adding MgO or $Mg(OH)_2$ to the CO_2-satd. soln. of K salt.

? 24-1950 Kl

5576. Effect of added salts upon the solubility of other salts in ethyl alcohol. Ralph T. Leonard and Walter C. Edwards. J. Am. Chem. Soc. 52, 3962-7 (1930). — The solubilities of KI, $KClO_4$ and $Na(NO_3)_2$ in the presence of other salts in EtOH have been measured and the results compared with those predicted by the inter-ionic attraction theory. Marked deviations from the original Debye-Hückel theory are shown and results agree qualitatively with that of Bjerrum.

C Q

24-1930 K2SO4

4593. Potassium salts. Kali-Chemie A.G. Fr. 682,685; Sept. 5, 1929. MgO is removed from crude K salts either wholly or in part in the form of phosphates of Mg and NH_4. Fr. 682,687 describes the recovery of sulfates as K_2SO_4 by introducing NH_3 into the solns. freed from phosphate of Mg.

25 - 1931

6/10/50

potash - zero

K_2CO_3

manuf of, [illegible], [illegible]

KCl - zero

K_2SiO_4 - zero

2.5 - 1931. K_2CO_3

781. Potassium carbonate, alcalina (con. amon.). Fr. 688,493, Jan. 20, 1930. K_2CO_3 is made by introducing MgO into a soln. of a K salt under a pressure of CO_2 equal to or higher than the critical pressure at which CO_2 is sol. in alk proportion in water. KCl is the preferred K salt so as to obtain MgCl at the same time.

25-1931 K_2CO_3

4367. Potassium carbonate. Verein für chemische und metallurgische produktion. Ger. 526,378, Dec. 7, 1928. This relates to the manuf. of K_2CO_3 by treating a soln. of KCl and $MgCl_2$ with NH_3 and CO_2 in such a way as to ppt. $KHCO_3 \cdot MgCO_3 \cdot 4H_2O$ and then decomp. the double salt. The improvement consists in using MgO, obtained from the double salt, to recover NH_3 from a corresponding amt. of the mother liquors from the ppn. of the double salt. These liquors contain NH_4Cl and some KCl, and when heated with MgO they yield NH_3 and a soln. contg. KCl and $MgCl_2$, which are used again. Cf. CA. 24, 1474.

? 26-1912 KCl 1/01 20

2:60. Potassium chlorate and potassium chloride. C. J. Shpitalskii and Z. A. Lotte. Russ. 4,554; granted Jan. 31, 1927; published July 31, 1928. Cl is made to react with K_2O, solns. of such a concn. that finally KCl precipitates out at high temp. The first stage of the process in which K_2CO_3 is acted with Cl, whereby bicarbonate is produced and the max. concn. of the hypochlorite is reached, is carried out at a medium flow of Cl and at a low temp.; the second stage is carried out at a gradually increasing temp. of the solns. and a simultaneously increasing velocity of the flow of Cl so as to obtain an acidic soln., which favors the transfer of hypochlorite into the chlorate.

LMP 24 - 1930 K_2CO_3

4361. Alkali chlorides are eliminated from solutions of crude K_2CO_3 by passing NH_3, preferably to satn., into the soln. and sepg. the ammoniacal layer which contains the chlorides.

26 - 1932

6/6/[illegible]

potash - zero

K_2CO_3 - zero

KCl

manuf. 4, 2580

K_2SO_4 - zero

C O

27 - 7933

potash - zero.

K_2CO_3

$KHCO_3$, manuf. of, 4353?

K_2CO_3, manuf. of, 4359?

KCl - zero.

K_2SO_4

manuf. of, 5154?, 5157?

27 F 1933 K_2CO_3 6[illegible]

4557. Potassium bicarbonate. I. G. Farbenind. A.-G. Brit. 386,351, Jan. 19, 1933. KCl reacts with CO_2, or with compds. of CO_2 and NH_3, in mixts. of NH_3 and H_2O, contg. at least sufficient H_2O to hydrolyze the carbonate to bicarbonate but more NH_3 than can be dissolved in the H_2O at room temp. and atmos. pressure, at temps. at which K carbonate would be decomposed under the conditions of working. In one example liquid NH_3, H_2O and powd. KCl are placed in a pressure vessel into which CO_2 at 10 atm. and room temp. is introduced.

n.r.i. [In a 2nd a mixt. of liquid NH_3 and H_2O is led through powd. KCl and NH_4HCO_3 at 25 atm. and 60°]. $KHCO_3$ forms the solid phase in each case, NH_4Cl being contained in the mother liquor.

77 -27-1933 K_2CO_3

2559 Potassium carbonate. Alfred Mentzel. Ser. 578,471, Aug. 27, 1930. A mixt. of K_2SO_4, C and CaO is heated to about 1000° in N to give a product containing KCN, which is then hydrolyzed with steam at 400-500° to produce K_2CO_3 and NH_3 in accordance with the equation:

$$2KCN + 4H_2O = K_2CO_3 + CO + H_2 + NH_3.$$

Addnl. NH_3 may be obtained by reconverting the hydrolysis product into cyanide and hydrolyzing. The residue from the extn. of the K_2CO_3 contains CaS, which may be treated in the known manner to yield $CaCO_3$ and H_2S. pooly! The latter may be oxidized to H_2SO_4 which may be combined with the NH_3.

9

27-1935 K_2SO_4 6/01

5154. Preparation of potassium sulfate and ammonium chloride from potassium chloride and ammonium sulfate. K. Chirkov, N. V. Solov'ev and M. S. Sokolova. Kalii (U.S.S.R.) 1935, no. 2, 19-24. — The most complete transformation of KCl into K_2SO_4 takes place at 70° and with an excess of not less than 46% of $(NH_4)_2SO_4$.

27 - 1933 K_2SO_4

5157. Potassium sulfate from potassium chloride. August Holz. U.S. 1,924,684, Aug. 15. A reacting mixt. of KCl and $(NH_4)_2SO_4$ is slowly passed through a zone heated at a temp. above the volatilization point of NH_4Cl and below the m.p. of K_2SO_4 and the resulting K_2SO_4 is continuously removed from the zone; the volatilized chloride is also continuously removed and is condensed, treated with lime, and the liberated NH_3 is absorbed in H_2SO_4 to prepare $(NH_4)_2SO_4$ for further continuation of the process. App. is described.

28 - 1954

potash - yes

K_2CO_3

manuf. of, p. 11494.

KCl - yes

K_2SO_4

manuf. of sulfates, 4193.

K_2SO_4, manuf. of, p. 6255

28 - 1934 - K-504

4,193. Potassium sulfate. Production from potassium chloride and sulfuric acid. C. J. Fox and J. W. Turrentine. Ind. Eng. Chem., 26, 493-6 (1934). Domestic economics and details of a process.

28 - 1934 K_2CO_3

1149. Potassium carbonate and sodium sulfate. Kali. chem. A.-G. Fr. 759,517, Sept. 25, 1933. K_2SO_4 is transformed to K_2CO_3 by means of $BaCO_3$, and the $BaSO_4$ is retransformed to $BaCO_3$ by means of Na_2CO_3 in aqueous suspension, preferably under pressure and heat. The mother liquor from the $BaCO_3$ is treated with CO_2 to ppt. $NaHCO_3$, and the mother liquor from the $NaHCO_3$ is cooled to ppt. Na_2SO_4. The $NaHCO_3$ is heated in the presence of water to form Na_2CO_3 and CO_2.

28 - 1934 K2SO4

6255. Potassium sulfate. John A. Simpson, Lon L. Clifford, Albert C. Cochrane and Imperial Chemical Industries Ltd. Brit. 410,930, May 25, 1934. K_2SO_4 is made by the cyclic process: (1) KCl, in part fresh material and in part returned from (4), and glaserite from (2) and (4), are reacted in the presence of H_2O at an elevated temp., e.g., 100°, KCl being used, after cooling to 5–55°; (2) the mother liquor from (1) is worked up by adding Na_2SO_4 and, optionally, some KCl, to yield glaserite at below 55° and a sulfate liquor; (3) the mother liquor from (2), after addn. of the mother liquor from (4), is evapd. to sep. NaCl; and (4) the mother liquor from (3) is cooled to sep. KCl and glaserite for return to (1) and a mother liquor for return to (3).

29 - 1935

potash - zero.

K_2CO_3

system, $K_4Fe(CN)_6$ - K_2SO_4 - H_2O, solubilities in, 82487.

KCl - zero.

K_2SO_4.

manuf of, P 37899.

C 9

n. 9. 29 - 1935 K_2CO_3

8246°. The solubilities in the system potassium ferrocyanide - potassium carbonate - potassium sulfate - water at 25°. N. A. Fleisher and E. F. Plaksina. Trans. State Inst. Applied Chem. (U.S.S.R.) no. 26, 48-51. — The solubilities are given in tables and curves. With increasing concn. of K_2CO_3 the solubilities of K_2CO_3 and $K_4Fe(CN)_6$ are greatly reduced. At a concn. of 34% K_2CO_3 the concn. of $K_4Fe(CN)_6$ falls to 0.26%. No double point was obtained at which the 2 salts are in solid phase.

29 - 1935 K_2SO_4. [illegible]

3799. Potassium sulfate. Palestine Potash Ltd. Fr. 776,937, Feb. 7, 1935. Finely divided sol. anhydrite or semi-hydrated $CaSO_4$ is agitated carefully for a short time with a solution of KCl. The syngenite is sepd. from the soln. of $CaCl_2$ and the remaining KCl and decomposed to K_2SO_4.

prob!

C O

30 - 1936

potash - zero.

K_2CO_3 - zero.

KCl

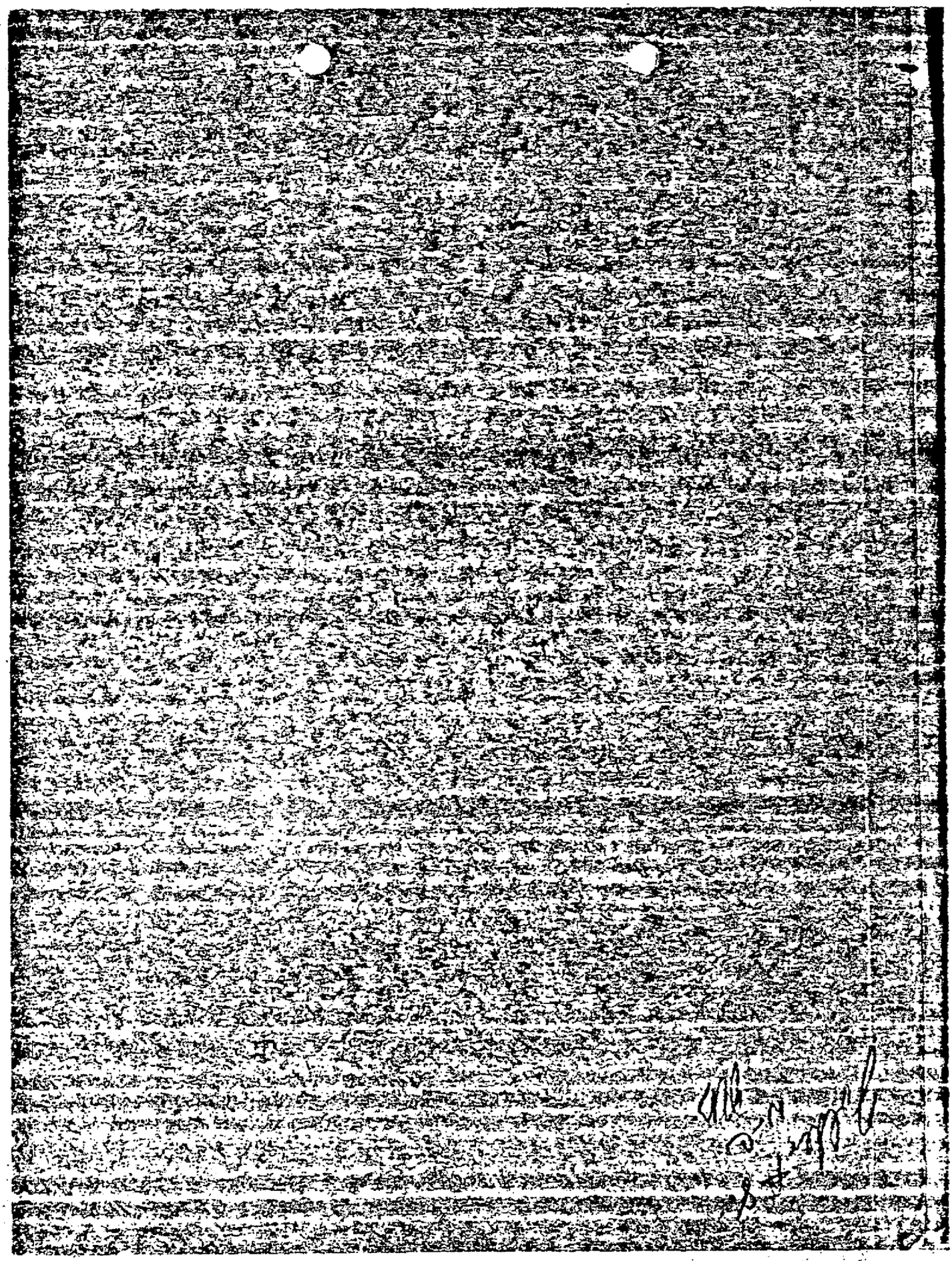
sepn. from Kainit Na salts, 77897.

K_2SO_4

6/6/50

Browning

63-4307-1-B-120 #8



SAC, PHILADELPHIA

July 7, 1950

T. SCOTT MILLER, SA

HARRY GOLD, was.,
ESP - R

65-4307-1B 12 (1) Folder No. 8

GOLD identified the material in this folder on June 24, 1950.

The letter dated September 15, 1947 from JULIAN PAUL BRODIE to BROTHMAN, GOLD said, was in connection with some work that BROTHMAN's firm was doing for BRODIE which was an attempt to develop a men's vanishing cream. GOLD explained that the firm was having difficulty in making the cream with the qualities that BRODIE desired the cream to have, such as a medicinal effect on the face as well as leaving the face with a definite tanned appearance. GOLD said this letter was written by BRODIE after it was apparent by both parties that the vanishing cream could not be produced.

GOLD said that the remainder of the material in this folder dealt with his work at the Philadelphia General Hospital and his courses in pharmacology at the U. of Pa. Medical School.

TSM:EMC
65-4307

10-18-48

Materials List for Heart Station

Quantity	Hausser Cat. No.	Description	Price
1	H-29900	Beckman pH meter, model G; complete with batteries, electrodes, solutions, standard cell and mp.	# [illegible] 245.00
2	H-29040	Hypodermic glass electrodes	# [illegible] 30.00
1	H-14200	Keele - Summerson colorimeter, clinical model Two H-1428 Keele - Summerson filters, nos. K-S 54 and K-S 64 are included	# 148.00
12	H-10640	Blood Volume tubes centrifuge tubes	# [illegible] 10.48
2	H-6750	Koch micro - burets; standard taper joints, two interchangeable outlet tips — capacity, 5 ml.	# [illegible] 29.00
12	H-34640	Volumetric flasks; standard taper glass stoppered — capacity, 100 ml.	# [illegible] 7.92

Materials List for Heart Station (continued)

Quantity	Catalogue No.	Description	Price
6	H-17461	Cylinders of standard type glass stoppered, spout ... — 11 ml capacity.	$ each 10.20

Insert p. 6

Note: The above items are all to be ordered from the Hamilton Scientific Company, 117 S. 17th St., Phila., Pa. They are standard laboratory items which sell at a fixed price, regardless of the supply house from which they are ordered.

See insert 4

In addition, there are needed:

1 . Filing cabinet

1 . Table, solidly built, size: length, 65", width 35", height, 3[illegible] approx.

1 - Sink - the present sink should be raised to a height of 36" (from floor to top), and the fittings replaced with an acid-proof type.

~~Wall~~ shelves are needed, in various locations in the room

Quantity	Harshaw cat no.	Description	Price
1	6404	Van Slyke manometric blood gas apparatus	$248.00
1		6 volt, 120 amp. hr. storage battery for use with Beckman model DU spectrophotometer	
1		Trickle charger for use with 6 volt, 120 amp. hr. storage battery	

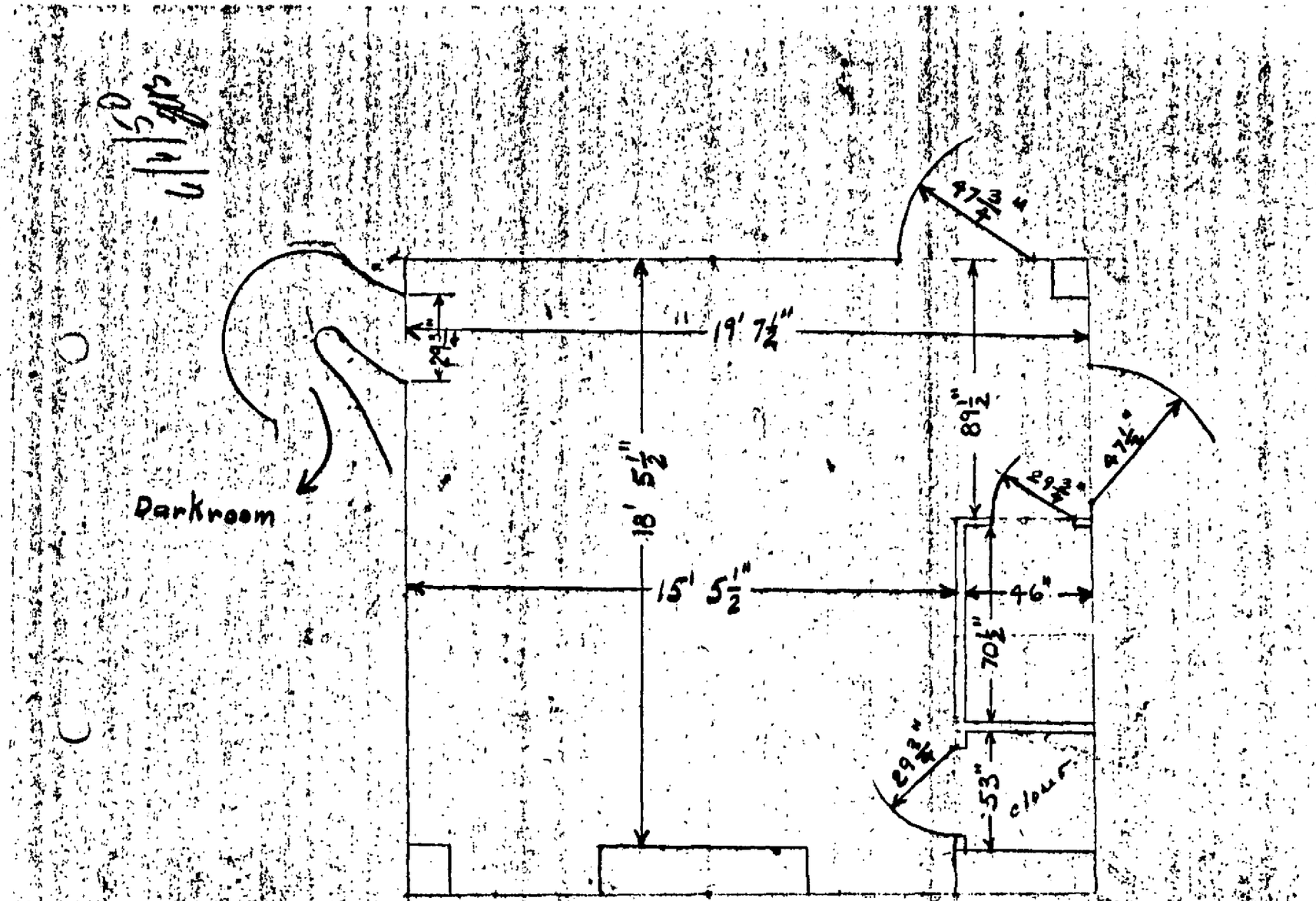
Other ~~firms~~ supply houses ~~from~~ where ~~they~~ these materials may be obtained are:

Arthur H. Thomas Co.
~~Washington Square~~ 230 S. 7th St.
Phila, Pa.

Williams, Brown & Earle
918 Chestnut St.
Phila, Pa.

Materials for Heart Station (additional)

Quantity	Harshaw Cat. no	Description	price
24	H-3800	Pyrex beakers — capacity, 20 ml	$ 6.48
2	H-11090	Double Castalloy Buret Clamps	$ 5.50
1	H-6110	Mohr Buret — capacity, 100 ml.	$ ~~5.08~~ 2.54
2	H-6280	Dispensing Buret	$ 13.32
1	H-60940	Buret Support, Fisher	$ 6.60
36	H-61610	Test Tubes, Pyrex — 15 mm. diameter 125 mm. length	$ 1.62



HEART STATION LABORATORY
SCALE 1/4" = 1 FOOT — 10-19-48

6/6/50

(1.3)

16

50

(2) 14.5
16.0
3.0
19.0

0.297 mg/10 cc

2.7 mg/100 cc

0.06
5.7 mg ×

2.7

6/6/50

J.B.C. 132 701-709 (1940)

Am. J. Physiol. 127 430-436 (1939)

J.B.C. 155 469-477 (1944)

Am. J. Physiol. 130 264-270

" " " 129 749-758

Am. J. Physiol. 132 801-809

9-27-48

Determination of Na and K in serum from Coma Project Patient

6/6/50

Patient - Ralph Parker

	Potassium, mg %	Sodium, mg %
1	24.5 (6.30 mEq.)	345 (mEq.)
2	14.5 (3.70 mEq.)	360 (mEq.)
3	12.5 (mEq.)	365 (mEq.)
4	12.5 (mEq.)	370 (mEq.)

When use pentothal - all respiratory failure
so use CO_2 [illegible]
nitrous - abdominal operation

6/6/50 [illegible]

also, when use cyclopropane - all bad ventilation
so use curare & can use low cyclopropane conc.

opposite types of effects

II Stimulants of nervous system (only C.N.S.)
in essence convulsant drugs = analeptics
counteract depression of C.N.S. → air

e.g. Strychnine
Caffeine - tri Me xanthine deriv.

atropine & camphor } formerly popular

all of above almost entirely supplanted by synthetic or other drugs — Hardly ever use strych. & even atropine &

use

Picrotoxin - no N
probably glucoside
no struct. formula known
↓ natural

counteracts depression by barbiturates

not effective against chloral hydrate & other like drugs

use intravenously { 2 parts / slow infusion
↓
because of latent period in onset of picrotoxin effect

metrazole — does not have latent period — was introd as cardiac stimulant (→ ?)

1. used as antidote for depressants
2. [illegible] as [illegible] barbiturates

Coramine (Nikethamide)

poorest of this group even tho' more popular

actual basis of action is presumably bound up with narcotic drug action

1. might displace narcotic drug from nerve — chemically or
2. " " neutralize "

but 1 & 2 are not true

3. action is a physiological one in which nerve cell is acted on by a contrary action to effect of the narcotic drug.
4. or indirectly by setting up strong reflexes — nerve impulses may be aroused — i.e. cf. cyanides — reflexes in carotid & aortic bodies.

most Recent Trend (analeptic action) — not only stimulate C.N.S. but → > b.p. (increase circulation)

Sympathomimetic Effects → mimic effects of —

get [illegible] in circulation → Benzedrine, etc.

Habitual Use of Drugs (9)

11-1-48

1/4/50

Habituation } etc.
Physical Dependence }

addiction is a psychic affliction of [illegible] - cannot be studied in animals.

synonymous
as chronic poisoning
with tolerance

not true def.

Dog - some not fondle of dog doesn't like it - but needs
vomits at first but gets accustomed
seeks it
morphine can be trained as to effects.

Cocaine - Dogs do not to like it

can make dogs tolerant to morphine but never addicted

Tolerance - can really get to be something
80 mg morphine daily
substance only
1.2 gm morphine in 40 min. I.V.
(ordinary fatal dose 0.05 gm).
is essentially a tissue tolerance - cells of body [illegible] accustomed to presence of drug - possibly oxidized more rapidly - fate of morphine same in [illegible].

Straub Effect -
perfuse heart with digitalis ([illegible]) & continuing
→ contract but if continued perfusion, heart no longer

Cont.

6/1/'50

action of drug depends on diff in conc. betw. inside & outside of cell. (e.g. – drug diffuses out

→ Reason why addicts once taken off drug sometimes die when start again.

Heroin – Diacetyl ester of morphine – supposed to produce addiction – but really – worst of all known

Everyone of effective morphine derivs. is known to cause addiction

Hypoth. – only ~~more~~ ~~[illegible]~~ useful

Colony (U.S.P.H.S.) Lex. Ky.

1. Withdraw drug → abstinence symptoms
- "cold turkey" – shakes
- nausea
- convulsions
- collapse

put small amts of morphine → & symptoms – disappear

So this way to test drugs for addiction (i.e. "Demerol" or methadone

Drastic test but there is no other way at present
- a – can't study animals
- b – can't try on population
- c – so utilize colony (to test newer synthetic analgesics)
  - none found which is non-addiction producing

Large no. would be needed

—

substances used for (effect on nervous syst.) (any which [illegible])

6/6/50
20

now 1. historically [illegible] worked out (Claude Bernard)

2. [illegible] no. of drugs act on nervous syst.

a - local anesthetics

b - sedatives

c - convulsant & anti-convulsants

d - analgesics

3. also - those which produce bad effects on nervous syst. (e.g. [illegible]

sulfonamides

streptomycin

4. Theories for action on c.n.s. - [illegible] to [illegible] the [illegible]

[illegible] background of pharmacology

[illegible]

I.

1. General

A. Inhalation

1. Ether - Centennial 1948

{ profoundly & completely unconscious
muscle completely relaxed
no conscious or unconscious movement
but, do not stop breathing or circulation } → surgical anesthesia

so too far → complete paralysis of c.n.s. → death

Ether (etc) selectively depress c.n.s. (more than heart)

also, selective within nervous system

2 Stages

a - diminished consciousness & drowsiness - can still feel pain

b - stage of excitement & delirium - partly conscious or unconscious - good deal of [illegible]

(discovery of [illegible] Crawford Long [illegible] effect)
[illegible] of U of P [illegible] → 1844

(First [illegible] case of [illegible])

c - surgical anesthesia - all [illegible] quiet down & patient [illegible] breathes [illegible] less - muscles completely

[illegible] depression of c.n.s.

(1) First higher centers are worked on — memory, thinking, etc.
(2) next, lower centers (primitive part of C.N.S.)
(3) paralysis of spinal cord → muscular relaxation
(4) most primitive part of C.N.S. — breathing slows down

6/4/50
20

I Why is the drug selective on C.N.S.?

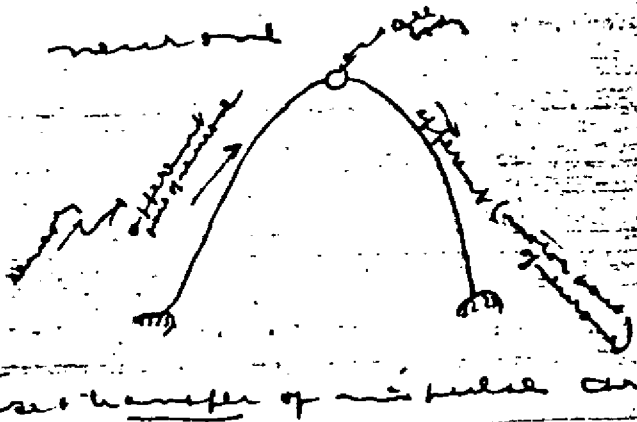
II Why a descending depression?

[illegible] alcohol have been studied more than any other drugs [illegible] ether

1. Reaction is not due to a chemical react. bet. drug + — no common chemical denominator
   a. diversity of drugs — organics of [illegible] amides, N_2O, [illegible] HCl, [illegible]
2. prompt & ready reversibility of reaction
3. diversity of tissues on which results can be observed — can be produced on bacteria, plants, sea urchins, protozoa [illegible] streaming, contraction of heart of dog [illegible] fermentation of sugar (N_2O, EtOH) & all of above
4. Degree of effect depends on conc. of anesthetic agent.

ordinarily mammalian C.N.S. is first worked on [illegible] living creatures.

→ Fundamental Organization of C.N.S.



set transfer of impulse along nerve [illegible]

(not continuity but neurons)

→ synapse

1. Synapse most susceptible portion [illegible]
[illegible] most susceptibility in the body

① 11-15-48

Action of Drugs on Circulation

Reasons

1. Disturbances of C.S. most common which M.D. deals
2. Large variety & no of drugs used
3. Tremendous mass of info available (because can measure objectively without difficulty)

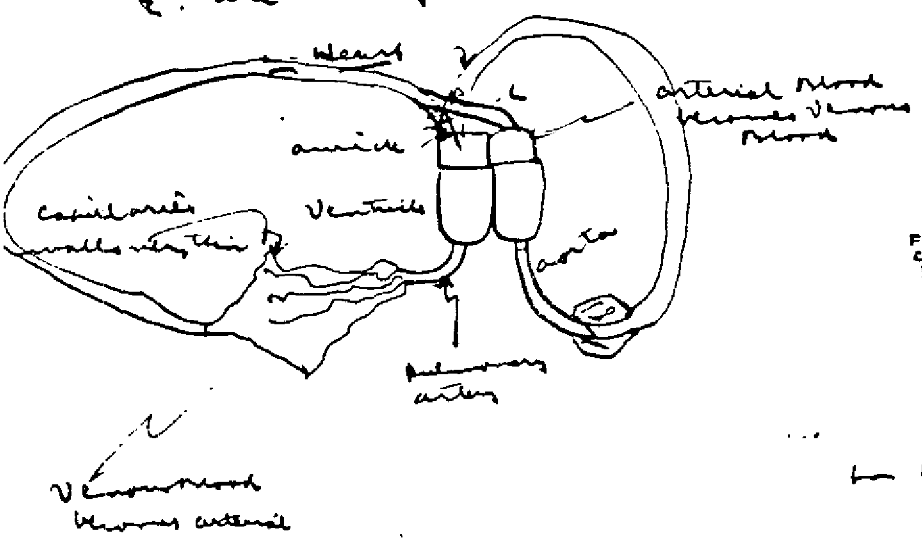
Basic underlying principles

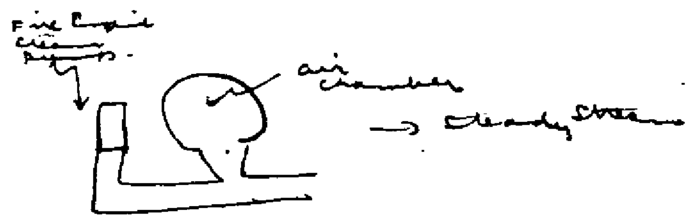
1. Environ of human being really consists of sea water environment around cells (cf primordial ancestors)

   Diffs
   - a- can heal itself
   - b- Red cells
   - c- buffer series
   - d- can remove prods of metabolism
   - e- White cells for dealing with infections.

   ∑ Case Study
   - a- blood level in administrations of drugs — cf. sulfonamides

2. are dealing with pump & tubing system





In blood vessels have elasticity of blood vessels.

- a- can't have anarchy — must have definite sequence of operations
- b- must have constant output — otherwise get edema, ...
  → outputs of both ventricles must be the same

3. Have pressure in tubes (major factors in controlling circulation)
   - a- Cardiac output of heart
   - b- Resistance of tubing system (cut down outflow) → caliber of
   - c- Viscosity of liquid (> viscosity & the greater pressure)

(2) 10-15-48

3. w[h]ere impulse is passed into a muscle (nerve)
4. ... where nerve fibre is (...)
5. ?

more cells involved in higher parts of C.N.S.
also more synapses involved
∴ the greater no. of units involved, the greater is the susceptib. to narcosis

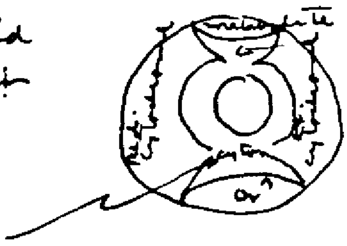
Theories of narcosis (anesthesia)

1. at first all in classical physical-chemical explanation
2. now look upon drugs as inhibitors (& relatively non-toxic) of cell oxidations
∴ get less free energy available for resp. cell functions
∴ get unsteady state of excitability

Recent work shows that || bet. O_2 uptake of brain & degree of functional activity of brain

Keilin expt of oxidation in cell. – see Diagram

Simplified Diagram



— dehydrogenated metabolite

cytochrome oxidase — how CN works

or cambered
complete snowball or blanketing of cell – then get
on dehydrogenases of expt

So Summary
1. narcotics act on dehyd enzymes of cell & cut down O_2 uptake
2. But why selectivity on C.N.S.? i.e. hi
 C.N.S. – & brain rep
 a – high O_2 requirements of C.N.S. to lack of O_2 (molecular O_2 from blood stream)
 b – brain more susceptible
 c – brain probably contains more cells than rest of body put together
 d – abundant blood supply of C.N.S. – brain gets more blood than any other body tissue except kidney

10-13-48

Relation of Sensation Functionability due to Decreased O_2 Uptake

last week – nerve cell as (chemical) amplifier

Ex acetyl choline cycle.
↓
chemical mediator

a.c.h. – liberated at periphery of nerve.

nerve impulse → K ions
↓
elect. (impulse) disturbance

(& a.c.h. is stored but is sensitive to K ions)

a.c.h. cell receptor substance is choline esterase

↓ free energy contrib by destruc of a.c.h.

But must replace a.c.h.

choline – from phospholipids in all body tissues

aerobic oxidn ↘

pyruvate $\xrightarrow[\text{co-carboxylase}]{O_2}$ acetate

or from citrate or hydrolysis of acetoacetate ↗

need also hi-energy phosphate (for comb of choline + acetate) → a.c.h.

& or for oxidn of pyruvate

a.c.h. can be considered as prototype of unstable chemical cpds which transmit nerve impulse & amplify

↓ read

unstable chemical cpd

Consideration of subs. used in producing anesthesia (10)
effect (minor)
Successions of 1000s Tried
→ Reason = most of 1000s have undesirable side effects
a - bad odor or taste
b - marked depression of heart
c - bad effect on liver or kidney
d - cannot control degree of depression produced.

A- 2. Only reagents that can be taken by inhalation can be used to produce surg. anesth. — reason, can control rate of absorp. & elim. by ~~breathing~~ (way of lungs)
→ { conc of (inhaled) gas in inhaled air
conc in alveolar (expired) air
∴ have complete control by operator
3. Signs & symptoms should be very readily recognized by anesthetist
4. Current Trend is to use combination
5. Safest single anesthetic is Et_2O — use others because of disagreeability & lonely after feeling.

B. newer Intrav. Anes.
1. pleasant to take — just prick
2. But do not block perception of pain — are not analgesics
So as surgeon works patient may make movements & anesthetist gives more → { 1. Removal of pain stimulus
2. → anesthetic may → respiratory failure

3. anesthesia is silent for patient — question by rectum — patient falls asleep in own bed & wakes up several hrs later
↓ not even needle prick
But now use small dose → unconsciousness then use nitrous oxide to complete ...

(6) 10-25-48

Cyclopropane now favorite of anesthetists

↳ use 10% in O2 (higher than in air)

↳ Has made thoracic surgery feasible.

4/6/50 [illegible]

D - Simple Sedatives - to produce sleep

↳ action like 1st stage of surgical anesthesia

assume all act in same way (more confession of ignorance than explanation)

Cont
a. Expose brain (experimental)
b. can pick up stimuli (elect. responses) at dose no. of diff areas in cortex.
c. > [illegible] & several areas — [illegible] complete
d. but Et2O & all [illegible] responses

but chloralose (p.s.) & can pick up impulses through C.N.S.

Simple Sedatives 1,000's tested

derivatives of barbituric acid have practically superseded all other classes of cpds.

reasons

1. Have low toxicity — do not damage circulatory syst or cause damage to kidney or heart

2. Easy to take - capsule.

3. Variety of choice — partic. with respect to duration of action

long acting — not if want to walk unhampered

↳ for epileptics etc.

4-6 hrs for [illegible]

ultra short - almost exclusively by i.v. to stop convulsions etc.

p. 3 3

alc. - conspicuous for producing state of euphoria — [transformed alcoholism]
cares go away, feel good
also produce considerable amt. of dilatation of
blood vessels - feel warmer at time.
can
but in lowers body temps & (if fallen gutter) then
get pneumonia.

worst of all - habituation - most conspicuous of
all mentioned so far

Only few are seriously addicted to barbiturate

Learned now for better info as how these things work
& not for "ideal" derivative.

evidence
1. Truth serum - pentothal → depresses higher centers of [illegible]
[illegible] site done individual considers more
freely. also used in mental hospitals for
cases of schizophrenia & dementia [illegible]
→ small dose → quite lucid (as [illegible] of
internal tension)

2. Distrib. of drugs in body (partic. barbiturates)
a - Excrete 20-30% of long acting barb. unchanged
in urine (pentobarbital, etc).

b. But if get shorter acting then get none
coming out in excreta - what happens?
Infectious Hepatitis ?? Look up.
detoxified in liver

c. But shorter acting ones — they act same
in animals & humans. - presumably
S H [illegible] not detoxified in liver etc.

a. none exists in S^R - Columbia
b. electrophotometric studies - for [illegible]

4

p. 6 Anti convulsants
convulsions — excitation of CNS has spread beyond
bounds - all stimulation goes on switchboard —
overall response all cells → generalized react.
of all body muscles

Suitable Dose of NaCN in Dog — goes through all
symptoms of [illegible] typical epileptic (mg/kilo dog)

also
[illegible] Denervate carotid & aortic bodies - so cannot
[illegible] [illegible] [illegible] happens

6

on other hand (

Convulsion may be due to increased ... in strength of stimulus (... decrease to spread of stimulus) (cause of)

now How prevent convulsion

6/6/50
20

E p. 3 when convulsions are already ... (i.e., tetany, etc)

note here - latent effects of barbiturates
... in longer acting barbiturates in rat.
Pentothal - short acting
Phenobarb - long acting

For chronic use - epilepsy — Phenobarbital
disadvantage → drowsiness
bromides not used much due to → bromide psychosis.

most Recent ones
D.H.S. (Diphenyl Hydantoin Na)

Tridione (most recent)

picrotoxin - convulsant drug.
now produce shock (elect) in brain of animal (skull)

set threshold dose (current)
then → drug & try current
→ "screening" test - keep only promising

try again & discard
Try again & discard

→ 1 remaining

Dilantin - Merritt & Putnam N.Y.
did not make individual study

usefulness not sound

Dilantin - major convulsions

Tridiol - minor (some gaining of control.)

[illegible] Habitual use of Drugs

6/6/50
[illegible]

Third way — interfere with [illegible] of [illegible] (blood vessels of kidney)

also,
In some individuals carotid sinus is sensitive of external pressure
↓
minutes
Trolley car conductor in Boston

6/6/50

I B 2 carotid & aortic bodies close to carotid sinus & aortic arch [illegible] (like [illegible] nervous tissue)
Chemoreceptor organisms can be stimulated by (a), (b) & (c)

(c) why lobeline & aminophylline act as [illegible] in [illegible] — ending takes dies
well-received as test to circulation time
breathe suddenly — lobeline least likely of (a)(b) & (c)
to do harm — "drug of choice"

3. Example
→ repeated doses of nicotine to animals → rise in b.p. initially, then continues to rise, then falls,
finally → paralysis.

Drug for blocking transfer impulses to [illegible] & [illegible] ganglia
Tetraethyl ammonium Cl. C[illegible]

4 Constrictor nerve endings (do they really exist we [illegible])

paralyzed by ergot group of alkaloids
(a?)
new drugs dihydroergot (cornine) for hypertension
early stages good. now being tried
dibenamine favorable

5. muscarine & muscarine drugs → vasodilatation

& muscarine action is removed by action of atropine

Puzzle — drugs have antidote which is not toxic
but later in chronic dose → [illegible] effects
(sweating, dilatation of heat muscles etc.)

nausea
6. Vomiting due to digitalis sign of excessive drug
↳ also loss of appetite (first [illegible])

7. Veratrum alkaloids used for ↓ b.p. for [illegible] by [illegible]
receptors in heart itself for ① & ② — ① in lungs.

8. a circulation [illegible] adapted to muscular activity — [illegible]
item in [illegible] reflex [illegible] → — [illegible]

[illegible] — drug action on ?

S.N.S. when stimulated is supposed to liberate or form sympathin (a chemical mediator) O 6/6/50

<u>Heart beat</u> - Heart has a rhythm of its own - i.e., does not depend on nerve impulses. (Expt. - use heart of frog & perhaps others there)
autonomous

sympathetic nerve - accelerator

Sinus node

Impulse begins at sinus node

no communication bet. muscles of auricle & ventricle - so impulse would die out if not for AV node

fine muscles spread all over & whole ventricles contract
(i.e., "rt or left bundle branch block")

Auriculo-ventricular node - interval .1 sec (no longer than $\frac{2}{10}$ sec if so have heart block

Inhibitory nerves - X (Vagus nerve)

So, have four extra cardiac pairs of nerves to regulate output of heart & of blood pressure

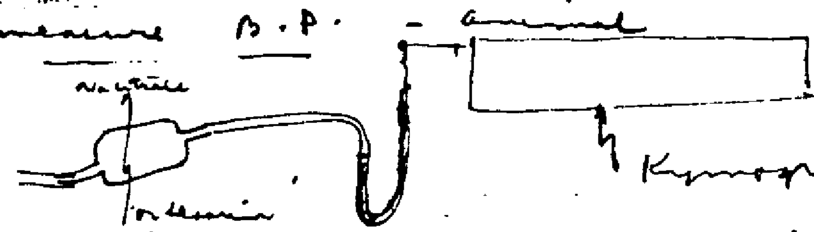
normal output - 4000 cc/min
Blood pressure - 120 mm Hg for top level (systolic)
(70) 80 mm Hg bottom level (diastolic)

exercise N.O. - 8 to 12 liters/min
B.P. { syst. - can go to 200

[illegible] circulation
(nervous mechanisms [illegible] regulatory mechanisms)

normal - ? mm. Hg.
affected by

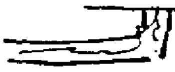
How measure B.P. - animal



But do not get both systolic & diastolic b.p.

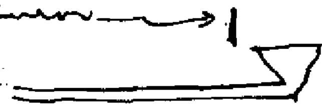
(4)

Hg column too much inertia — So use membrane manometer



— membrane (rubber) & recording film 6/4/50

Eventually by Hamilton manometer



mirror → | — chain [illegible] → to recording camera

modification — Lilly manometer

Heat two strain & amplify suitably (developed during war)
Do not need much (but amplify) &
so need only little change of only a few drops of blood & need only inserts a small needle (also [illegible] clotting)

membrane

another method — Strain Gage

[illegible] of elect. wire depends on cross section

M. 4.

M.D. uses inflatable cup + steth. — what is he doing?

puts on enough press to obliterate pulse in arm — when he hears 1st sound (systolic press) then listens longer for [illegible] → diastolic

pressure higher than in blood vessels

as air press falls

point highest [illegible] at which [illegible] pressure [illegible] then.

bangs

when all air pressure goes down don't hear anything

called Riva-Rocci method — one [illegible] obviously [illegible]

Can do on Rat's tail — don't listen [illegible] watch circulation under microscope.

Drug action

1. Drug actions on Heart itself — > or < activity } deal with
2. " " " Tonus Caliber of Blood Vessels
3. " " " , Viscosity of blood — no drugs. blood actions that are recognized — ability of SCN to lower b.p. when high. others.

(5)

4. Finally drugs which act on mechanisms of control & regulation — i.e. which act on ~~vasomotor~~ nerve mechanisms that control circulation;

6/4/50

I-A. Outline

1. Cardioinhibitory center stimulus — digitalis & drugs p. 2 II A-1.

other drugs which produce this are those veratrine group veratrum

produces marked slowing of heart, dilation of blood vessels & ? respirations.

C.C. d. mol

reciprocal innervation bet cardioaccelerator & cardioinhibitory centers — most marked by action of impulses → ? blood vessel dilation & ? cardiac output

I-A.

2. V.C.S & D

individual not breathing & given picrotoxin etc & b.p. rises then this is favorable sign — getting ready to [illegible]. But not true for [illegible] type — raises b.p. by peripheral type action

vasomotor center being stimulated;

V.C. — no. [illegible] — bitters in [illegible]

B In the Blood Vessels

1. when b.p. rises → inhibitory impulses (via ?) to [illegible] ... thermostat
- slow heart
- dilate blood vessels
- inhibit respiration

receptors in aortic arch & carotid [illegible]

cut [illegible] nerve in expt animal

b.p. → 300
fibrillation — values fall constantly
pulse goes 80 → 300

[illegible] one way to study high b.p. without arteries [illegible] ... → other mechanisms coming into play & b.p. — come down

Control of Circulation

1. Ideally the controlling circula- should maintain homeostasis [environ. in cells constant.
brought about by
a. change output of heart } but really can't do this for long.
b. change caliber of blood vessels

Components — cardiac output + vascular tone are regulated by two main types of influences. 6/6/50 20

a. chemical influences
b. Vasomotor influences

Chemical — blood vessels ~~of~~ of all parts of body are dilated by all kinds of metabolism

a. < O_2 tension
b. > CO_2 "
c. > acidity
d. > t°
e. acetylcholine
f. K-ions etc.

So, the more active a cell becomes the more the blood vessels dilate, i.e. kind automatic control.

Vasomotor Influences — diff than chemical

a. Vasoconstrictor — parasympathetic nervous
b. Vasodilator (belong to ~~central nervous~~ system)

belong to the sympathetic nervous system (vital factor in preparing body for emergencies) to involve whole sym. S.

So, some blood vessels in body that are strongly constricted by sym. S. & some that almost [illegible] (i.e., blood vessels supplying abdomen, skin) — but not brain & heart — flight muscles, don't need now (digestion + [illegible])

need blood here

cf. action of adrenaline & epinephrine

b. Vasodilator control — Belong to parasympathetic nervous system (are the main antagonists to sym. S. in its action)

necessity for function of individual isolated organisms (i.e., eat, [illegible] etc.)

when stimulated — supposedly — i.e. via Acetylcholine

9-15-47

Na & K by Flame Photometer (Perkin-Elmer)

6/4 5/20

A. Blood Prep
1. Remove clot
2. Centrifugal → serum

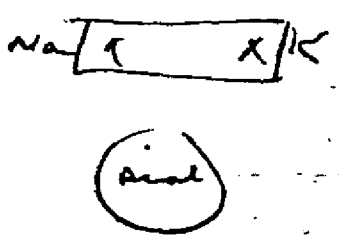
B. Stds
1. Na with K
2. no K with Na
3. also TCA

brown stoppered bottle

C. Sample

1. 4 cc TCA (10%)
2. add 2 cc sample (with a needle) serum [illegible]
3. add 4 cc distilled HOH (wider) (shake)
4. Fill [illegible] 400 x 42

(5) K Stds 4, 5 & 6.



K X

Dial Hoff
5(a) [illegible] Dial Hoff (machine) - only [illegible]
6. Remove F.A. - Remove funnels
7. Turn dial 0
8. [illegible] set to 0 with upper knob K
9. [illegible] (HOH [illegible]) then [illegible]
[illegible]

[illegible] / [illegible]

4/4/50

/ 80

Pat.

39 | 100

(2) 4 4

Na

3000 / 100

1/2 + 9 1/2 1+0 4

[illegible]

1 – 100 [illegible]

[illegible]

Protein (Serum)

alk [illegible] soln [illegible] cc [illegible]
(0.1 cc serum (CO [illegible] pipet) [illegible]
[illegible] E[illegible]
[illegible] tt using same rubber stopper for all tubes
centrifuge [illegible] min

6/4/50 [illegible]

Klett - Summerson Photelometer

use 540 mμ filter (adjust to zero for each filter)
use Klett colorimeter tubes (individually calibrated)
run blank 1st then samples.
rinse tubes 1st in H_2O water then dry & read

Table for values
Kjeldahl serum of known values

$\frac{1000}{50}$ =

$\frac{1000}{50}$ = [illegible]

4/6/50

$\frac{1000}{100}$ =

$\frac{18}{20}$

$\frac{18}{20} \times 5 = 4.5$

$\frac{16}{20} \times 5 = 4.0$

$\frac{14}{20} \times 5 = 3.5$

$\frac{12}{20} \times 5 = 3.0$

$\frac{10}{20} \times 5 = 2.5$

60 → 4 | 100

150 → = 50

$\frac{8}{10} \times 5 = 4.0$

$\frac{6}{10} \times 5 = 3.0$

$\frac{4}{10} \times 5 = 2.0$

$\frac{2}{10} \times 5 = 1.0$

C.A. 41, 2150c (1947)

J. Biol. Chem. 167, 499-513 (1947) 6/6/50 ajp

Pauline M. Hald

The Flame Photometer for the measurement of Na and K in Biol. materials

also,

C.A. 40, 4756' (1946)

J. Biol. Chem. 163, 429-434 (1946). P on H. notes on comm. data of Na & K.

C.A. 41, 6595c (1947)

J. Biol. Chem. 168, 641-649 (1947)

R. Overman & A.K. Davis (Univ. Tenn. Coll. Med.)

application of Flame Photometry to Na & K determ in Biological Fluids

U.S.I. with Perkin-Elmer flame photometer model 17 for determ of Na & K in blood, plasma and blood cells & urine with approx. the same accuracy as by chemical methods.

C.A. 41, 2787f (1947) Det. 0.05 mg/ml.

Biochem. J. 40, 828-831 (1947)

R.J. Barnes (Postgrad. Med. School, London)

colorimetric determ of Mg in Plasma or Urine by means of Titan Yellow

7.0
3) 25.0
8.3

8.0
3.0
6.0
3) 19.0
6.3

7.0
6.5
6.5
3) 20.0
6.6

3.0
2.0
1.5
3) 6.4
2.1

6.0
4.5
5.5
3) 16.0
5.3

In conclusion sensory fibers less ~~conducting~~ conducted than motor (efferent) fibers

Counterpart — leg goes to sleep — can move leg but can't feel any

6/4/50 20

~~also~~ Further

pain knocked out before pressure impulses
by impulses
— air
Reason smaller fibers (matter of diffusion)

~~tested~~ Local anesthetic tested on p.5

Situation like barbiturates = adequate but will not likely get ideal

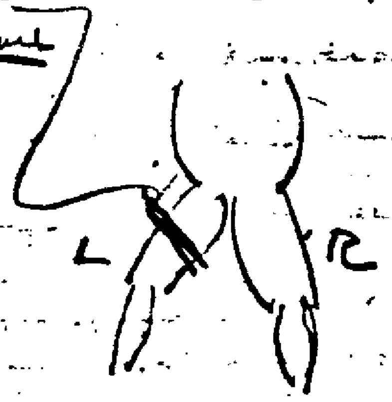
Note p.5 — Specific neuromuscular blocking agents

Means block bet. nerve & muscle

Curare or curare-like action

Famous exp. of Claude Bernard

1. Gave curare to Frog — Respiratory paralysis & limpness
2. Is effect on CNS or is it peripheral?
   put rubber band around thigh to obstruct circulation
   before curare



Ant. reflex	L	R
	+	+
after curare	+	0

normal response in frog

protected side still reacts normally.

Curare — produces paralysis
but is not anesthetic
to "pith" animal
then cut brain & cord
destroy other

11-1-49

a- Demerol (U.S.P.) not antispas (?) → similar to its action

sif? Insufficient

also has danger of addiction

Ad. Pont ?? → lacks effect on smooth muscle.

6/6/50 JM

b- amidone

most effective synthetic analgesic

most effective analgesic not free from danger of addiction

over p.4

C- miscellaneous depressants

1. Scopolamine (levo-hyoscyamine)

→ has atropine like action on autonomic lines

but can depress C.N.S. & produce sleep

potent dose 1/2 mg

Hyoscine - will prevent sea-sickness & air-sickness (found out during war)

but results largely due to suggestion? No definite ability in it to prevent motion-sickness.

also used as truth serum."

2. Apomorphine HCl - split out H_2O from morphine with conc. acid

causes

a- strong vomiting effect to man (only 15 mg.)

b- but has not removed the depressant effect - (i.e., can kill animals)

3. Bulbocapnine - produces catatonia (an animal in any position)

used as gd sedative for horses (morphine actually excites)

4. $MgCl$ - anion doesn't matter

but large enough dose → respiratory failure

(but must inject - can't pass through intestinal wall & reason for cathartic effect of Mg salts)

(2) 11-1-47

can produce [illegible] by O_2
(overall can be [illegible] in reaction)

Hormonal defense [illegible] breaking down

6/6/50
JLD

p. 5 Cannabis
(1) no therapeutic effect

p. 5. Local anesthetics

a. produce insensibility to pain at site at which applied
(not like gen'l anesthetics which are carried thru body)
b. act locally because they are applied locally (& are [illegible] there)
c. Have predilection for nerve tissue.
d. Do not use to produce gen'l anesthesia
(1) get convulsions → collapse
(2) collapse without any preliminary convulsions.
Do not want these substances absorbed.

How Used

1. Terminal anesthesia — apply to [illegible]
or conjunctiva [illegible]

[illegible] applications drug

2. Infiltration — [illegible] under skin [illegible]
(afferent) [illegible] to establish contact with nerve endings
substances [illegible]

relatively
very dilute solutions (1% or less)
procaine = novocaine

absorption [illegible]
1. Reduces local conc. } So add constrictor — epinephrine
2. → collapse or adrenalin
[illegible]

<u>outline</u> 6/4/50

F. analgesics
(Diminish or block perception of pain)
How Done
1. Block or abolish pain impulses (cut nerves or local anesthetic)
(deposition in a nerve to block conduction)
2. Block conduction within [illegible]
(salicylic acid series)
↳
acetanilid etc
p. 4 — 2 also are antipyretics (but only in presence of fever – not for normal temp).

3. modifying reaction to pain impulses = —— production of euphoria (sensation of comfort & well-being)
i.e. – morphine (reaction to pain is modified)
characteristic of opiates
Dangerous condition – can likely lead to habituation.
no explanation for habituation
morphine alkaloids differ
codeine – weakest
[illegible] – strongest (& worst as far as addiction)
[illegible] alleged drug traffic

<u>Drawbacks</u>
a. Danger of addiction
b. Far reaching effects on smooth (involuntary) muscle ⟶ nausea, vomiting, constipation
c. – ~~[illegible]~~ Natural source of these drugs (poppy plant) has got out of control. [illegible]
d. – Also many plant poppies for edible oil – but these contain morphine (all with [illegible])

3rd [illegible] middle p 44

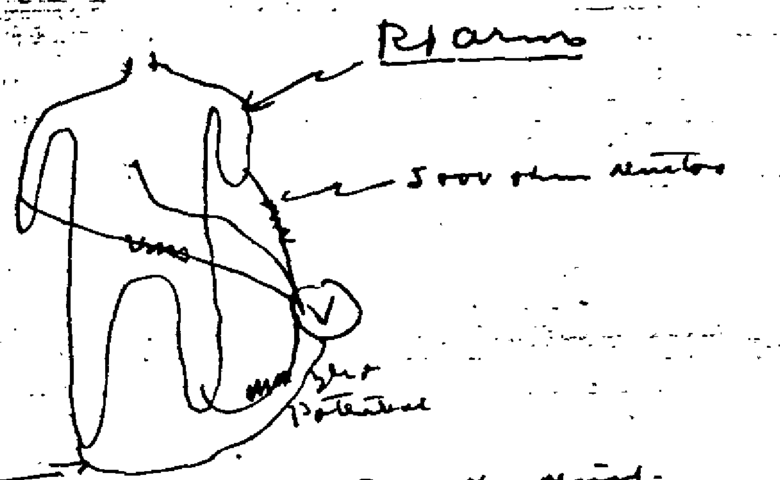
E.K.G.

6/4/50

C L — not satisfactory
C F — used in many shops but not ideal.

C R

V — unipolar leads

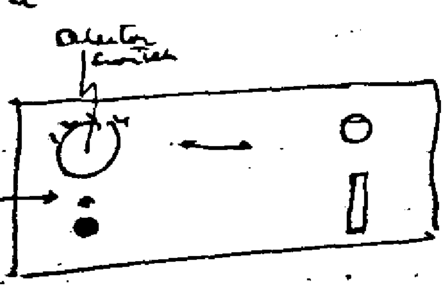


Wilson lead — 5000 ohm resist.

Goldberger leads — no resist. — just as accurate

1. Std leads
2. precordial chest leads (as am. Ht. assn)
3. unipolar chest leads
4. unipolar extremity leads
5. augmented unipolar extremity leads

How take E.K.G.



Potentiometer switch — for recording + millivolt alone

Standardize machine

6/6/50

E-K-G.

Uses

1. Detect & Treat arrhythmia
2. Digitalis Treat.
3. Detect previous myocardial disease
4. occasionally etiological diagnosis

orthodiagram

cardiac silhouette with fluoroscope

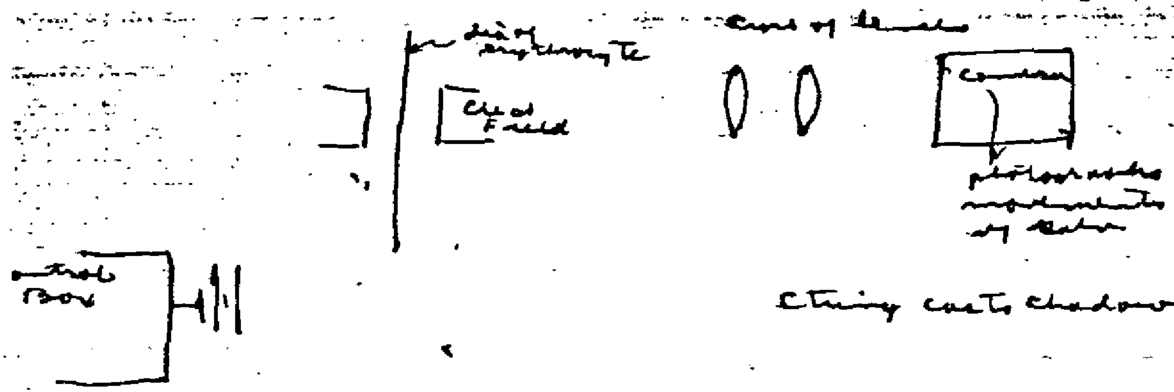
History

1887 Ludwig →

1903 Einthoven used

String galv.

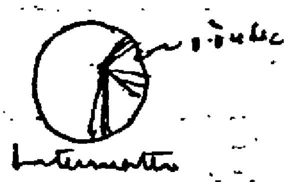
Quartz fiber - coated



String casts shadow on film

Types — uses by standardization &

1. String galv. + camera
2. mirror →
3. direct writer
4. Vac tube.



Precordial leads

Posi. 1 4th interspace at border of sternum

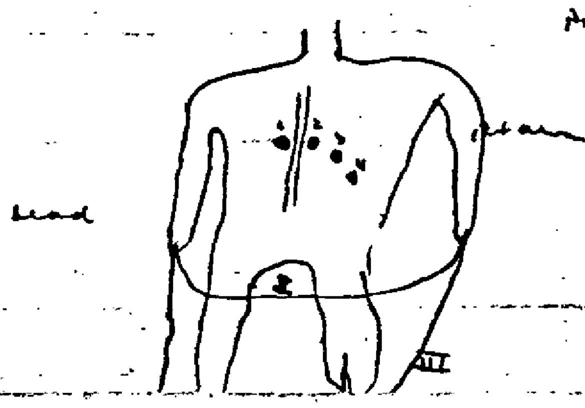
Posi. 2

Pos 3

4

5

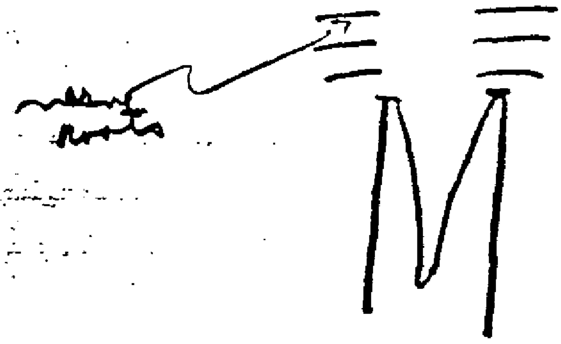
6



Epinephrine may itself have local anesthetic effect.
Due to ?

6/6/50

3. Conduction anesthesia
Block conduct of nerve impulses along a nerve trunk
(Have anesthesia in peripheral distribution of nerve)
or still in injecting nerve (of
Spinal anesthesia (lumbar region) — inject drug substance in cerebral spinal space — & drugs pass up & down & contact nerve roots (& block conduction)
of spinal cord



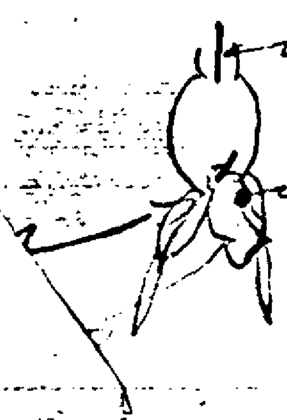
add glucose (make heavier than spinal fluid)
& hold patient head down

Cameron performs ... operations in head pain in tongue — but not safe

Surgeons nowadays will not use spinal anesthesia for chest higher than abdomen (higher than diaphragm)

Reason get to thoracic region & paralyze sympathetic nerves & get down B.P. → collapse

Difference in sensitivity of diff nerve fibers to same anesthetics



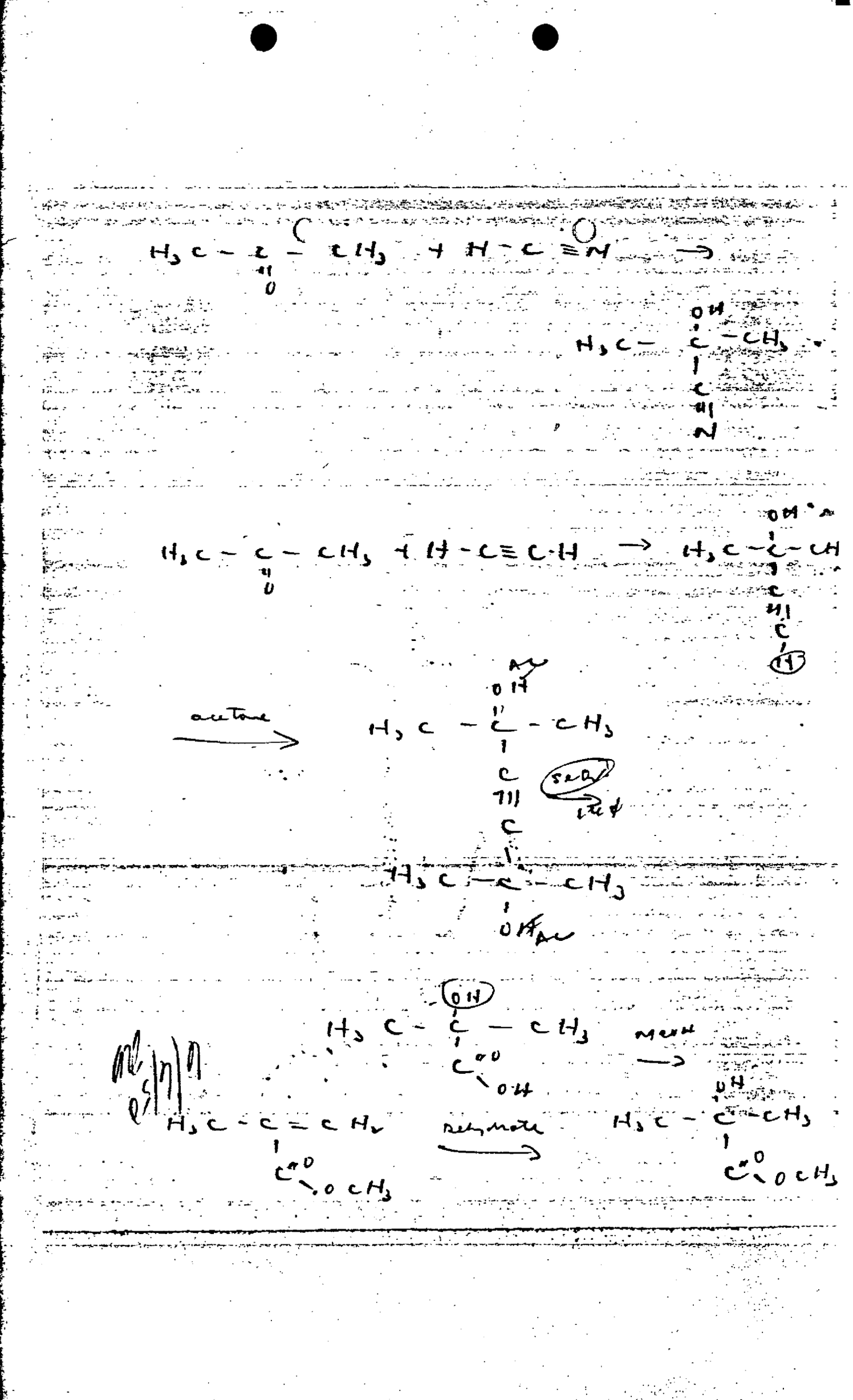
Kiessmann ("Pithing")

test acid response time

R L
2" 2"

put cocaine + procaine

1 hour 2



6/6/50
JW

(4C)

File cabinet(

✓ Sink (??)

✓ Shelves

✓ Mattresses

✓ Kett

✓ Table

Vanslyke

✓ pH app.

✓ Door

✓ ~~[illegible]~~

Chemicals { and parts. ✓

Balance

Hematocrit

10-16-47

1. K → C-blood & urine ○

Introduce
of
following Heart Failure

Kamen's
Wire Book

Control Diet

(meningeal casts)

6/6/50 / NB

---

2. K in Diabetic acidosis – was hi
administration use of K → normal ⟶ low.

---

3. pH on Vomiting cases

---

4. P

---

5. mercipurin cases
Follow at least 1 or 2 more – use fractional
bloods & urines

Action of Drugs on Respiratory System

Respiration — gas exchange bet. living organism & its environment, i.e. uptake of O_2 & exhalation of CO_2.

In pharmacology — refers to respiratory movements in higher animals or man

1. Single cell (historic precursor)

Seawater surrounds
O_2 diffuses in

6/4/50

2. Combination of cells

pumps sea water in

need transport mechanism

3. Then needed to > area of contact

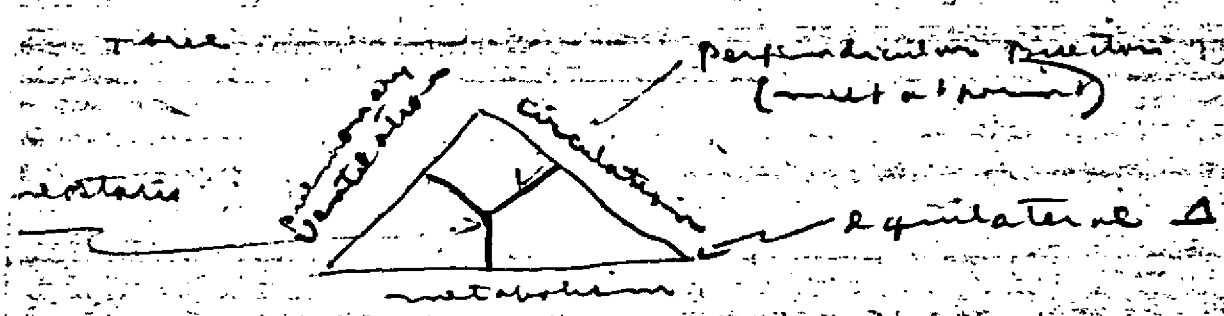
in aquatic organisms had gills

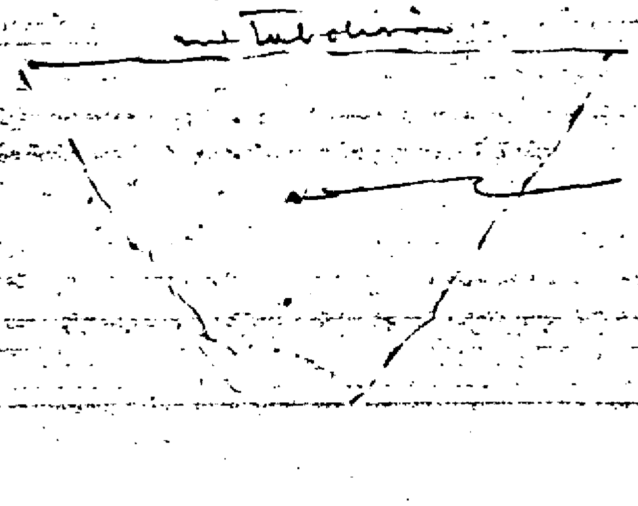
in air breathing animals had lungs — thin layers of air cells

tremendously large area.

4. Then came rhythmic respiratory movements (of air in & out of lungs)

There





But internal environment of body cells would remain constant.

Krebs cycle — ? 6/6/50

↳ Fixation of CO_2

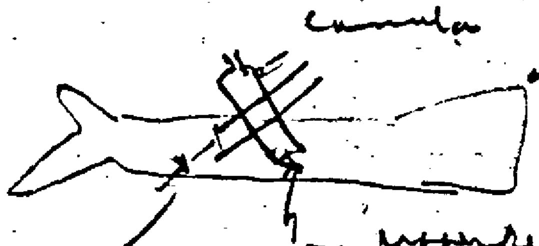
1. Reduced O_2 tensions are not stimulants to respiratory centers — actually is a depression.
2. If is more cent depressant respiration [illegible]
   O_2 extent is slight & [illegible]

3. CO_2 → [illegible] in keeping activity of center rhythmic.

How CO_2 works

1. Hering – Breuer reflexes – check inspiration of air when lungs are filled satisfactorily

2. Kretschmer reflexes – irritation of lungs will check inspiration.



in will [illegible]

Passing Et_2O will stimulate action of lungs

Passing Et_2O & will stop breathing (inhibit breathing)

also SO_2, NH_3, I_2

Carotid & aortic nodes (arteries) area are stimulated by air rate
1. low O_2 — low O_2 most powerful stimulant
2. > CO_2
3. > acidity Conclusion?

Carotid & aortic nodes stimulated by [illegible] of Drugs
[illegible] lobeline (little [illegible])

(2)

4. - CO_2 poisoning is coming to be a recognized clinical entity.

6/4/50 JD

Tube in Trachea

completely saturate hemoglobin with O_2 but ... provision for removal of CO_2 & ... may go by ... normal tension ... 90 to 140 ... Hg. ... will ... tho' he looks fine

check by arterial blood specimen.

5. - Treatment of cough

(method of getting rid of ...)

action

a - Inspiration of air

b -

c - Explosive exhalation.

can use (depressant drugs

a - Codeine (...

b - Barbiturate ... (as ... depressant)

... on ...

so Try to remove source of irritation

a - Idea of demulcent coating of upper passages (mucous membranes)

(cough syrups) (lozenges)

b - Expectorants (Idea - increase secretions of respiratory tract)

no real scientific background

nauseating agents ... etc

NH_4Cl

$NaHCO_3$

Terpene derivs - volatile oils

of sympathomimetic drugs — (epinephrine / adrenalin [illegible] / ephedrine / [illegible]) 6/6/50

to minimize effect of sympathetic nervous system

maybe the 1 inhalation of epinephrine spray may be even more effective than s.c. — relaxation effect — explain??

Hemoglobin : methemoglobin

Fe^{++} → Fe^{+++}

cannot longer combine with O_2

slate gray color of [illegible] addicts (can also be caused by sulfa drugs)

also, for combining with hemoglobin

$CO : O_2 = 1 : 210$

∴ CO bad

also { 1. [illegible] feel good
2. rosy pinkish color (CO hemoglobin)
3. Doesn't give any warning

CO poisoning (O_2 tension is normal [illegible] CO present [illegible] [illegible] to O_2 [illegible])

---

anemia — 4.5 - 5.0 million red blood cells/cu. mm. normal

a severe anemia may be reduced to [illegible] 2.0

[illegible] $FeSO_4$ / Fe gluconate (easiest to take)

(7) 11-8-49

2. Hypokinemic anoxia - difficulty due to circulation - i.e. cardiovascular fault.

Can be
a - ischemic (arterial)
b - congestive (venous)

3. Overutilization anoxia - more demand for O_2 than can get - i.e. muscles while [illegible] - occurs at tissue level.

4. Histotoxic anoxia - Tissue enzymes which activate O_2 can no longer take it up. i.e. caused by H_2S & cyanide.

What does it look like ??

a - Simulates drunkenness ( ) Joseph Barcroft 50 yrs ago

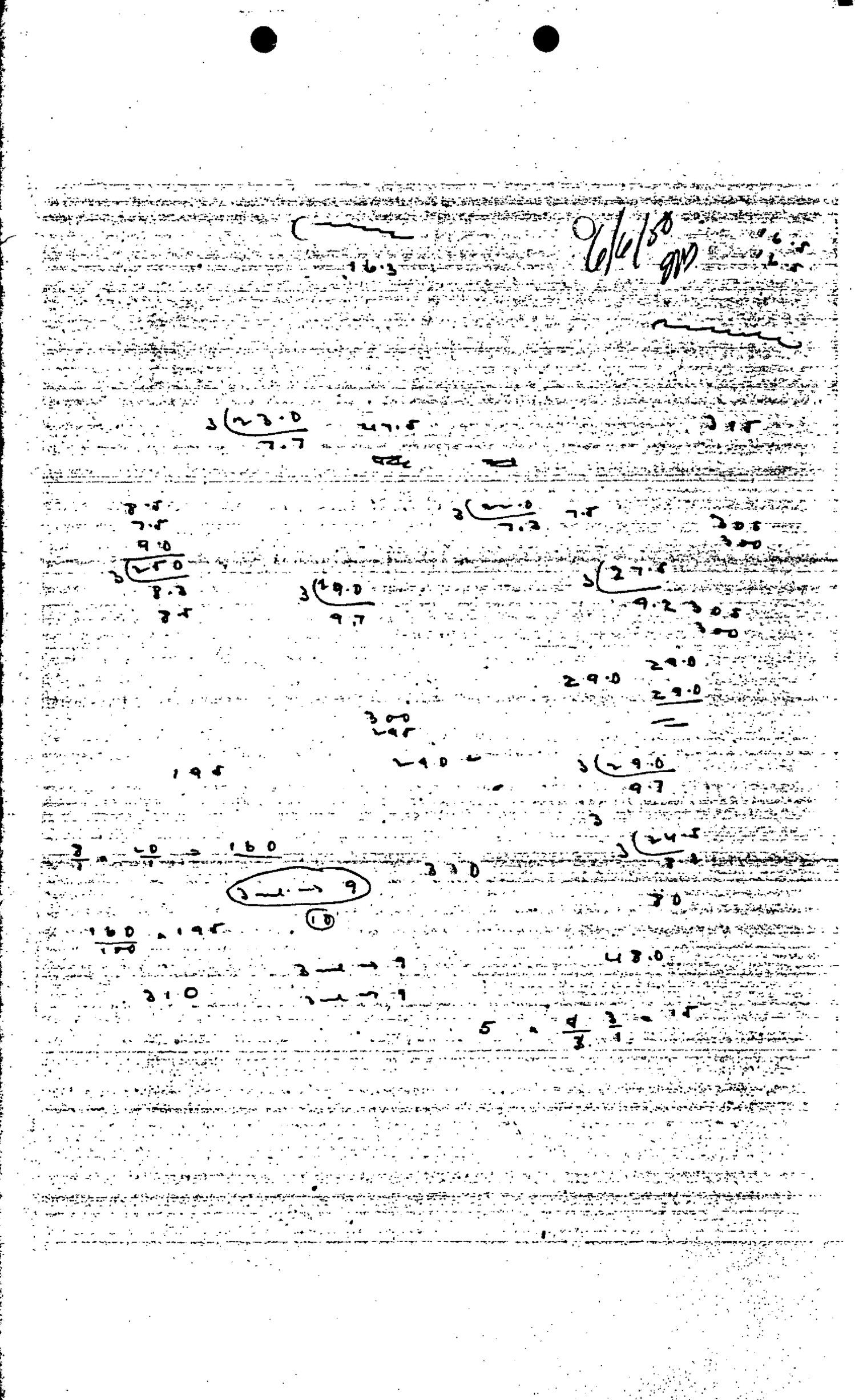
i.e. individuals vary from sleepiness to aggressiveness & are completely unaware of their poor judgement. (air pilots in war)

b - Can even deceive physician - patient (due to euphoria) says he feels better

During war

a. Ways of giving O_2 other than by mask - more successful { swallowing H_2O_2 & other chemical methods for improving altitude tolerance.

b. Niacin, carbohydrate diets, caffeine (attempts to train organisms)
A.A.F. attitude is [illegible] as training because can't train)



Materials list for Heart Station.

Quantity	Harshaw Catalogue No.	Description	Price
1	H-26900	Beckman PH meter, model G; complete with batteries, electrodes, solutions, standard cell and cup.	$245.00
2	H-29040	Hypodermic Glass Electrodes	$30.00
1	H-14200	Klett - Summerson colorimeter, clinical model. Two H-1428 Klett - Summerson filters, nos. K-S 54 and K-S 64 are included.	$148.00
12	H-10640	Blood volume index centrifuge tubes	$ 10.48
2	H-6350	Kock micro- Burets/ standard taper points, two interchangeable outlet tips - capacity, 5 ml.	$ 29.30
12	H-24640	Volumetric Flasks; standard taper glass stoppered - capacity, 100 ml.	$ 28.62
6	H-18460	Cylinders; standard taper glass stoppered, pyrex glass - 10 ml. capacity.	$ 10.20
1	6404	Van Dyke manometric blood gas apparatus	$248.00

6/4/50

Materials list for Heart Station

Quantity	Harshaw Catalogue No.	Description	Price
1	H-28900	Beckman PH water, model G; complete with batteries, electpodes, solutions, standard cell and cup.	$245.00
2	H-29040	Hypodermic Glass Electrodes	$30.00
1	H-14200	Klett - Summerson colorimeter, clinical model. Two H-1428 Klett - Summerson filters, nos. K-S 54 and K-S 64 are included.	$148.00
12	H-10640	Blood volume index centrifuge tubes	$ 10.48
2	H-6350	Kock micro- Burets/ standard taper joints, two interchangeable outlet tips - capacity, 5 ml.	$ 29.30
12	H-24640	Volumetric Flasks; standard taper glass stoppered - capacity, 100 ml.	$ 28.62
6	H-18460	Cylinders; standard taper glass stoppered, Pyrex glass - 10 ml. capacity.	$ 10.20
1	6406	Van Slyke monometric blood gas apparatus	$248.00

Materials list for Heart Station (cont.)

Quantity	Marshaw Catalogue No.	Description	Price
1		6 volt, 120 amp. hr. Storage battery for use with Beckman model DU Spectrophotometer.	
1		Trickle charger for use with 6 volt, 120 amp. hr. storage battery.	

NOTE: The above can all be ordered from the Marshaw Scientific Company,
117 S. 17th Street,
Philadelphia, Penna.
They are standard laboratory items which sell at a fixed price, regardless of the supply house from which they are ordered.

Other supply houses where these materials may be obtained are:

Arthur H. Thomas Company,
230 S. 7th Street,
Philadelphia, Penna.

Williams, Brown and Earle,
918 Chestnut Street,
Philadelphia, Penna.

In addition, there are needed:

1 - Filing cabinet

1 - Table, solidly built, approx. size: length, 65", width 35", height, 36".

1 - Sink - the present sink should be raised to a height of 36" (from floor to tap).

Materials list for Heart Station (cont.)

Quantity	Marshaw Catalogue No.	Description	Price
1		6 volt, 120 amp. hr. Storage battery for use with Beckman model DV Spectrophotometer.	~~25~~ 38.45
1		Trickle charger for use with 6 volt, 120 amp. hr. storage battery.	19.25

NOTE: ~~The above can all be ordered from the Marshaw Scientific Company,~~
117 S. 17th Street,
Philadelphia, Penna.

~~They are standard laboratory items which sell at a fixed price~~, regardless of the supply house from which they are ordered.

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1 - Sink - the present sink should be raised to a height of 36" (from floor to tap).

Materials list for Heart Station

Quantity	Marshaw Catalogue No.	Description	Price
24	M-5800	Pyrex Beakers - capacity, 20 ml.	$6.48
2	M-11090	Double castalloy Buret clamps	$5.00
1	M-6110	Mohr Buret - capacity, 100 ml.	$2.54
2	M-6280	Dispensing Buret	$13.32
1	M-60940	Buret Support, Fisher	$ 6.60
36	M-61610	Test tubes, Pyrex 15 mm. diameter 125 mm. length	$ 1.62
1		Mechanical Refrigerator - capacity approx. 6 cu. ft.	

Materials list for Heart Station

Quantity	Marshay Catalogue No.	Description	Price
24	M-3800	Pyrex Beakers - capacity, 20 ml.	$6.48
2	M-11090	Double castalloy Buret clamps	$5.00
1	M-6110	Mohr Buret - capacity, 100 ml.	$2.54
2	M-6280	Dispensing Buret	$13.32
1	M-60940	Buret Support, Fisher	$ 6.60
36	M-61610	Test tubes, Pyrex 15 mm. diameter 125 mm. length	$ 1.62
1		Mechanical Refrigerator - capacity approx. 6 cu. ft.	

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Mr. Harry Gold
6823 Kindred St.
Philadelphia 24, Pa.

6/6/50

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THE ENGINEERS CLUB

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PARKWAY ENTRANCE

PROGRAM

Thursday, October 28, 1948, 7:30 P. M.

"The Present Status of Fundamental Particles in Physics—A Survey"

Speaker to be announced

Tuesday, November 9, 1948, 7:30 P. M.

"The Medical Use of Radioisotopes for Tracing and Therapy"

RICHARD H. CHAMBERLAIN, M. D.
Department of Radiology, Hospital of the University of Pennsylvania

Tuesday, November 30, 1948, 7:30 P. M.

"Some Dividends for Fundamental Physics from War-time Investments in Microwave Technology"

DR. CHARLES H. TOWNES
Associate Professor of Physics, Columbia University

Wednesday, December 8, 1948, 7:30 P. M.

"The Synchrotron Accelerator Project at Brookhaven"

DR. G. KENNETH GREEN
Physicist, Accelerator Project, Brookhaven National Laboratory

ALL LECTURES will be held in the Lecture Hall of The Franklin Institute beginning at 7:30 P. M.

The fee for this symposium will be $3.25 for members of either The Franklin Institute or The American Institute of Electrical Engineers. The fee for single lectures will be $1.00, and the fee for non-members for the series will be $4.00. Attendance will be limited to 350.

Please use the reply card on the back of this page for registration.

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Title Practical physiological chemistry Edition 12

612.014 D647 C02 Author Dixon, Malcolm

Title manometric methods

MEMBER'S NAME Harry Gold

JULIAN PAUL BRODIE

September 15, 1947

6/6/50
320

Dear Mr. Brothman:

I think you will agree with me that I have been more than patient in waiting for you to develop a men's vanishing cream which you were supposed to complete for me within three months or less from September 13, 1946. There must be an end to all things, and I think in all fairness to me that you should either complete the job or advise me frankly that you cannot proceed and return the $650 I paid you.

Under the circumstances, I will make this final request that you deliver the completed product to me within ten days from date hereof or, if you are unable to do so, to return my $650, and let us call the deal off.

Sincerely,

Julian P. Brodie

Mr. A. Brothman
A. Brothman and Associates
85-03 57th Avenue
Long Island City, New York

File this return with Collector of Internal Revenue on or before March 15, 1947. Any balance of tax due (item 9, below) must be paid in full with return. See separate instructions for filling out return.

Page 1

FORM 1040
Treasury Department
Internal Revenue Service

U. S. INDIVIDUAL INCOME TAX RETURN
FOR CALENDAR YEAR 1946

1946

For fiscal year beginning _____, 1946, and ending _____, 1947

EMPLOYEES.—Instead of this form, you may use your Withholding Statement, Form W-2, as your return, if your total income was less than $5,000, consisting wholly of wages shown on Withholding Statements or of such wages and not more than $100 of other wages, dividends, and interest.

Do not write in these spaces

File Code

Serial No.

District

(Cashier's Stamp)

Name _____ (PLEASE PRINT. If this return is for a husband and wife, use both first names)

ADDRESS _____ (PLEASE PRINT. Street and number or rural route)

(City or town, postal zone number) (County) (State)

Occupation _____ Social Security No. _____

Your Exemptions

List your own name.
If married and your wife (or husband) had no income, or if this is a joint return of husband and wife, list name of your wife (or husband).

List names of other close relatives (as defined in instruction 1) with 1946 incomes of less than $500 who received more than one-half of their support from you. If this is a joint return of husband and wife, list dependent relatives of both.

1.	Name (please print)	Relationship	Name (please print)	Relationship
	Your name			

Your Income

Enter your total wages, salaries, bonuses, commissions, and other compensation received in 1946, BEFORE PAY-ROLL DEDUCTIONS for taxes, dues, insurance, bonds, etc. Members of armed forces and persons claiming traveling or reimbursed expenses, see instruction 2.

2.	Print Employer's Name	Where Employed (City and State)	Amount	
			$	

Enter total here → $ _____

3. Enter here the total amount of your dividends _____

4. Enter here the total amount of your interest (including interest from Government obligations unless wholly exempt from taxation) _____

5. If you received any other income, give details on page 2 and enter the total here _____

6. Add amounts in items 2, 3, 4, and 5, and enter the total here _____ $ _____

How to Figure Your Tax

IF YOUR INCOME WAS LESS THAN $5,000.—You may find your tax in the tax table on page 4. This table, which is provided by law, automatically allows about 10 percent of your total income for charitable contributions, interest, taxes, casualty losses, medical expenses, and miscellaneous expenses. If your expenditures and losses of these classes amount to more than 10 percent, it will usually be to your advantage to itemize them and compute your tax on page 3.

IF YOUR INCOME WAS $5,000 OR MORE.—Disregard the tax table and compute your tax on page 3. You may either take a standard deduction of $500 or itemize your deductions, whichever is to your advantage.

HUSBAND AND WIFE.—If husband and wife file separate returns, and one itemizes deductions, the other must also itemize deductions.

Tax Due or Refund

7. Enter your tax from table on page 4, or from line 12, page 3 _____ $ _____

8. How much have you paid on your 1946 income tax?
   (A) By withholding from your wages _____ $ _____
   (B) By payments on 1946 Declaration of Estimated Tax _____
   Enter total here → $ _____

9. If your tax (item 7) is larger than payments (item 8), enter BALANCE OF TAX DUE here _____ $ _____

10. If your payments (item 8) are larger than your tax (item 7), enter the OVERPAYMENT here _____ $ _____
    Check (✓) whether you want this overpayment: Refunded to you ☐; or Credited on your 1947 estimated tax ☐

If you filed a return for a prior year, what was the latest year? _____

To which Collector's office was it sent? _____

To which Collector's office did you pay amount claimed in item 8 (B), above? _____

Is your wife (or husband) making a separate return for 1946? _____ ("Yes" or "No")
If "Yes," write below:
Name of wife (or husband) _____

Collector's office to which sent _____

I declare under the penalties of perjury that this return (including any accompanying schedules and statements) has been examined by me and to the best of my knowledge and belief is a true, correct, and complete return.

(Signature of person (other than taxpayer or agent) preparing return) (Date) (Signature of taxpayer) (Date)

(Name of firm or employer, if any) (If this is a joint return of husband and wife, it must be signed by both)

20-00000-1

Do not itemize deductions if (1) You determine your tax from the tax table on page
(2) Your total income is $5,000 or more and you claim the $500 standard deduction.
If husband and wife filing together at end of year file separate returns and one itemizes deductions, the other must file his or her return on Form 1040, and must also itemize deductions.

DEDUCTIONS

Describe deductions and state to whom paid. If more space is needed, list deductions on separate sheet of paper and attach to this return.

		Amount
Contributions		
	Allowable Contributions (not in excess of 15 percent of item 6, page 1)	$
Interest		
	Total Interest	
Taxes		
	Total Taxes	
Losses from fire, storm, shipwreck, or other casualty, or theft.		
	Total Allowable Losses (not compensated by insurance or otherwise)	
Medical and dental expenses		
	Net Expenses (not compensated by insurance or otherwise)	$
	Enter 5 percent of item 6, page 1, and subtract from Net Expenses	
	Allowable Medical and Dental Expenses. See Instruction for limitation	
Miscellaneous (See Instructions)		
	Total Miscellaneous Deductions	
	TOTAL DEDUCTIONS	$

TAX COMPUTATION—FOR PERSONS NOT USING TAX TABLE ON PAGE 8

1. Enter amount shown in item 6, page 1. This is your Adjusted Gross Income	$
2. Enter DEDUCTIONS (If deductions are itemized above, enter the total of such deductions; if adjusted gross income (line 1, above) is $5,000 or more and deductions are not itemized, enter the standard deduction of $500)	
3. Subtract line 2 from line 1. Enter the difference here. This is your Net Income	$
4. Enter your exemptions ($500 for each person whose name is listed in item 1, page 1)	
5. Subtract line 4 from line 3. Enter the difference here	$
6. Use the tax rates in instruction sheet to figure your combined tentative normal tax and surtax on amount entered on line 5. Enter the tentative tax here. (If line 3 above includes partially tax-exempt interest, see Tax Computation Instructions)	$
7. Enter here 5 percent of amount entered on line 6	
8. Subtract line 7 from line 6. Enter the difference here. This is your combined normal tax and surtax. (If alternative tax computation is made on separate Schedule D, enter here tax from line 12 of Schedule D)	$
IF YOU USED THE $500 STANDARD DEDUCTION IN LINE 2, DISREGARD LINES 9, 10, AND 11, AND COPY ON LINE 12 THE SAME FIGURE YOU ENTERED ON LINE 8.	
9. Enter here any income tax payments to a foreign country or U. S. possession (attach Form 1116)	$
10. Enter here any income tax paid at source on tax-free covenant bond interest	
11. Add the figures on lines 9 and 10 and enter the total here	
12. Subtract line 11 from line 8. Enter the difference here and in item 7, page 1. This is your tax	$

Do not use this page if your income is wholly from salaries, wages, dividends, and interest

Schedule A.—INCOME FROM ANNUITIES OR PENSIONS

1. Cost of annuity (total amount you paid in)	$	4. Total amount received this year	$
2. Amount received tax-free in prior years		5. Excess, if any, of line 4 over line 3	
3. Remainder of your cost (line 1 less line 2)	$	6. Enter line 5, or 3 percent of line 1, whichever is greater (Attach separate schedule for each additional annuity or pension)	$

Schedule B.—INCOME FROM RENTS AND ROYALTIES

1. Kind of property	2. Amount of rent or royalty	3. Depreciation or depletion (explain in Schedule F)	4. Repairs (explain in Schedule G)	5. Other expenses (itemize in Schedule G)
	$	$	$	$
Net profit (or loss) (col. 2 less sum of cols. 3, 4, and 5)	$	$	$	$

Schedule C.—PROFIT (OR LOSS) FROM BUSINESS OR PROFESSION. (Farmers should obtain Form 1040F)

(State (1) nature of business ________; (2) business name ________)

1. Total receipts ________ $

COST OF GOODS SOLD

(To be used where inventories are an income-determining factor)
(Enter the letters "C" or "C or M" on lines 2 and 8 if inventories are valued at either cost, or cost or market, whichever is lower)

2. Inventory at beginning of year	$
3. Merchandise bought for sale	
4. Labor	
5. Material and supplies	
6. Other costs (explain in Schedule G)	
7. Total of lines 2 to 6	$
8. Less inventory at end of year	
9. Net cost of goods sold (line 7 less line 8)	$
10. Gross profit (line 1 less line 9)	$

OTHER BUSINESS DEDUCTIONS

11. Salaries and wages not in line 4	$
12. Interest on business indebtedness	
13. Taxes on business and business property	
14. Losses (explain in Schedule G)	
15. Bad debts arising from sales or services	
16. Depreciation, obsolescence and depletion (explain in Schedule F)	
17. Rent, repairs, and other expenses (explain in Schedule G)	
18. Amortization of emergency facilities (attach statement)	
19. Net operating loss deduction (attach statement)	
20. Total of lines 11 to 19	$
21. Total of lines 9 and 20	$
22. Net profit (or loss) (line 1 less line 21)	

Schedule D.—GAINS AND LOSSES FROM SALES OR EXCHANGES OF CAPITAL ASSETS, ETC.

1. Net gain (or loss) from sale or exchange of capital assets (from separate Schedule D)
2. Net gain (or loss) from sale or exchange of property other than capital assets (from separate Schedule D)

Schedule E.—INCOME FROM PARTNERSHIPS, ESTATES AND TRUSTS, AND OTHER SOURCES

1. Name and address of partnership, syndicate, etc. ________ Amount, $
2. Name and address of estate or trust ________ Amount,
3. Other sources (state nature) ________ Amount,
4. Total

Total income from above sources (Enter as item 5, page 1) ________ $

Schedule F.—EXPLANATION OF DEDUCTION FOR DEPRECIATION CLAIMED IN SCHEDULES B AND C

1. Kind of property (if buildings, state material of which constructed)	2. Date acquired	3. Cost or other basis (do not include land or other nondepreciable property)	4. Assets fully depreciated in use at end of year	5. Depreciation allowed (or allowable) in prior years	6. Remaining cost or other basis to be recovered	7. Estimated life used in accumulating depreciation	8. Estimated remaining life from beginning of year	9. Depreciation allowable this year
		$	$	$	$			$

Schedule G.—EXPLANATION OF COLUMNS 4 AND 5 OF SCHEDULE B, AND LINES 6, 14, AND 17 OF SCHEDULE C

1. Column or Line No.	2. Explanation	3. Amount	1. Column or Line No.	2. Explanation	3. Amount
		$			$

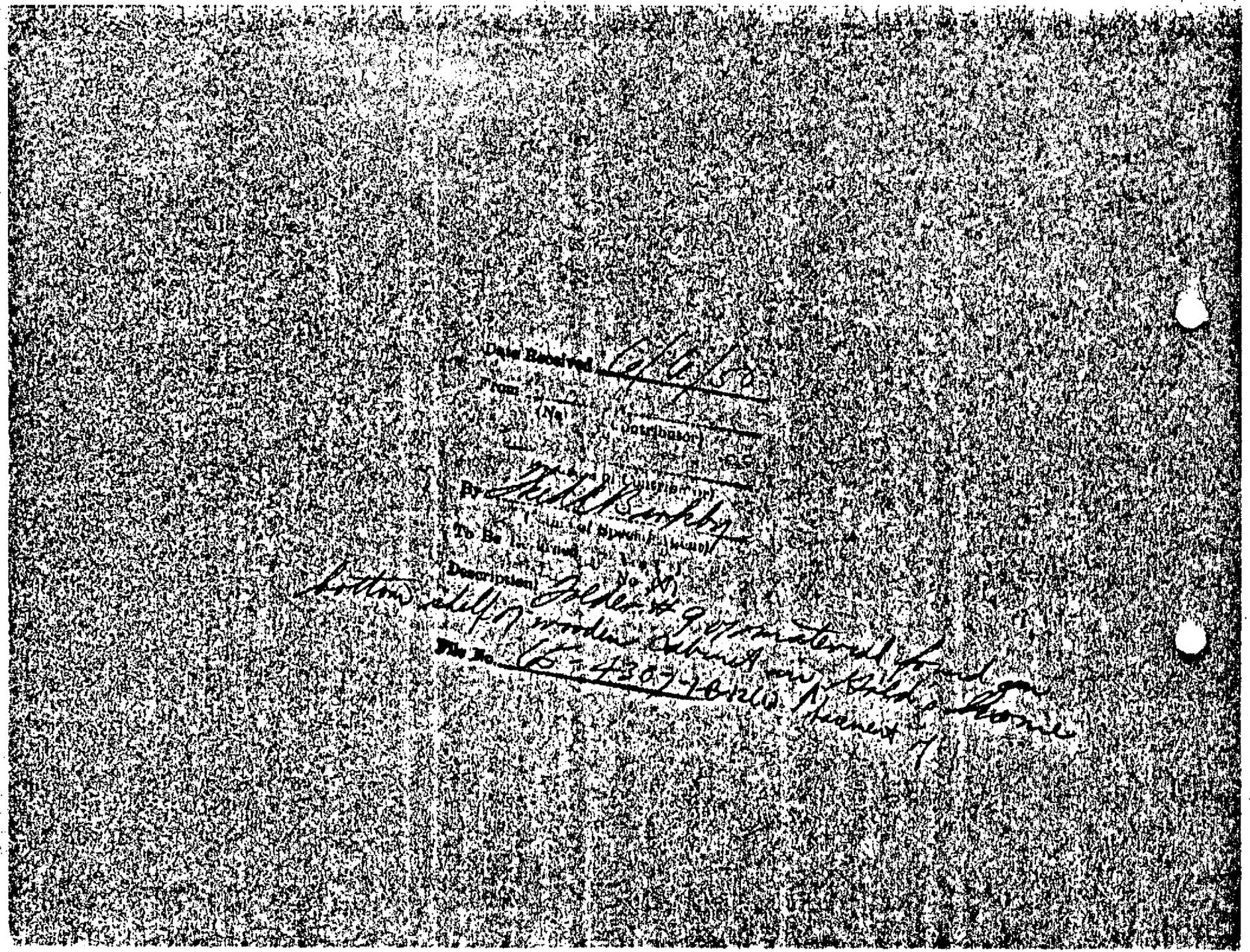
If you use this table, tear off this page and file only pages 1 and 2

TAX TABLE

FOR PERSONS WITH INCOMES UNDER $5,000 NOT COMPUTING TAX ON PAGE 2

Read down the shaded columns below until you find the line covering the total income you entered in Item 6, page 1. Then read across to the column headed by the number corresponding to the number of persons listed in Item 1, page 1. Enter the tax you find there in Item 7, page 1.

If total income is Item 6, page 1, is—		And the number of persons listed in Item 1, page 1, is—				If total income is Item 6, page 1, is—		And the number of persons listed in Item 1, page 1, is—								
At least	But less than	1	2	3	4 or more	At least	But less than	1	2	3	4	5	6	7	8	9 or more
		Your tax is—						Your tax is—								
$0	$550	$0	$0	$0	$0	$2,225	$2,250	$288	$193	$98	$3	$0	$0	$0	$0	$0
550	575	1	0	0	0	2,250	2,275	292	197	102	7	0	0	0	0	0
575	600	5	0	0	0	2,275	2,300	296	201	106	11	0	0	0	0	0
600	625	10	0	0	0	2,300	2,325	300	205	110	15	0	0	0	0	0
625	650	14	0	0	0	2,325	2,350	305	210	115	20	0	0	0	0	0
650	675	18	0	0	0	2,350	2,375	309	214	119	24	0	0	0	0	0
675	700	23	0	0	0	2,375	2,400	313	218	123	28	0	0	0	0	0
700	725	27	0	0	0	2,400	2,425	318	223	128	33	0	0	0	0	0
725	750	31	0	0	0	2,425	2,450	322	227	132	37	0	0	0	0	0
750	775	35	0	0	0	2,450	2,475	326	231	136	41	0	0	0	0	0
775	800	40	0	0	0	2,475	2,500	330	235	140	45	0	0	0	0	0
800	825	44	0	0	0	2,500	2,525	335	240	145	50	0	0	0	0	0
825	850	48	0	0	0	2,525	2,550	339	244	149	54	0	0	0	0	0
850	875	52	0	0	0	2,550	2,575	343	248	153	58	0	0	0	0	0
875	900	57	0	0	0	2,575	2,600	347	252	157	62	0	0	0	0	0
900	925	61	0	0	0	2,600	2,625	352	257	162	67	0	0	0	0	0
925	950	65	0	0	0	2,625	2,650	356	261	166	71	0	0	0	0	0
950	975	70	0	0	0	2,650	2,675	360	265	170	75	0	0	0	0	0
975	1,000	74	0	0	0	2,675	2,700	365	270	175	80	0	0	0	0	0
1,000	1,025	78	0	0	0	2,700	2,725	369	274	179	84	0	0	0	0	0
1,025	1,050	82	0	0	0	2,725	2,750	373	278	183	88	0	0	0	0	0
1,050	1,075	87	0	0	0	2,750	2,775	377	282	187	92	0	0	0	0	0
1,075	1,100	91	0	0	0	2,775	2,800	382	287	192	97	2	0	0	0	0
1,100	1,125	95	0	0	0	2,800	2,825	387	291	196	101	6	0	0	0	0
1,125	1,150	100	5	0	0	2,825	2,850	391	295	200	105	10	0	0	0	0
1,150	1,175	104	9	0	0	2,850	2,875	396	299	204	109	14	0	0	0	0
1,175	1,200	108	13	0	0	2,875	2,900	401	304	209	114	19	0	0	0	0
1,200	1,225	112	17	0	0	2,900	2,925	405	308	213	118	23	0	0	0	0
1,225	1,250	117	22	0	0	2,925	2,950	410	312	217	122	27	0	0	0	0
1,250	1,275	121	26	0	0	2,950	2,975	415	317	222	127	32	0	0	0	0
1,275	1,300	125	30	0	0	2,975	3,000	419	321	226	131	36	0	0	0	0
1,300	1,325	129	34	0	0	3,000	3,050	427	327	232	137	42	0	0	0	0
1,325	1,350	134	39	0	0	3,050	3,100	436	336	241	146	51	0	0	0	0
1,350	1,375	138	43	0	0	3,100	3,150	445	344	249	154	59	0	0	0	0
1,375	1,400	142	47	0	0	3,150	3,200	455	353	258	163	68	0	0	0	0
1,400	1,425	147	52	0	0	3,200	3,250	464	361	266	171	76	0	0	0	0
1,425	1,450	151	56	0	0	3,250	3,300	474	370	275	180	85	0	0	0	0
1,450	1,475	155	60	0	0	3,300	3,350	483	379	284	189	94	0	0	0	0
1,475	1,500	159	64	0	0	3,350	3,400	492	388	292	197	102	7	0	0	0
1,500	1,525	164	69	0	0	3,400	3,450	502	397	301	206	111	16	0	0	0
1,525	1,550	168	73	0	0	3,450	3,500	511	407	309	214	119	24	0	0	0
1,550	1,575	172	77	0	0	3,500	3,550	521	416	318	223	128	33	0	0	0
1,575	1,600	176	81	0	0	3,550	3,600	530	425	326	231	136	41	0	0	0
1,600	1,625	181	86	0	0	3,600	3,650	539	435	335	240	145	50	0	0	0
1,625	1,650	185	90	0	0	3,650	3,700	549	444	343	248	153	58	0	0	0
1,650	1,675	189	94	0	0	3,700	3,750	558	454	352	257	162	67	0	0	0
1,675	1,700	194	99	4	0	3,750	3,800	568	463	361	266	171	76	0	0	0
1,700	1,725	198	103	8	0	3,800	3,850	577	472	369	274	179	84	0	0	0
1,725	1,750	202	107	12	0	3,850	3,900	586	482	378	283	188	93	0	0	0
1,750	1,775	206	111	16	0	3,900	3,950	596	491	387	291	196	101	6	0	0
1,775	1,800	211	116	21	0	3,950	4,000	605	501	396	300	205	110	15	0	0
1,800	1,825	215	120	25	0	4,000	4,050	615	510	406	308	213	118	23	0	0
1,825	1,850	219	124	29	0	4,050	4,100	624	520	415	317	222	127	32	0	0
1,850	1,875	223	128	33	0	4,100	4,150	633	529	424	325	230	135	40	0	0
1,875	1,900	228	133	38	0	4,150	4,200	642	538	434	334	239	144	49	0	0
1,900	1,925	232	137	42	0	4,200	4,250	652	548	443	342	247	152	57	0	0
1,925	1,950	236	141	46	0	4,250	4,300	662	557	453	351	256	161	66	0	0
1,950	1,975	241	146	51	0	4,300	4,350	671	567	462	360	265	170	75	0	0
1,975	2,000	245	150	55	0	4,350	4,400	680	576	471	368	273	178	83	0	0
2,000	2,025	249	154	59	0	4,400	4,450	690	585	481	377	282	187	92	0	0
2,025	2,050	253	158	63	0	4,450	4,500	699	595	490	386	290	195	100	5	0
2,050	2,075	258	163	68	0	4,500	4,550	709	604	500	395	299	204	109	14	0
2,075	2,100	262	167	72	0	4,550	4,600	718	614	509	405	307	212	117	22	0
2,100	2,125	266	171	76	0	4,600	4,650	727	623	518	414	316	221	126	31	0
2,125	2,150	271	176	81	0	4,650	4,700	737	632	528	423	324	229	134	39	0
2,150	2,175	275	180	85	0	4,700	4,750	746	642	537	433	333	238	143	48	0
2,175	2,200	279	184	89	0	4,750	4,800	756	651	547	442	342	247	152	57	0
2,200	2,225	282	188	[illegible]	0	4,800	4,850	765	661	556	[illegible]	350	255	160	65	0
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	4,850	4,900	774	670	565	[illegible]	359	264	169	74	0
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	4,900	4,950	784	679	575	470	367	272	177	82	0
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	4,950	5,000	793	689	584	480	376	281	186	91	0



SAC, PHILADELPHIA

July 7, 1950

T. SCOTT MILLER, SA

HARRY GOLD, was.,
ESPIONAGE - R

65-4307-1B 12 (1) Folder No. 9

GOLD advised on June 24, 1950 that the material in this folder are notes and material in connection with a course given by Dr. CARL SCHMIDT, Professor in Pharmacology at the University of Pennsylvania Medical School. GOLD said that he took this course in the Fall of 1948 which was given by the Philadelphia Section of the American Chemical Society and paid $10.00 to take the course.

GOLD said he thought that he needed this course in connection with his position at the Philadelphia General Hospital.

The notes in this folder are in the handwriting of HARRY GOLD.

TSM:ELC
65-4307

6/6/50

CHEMOTHERAPY

(Specific treatment of diseases due to living organisms by chemical agents that are more toxic to the tissues of the invading organisms than to those of the host).

I. Anthelmintics (drugs used against parasitic worms).

A. Against intestinal parasites

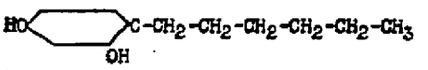
Natural (vegetable) products: Aspidium, pomegranate (pelletierine), chenopodium, santonin, thymol, fig latex (ficin).

Synthetic products:-

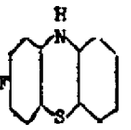
a. Carbon tetrachloride USP $C-Cl_4$

b. Tetrachlorethylene USP $Cl_2C:CCl_2$

c. Hexylresorcinol USP

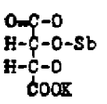


d. Phenothiazine NF

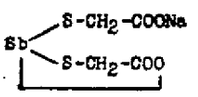


B. Against tissue parasites (leishmaniasis, filariasis etc.)

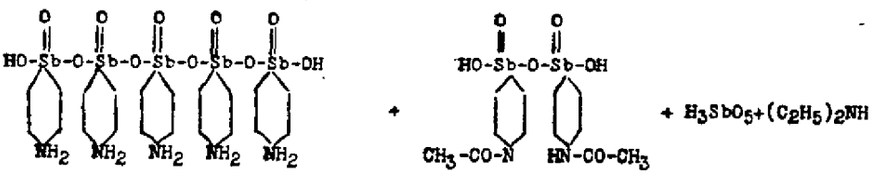
Antimony Potassium Tartrate USP
(Tartar emetic)



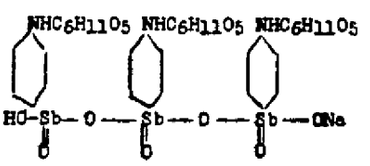
Antimony Sodium Thioglycollate USP



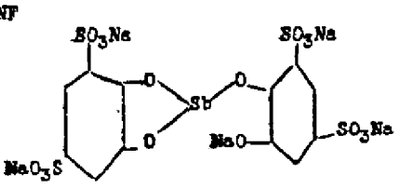
Ethylstibamine MNR
("Neostibosan")



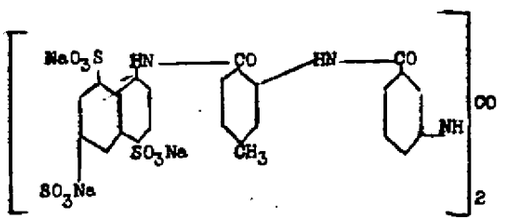
Stibamine Glucoside MNR
("Neostam")



Stibophen NF
("Fuadin")

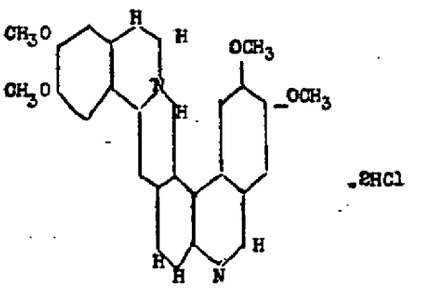


Suramin Sodium USP
(Bayer 205, Germanin, Naphuride)
$C_{51}H_{34}O_{23}S_6Na_6$

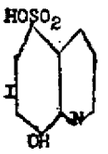


C. Against amebae

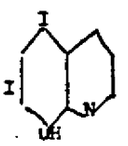
Emetine Hydrochloride
($(C_{29}H_{40}N_2O_4.2HCl)$) USP



Chiniofon USP
("Yatren")

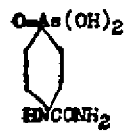


Diiodo-hydroxyquinoline NNR
("Diodoguin", "Yodoxin")

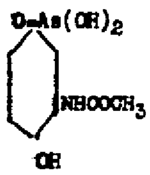


Iodochlorohydroxyquinoline NF

Carbarsone USP



Acetarsone NF
("Stovarsol")

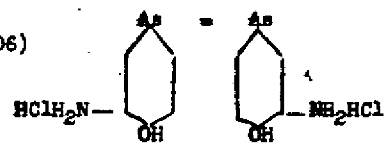


II. <u>Against Syphilis</u>

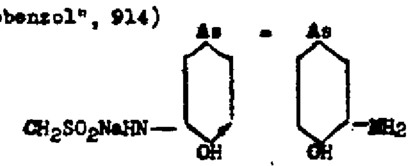
A. Preferred treatment at present is <u>Penicillin</u> (see Antibiotics under Bacterial Chemotherapy)

B. <u>Organic Arsenic Derivatives</u>

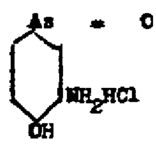
Arsphenamine USP
("Salvarsan", "Arsenobenzol", 606)



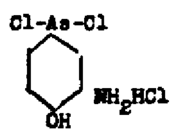
Neoarsphenamine USP
("Neosalvarsan", "novarsenobenzol", 914)



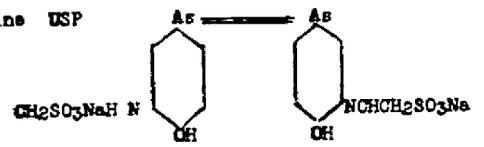
Oxyphenarsine Hydrochloride USP
("Mapharsen")



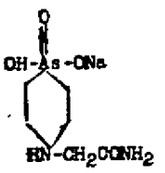
Dichlorophenarsine Hydrochloride USP
("Chlorarsen")



Sulfarsphenamine USP

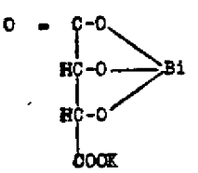


Tryparsamide USP

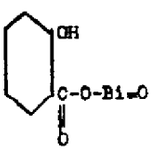


C. Bismuth Preparations

Bismuth Potassium Tartrate USP



Bismuth Subsalicylate USP



Iodobismuthite Sodium NNR
("Iodobismitol") Na_2BiI_5

Sobisminol Mass NNR

Bismuth Camphocarboxylate NNR

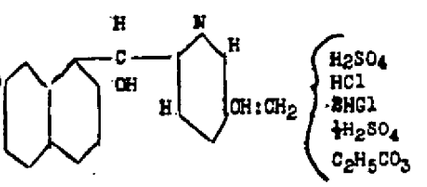
Bismuth Ethyloamphorate NNR

Bismuth Sodium Triglycollamate NNR

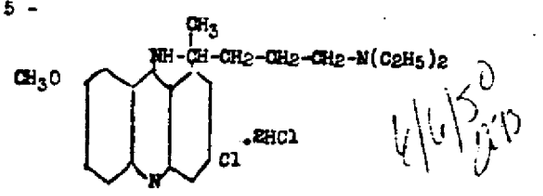
Quinine Bismuth Iodide NNR

III. Against Malaria

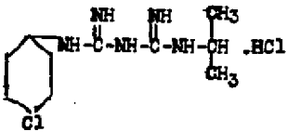
Quinine ($C_{20}H_{24}N_2O_2$) (Bisulfate; Hydrochloride; Dihydrochloride; Sulfate; Ethyl carbonate) USP



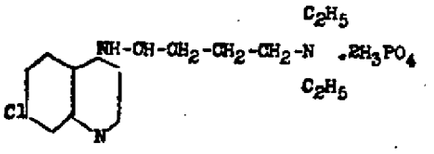
Quinacrine Hydrochloride USP
(Mepacrine, "Atabrine")



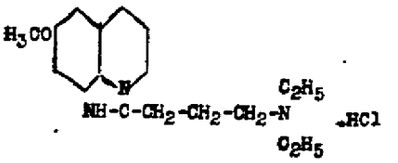
Chlorguanidine Hydrochloride NNR



Chloroquinine Diphosphate NNR
("Aralen", SN7618)



Pamaquin Naphthoate NF
("Plasmochin","Aminoquin")



IV. Against Bacteria

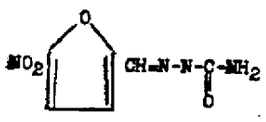
A. For local use (antiseptics, disinfectants, germicides)

1. Phenol, cresol, resorcinol, picric acid etc.
2. Alcohols (ethyl, isopropyl)
3. Aldehydes (formaldehyde and methenamine)
4. Acids (HCl, HNO_3, H_2SO_4. Particularly H_3BO_3, benzoic, salicylic, acetic and mandelic acids)
5. Halogens and halogen - containing compounds.
   Chlorinated lime, sodium hypochlorite, chloramine-T, dichloramine-T, chloroazodin ("azochloramid"), halazone, succinchlorimide. Iodine, iodoform, thymol iodide, iocamfen, vioform.
6. Oxidizing agents
   (Peroxides of hydrogen, sodium, calcium, zinc. Perborates. Permanganates. Chlorates.)
7. Heavy metals and derivatives.
   Inorganic mercuric chloride, oxide, cyanide, iodide.
   Organic - merourochrome, merthiolate, meroresin, metaphen, merphenyl.
   Silver, silver nitrate and picrate. Colloidal silver protein, chloride and iodide
   Zinc oxide, chloride, sulfate and stearate.
   Copper, copper sulfate.
8. Surface-active (detergent) agents
   Benzalkonium chloride USP ("Zephiran")
   Cetyl Pyridinium Chloride NNR ("Ceepryn")
   Benzethonium Chloride NNR ("Phemerol")

Hexylresorcinol USP
Sodiumtetradecyl sulfate NNR

9. Dyes
   Azo compounds
     Scarlet Red NF (Sudan IV)
     Dimazon, pyridium
   Acridine derivatives
     Acriflavine NF
     Dymixal NNR
     Proflavine NF
   Triphenylmethane (Rosaniline) Derivatives
     Methylrosaniline Chloride USP
     (Gentian violet, methyl violet, crystal violet)
     Carbolfuchsin NNR

10. Miscellaneous
    Sulfur and derivatives.
    Volatile oils, camphor and thymol; chlorbutanol.
    Nitrofurazone NNR
    ("Furacin")

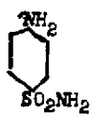


Tyrothricin (see Antibiotics)

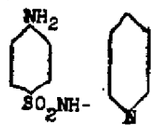
B. Antibacterial Agents Used Systemically

1. Sulfonamides

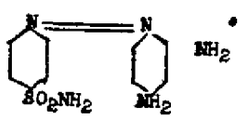
Sulfanilamide USP



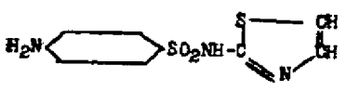
Sulfapyridine NF
("Dagenan", M and B693)



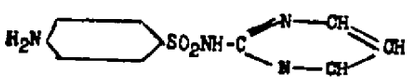
Prontosil NO
("Streptozon", "Rubiazol")



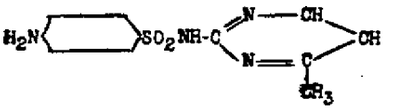
Sulfathiazole USP



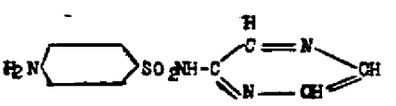
α—Sulfadiazine USP



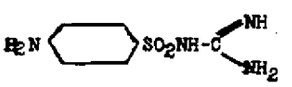
b Sulfamerazine USP



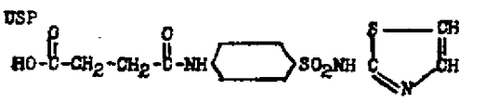
c Sulfapyrazine NNR



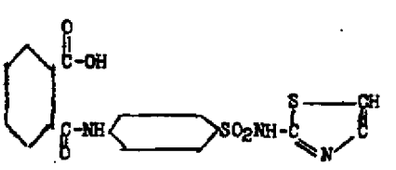
d Sulfaguanidine USP



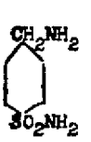
e Succinylsulfathiazole USP
("Sulfasuxidine")



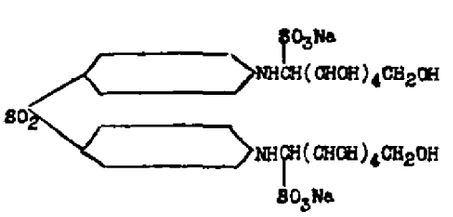
f Phthalylsulfathiazole NNR



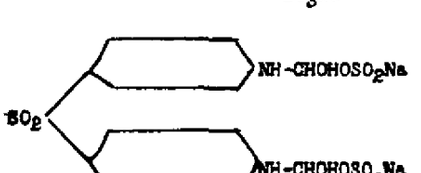
g Sulfamylan NO
("Marfanil")



h Promin NO



i Diasone NO

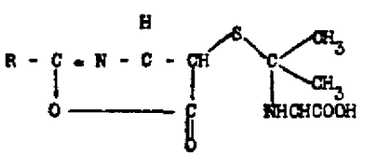


j Promizole NO

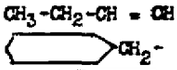
k Paraaminobenzoic acid NNR
("Paba")

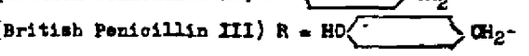
2. Antibiotics

Penicillin USP



In Penicillin F (British Penicillin I) R = $CH_3-CH_2-CH=CH-CH_2-$

In Penicillin G (British Penicillin II) R = 

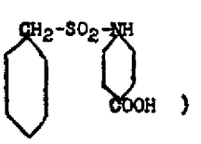
In Penicillin X (British Penicillin III) R = 

In Penicillin K (No British equivalent) R = $(C_6H_{13})CH_2-$

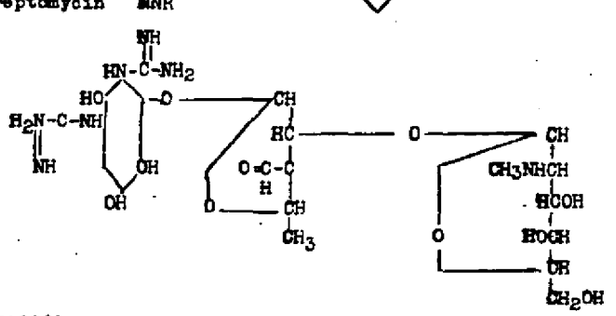
Used as Na or Ca salt

(To slow renal excretion of penicillin:

Caronamide ("Retentin") NO



Streptomycin MNR



Streptidine
$C_8H_{18}N_6O_4$

Streptose
$C_6H_{10}O_5$

Methylglucosamine
$C_7H_{15}NO_5$

Used as Sulfate or Hydrochloride

Tyrothricin MNR
(Mixture of polypeptids. Used locally only)

Bacitracin NO (Polypeptides)

Aureomycin NO
("Duomycin")

Chloromycetin NO

Aerosporin (Polymyxin) NO

THERAPEUTIC VALUE OF PRINCIPAL ANTIBIOTICS

Penicillin

Best agent vs:
Staphylococci
Streptococci (hemolytic and anaerobic)
Clostridia
Pneumococci
Meningococci
Gonococci
B. Anthracis
Spirochetes (syphilis, yaws)

Moderately effective vs:
Actinomycosis
Diphtheria
Strep. viridans (bact. endocard.)
Leptospidrosis
Psittacosis

Ineffective vs.
Viruses (all)
Gram neg. rods
Yeasts, molds
T-b., leprosy
Ulcerative colitis
Tularemia
Rheumatic fever
Malaria
Neoplasms

Toxicity:-
Lowest of all chemother. agents. Sensitivity reactions (skin rash, asthma, etc.). No serious results reported.

Bacitracin

Like penicillin in general, but early promise in syphilis not borne out (probably valueless here).
Effective vs.
Some penicillin-resistant strains. Also effective vs. amebiasis (value here uncertain)
Difficulties over quantity production and toxicity (damage to liver and kidney reported in animals and man)
These may or may not be due to impurities.
(wait and see)

Streptomycin

Best agent vs:
Tularemia
Miliary T-b
and T-b meningitis
E. Coli infections (urinary tract peritonitis, etc.)
H. Influensae infections (pneumonia, meningitis)

Moderately Effective vs.
Pulmonary and renal T-b.
Penicillin-resist. strep., staph.

Questionable vs.
Bacillary dysentery
Typhoid
Undulant fever
Chronic T-b

Ineffective vs.
Amebas.
Clostridia
Rickettsiae
Malaria
Ulc. colitis
Viruses
Spirochetes

Toxicity
Like penicillin; more serious:-
Injury to auditory nerve (may be persistent or even permanent).

Aureomycin (Duomycin)

Preliminary data indicates great value vs.
Lymphogram. venereum
Rocky Mt. fever
Undulant fever (acute and chronic)

Questionable vs.
Virus pneumonia
Typhoid fever

Toxicity
Only temporary anemia thus far reported.

Chloromycetin

Preliminary data indicates great value vs.
Rickettsiae (typhus, scrub typhus)
Typhoid
Rocky Mt. ~~spotted~~ fever.

Aerosporin (Polymyxin)

Preliminary data indicates great value vs.
Pertussis
Typhoid
Influensa
Colon infections

Ineffective vs.
T-b; but is said to be more effective than streptomycine vs. Gram neg. rods.

Toxicity
In animals considerably more toxic than streptomycin, but much more effective - ratio favorable to aerosporin.

Tyrothricin

Local use only (ineffective by mouth, dangerous by injection).
Value demonstrated vs.
Ulcers of skin
Mastoiditis
Empyema
Sinusitis
(Local bacitracin may be as good or better.

MAJOR ANTIBIOTIC AGENTS

	NAME	SOURCE	DATE	SPECTRUM	PRACTICAL VALUE
Bacteria	Pyocyanase	Ps. Aeruginosa	1899	Gram pos. and neg. cocci and rods	None (very toxic)
	Pyocyanin	Ps. Aeruginosa	1924	Mainly Gram pos.	None (very toxic)
	Tyrothricin	B.Brevis	1939	Gram pos. and neg.	++ (local use only)
	Gramicidin S	B.Brevis	1944	Gram pos. and neg.	? (local use only)
	Bacitracin	B.Subtilis	1943	Gram pos. and neg. cocci	++? (production troubles)
	Subtilin	B.Subtilis	1945	Gram pos. and neg. cocci, diph., t-b.	? (scanty information)
	Eumycin	B.Subtilis	1946	T-b, diph., fungi	? (local use only)
	Aerosporin (Polymyxin)	B.Aerospora (polymyxa)	1947	Gram neg. rods	++? (preliminary)
Molds And Fungi	Penicillic acid	Pen. Puberulum	1913	Gram pos. and neg. cocci and rods	None (no information)
	Penicillin	Pen. Notatum	1929	Gram pos. and neg. cocci rods, spiro.	++++ (unquestionable)
	Citrinin	Pen. Citrinum	1931	Non-selective	None (very toxic)
	Gliotoxin	Trich. Lignorum	1936	Gram pos. cocci, fungi	None (very toxic)
	Claviformin	Pen. Claviforme	1942	Probably identical, active vs. Gram pos. and neg. cocci, some fungi	None (toxic - may have some value for local use)
	Clavacin	Asper. Clavatus	1942		
	Patulin	Pen. Patulum	1942		
	Fumigacin	Asper. Fumigatus	1942	Mainly Gram pos.	None (toxic to liver)
	Aspergillic acid	Asper. Flavus	1943	Gram pos. cocci and rods	None (toxic)
	Flavicin	Asper. Flavus	1943	Similar or identical Activity like Penicillin	None (no information)
	Flavocidin	Asper. Flavus	1943		
	Gigantic acid	Asper. Giganteus	1943		
	Chaetomin	Chaet. Cochliodes	1944	Mainly Gram pos. cocci and rods	None (inactive in vivo)
Actinomycetes	Actinomycetin	Act. (unident.)	1924	Gram pos. and neg. cocci	None (toxic)
	Actinomycin	Act. Antibioticus	1940	Gram pos. cocci and rods	None (toxic)
	Streptothricin	Act. Lavendulae	1942	Mainly Gram neg. cocci and rods	? (local use only)
	Streptomycin	Act. Griseus	1944	Gram pos. and neg. cocci and rods, T-b.	+++ (toxicity?)
	Nocardin	Noc. Coeliaca	1948	T-b group	? (No information)
	Chloromycetin	Streptomyces—?	1947	Typhoid, typhus some viruses	+++ ? (preliminary)
	Aureomycin	Strep. Aureofaciens	1948	Lymphogran. brucellosis, virus pneumonia	+++? (preliminary)
	Actidione	Strep. Griseus	1948	Pathogenic yeasts	? (No information)
Others	Lysozyme	Animal cells	1922	- - - - - -	None (glycolytic enzyme)
	Chlorellin	Algae	1944	Gram pos. and neg. cocci and rods	None (No information)
	Canavalin	Jack beans	1944	Gram pos. and neg. cocci	None (No information)
	Allicin	Garlic	1944	Gram pos. and neg. cocci	None (No information)
	Tomatin	Tomato	1946	Pathogenic molds and fungi	None (No information)

REPRESENTATIVE DRUGS USED CHIEFLY FOR ACTIONS ON CENTRAL NERVOUS SYSTEM

(USP = U.S. Pharmacopoeia XIII; NF = National Formulary VIII; NNR = New and Nonofficial Remedies 1948; NO = Not Official)

I. Depressants of Nervous System

1. General (as opposed to Local) Surgical Anesthetics

A. Inhalation Anesthetics

Ether (diethyl oxide, $C_2H_5.O.C_2H_5$) USP

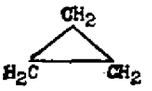
Vinyl Ether (divinyl oxide, CH_2: CH.O.CH:CH_2) USP

Chloroform (trichlormethane, $CHCl_3$) USP

Ethyl Chloride (monochlorethane, $CH_3.CH_2.Cl$) USP

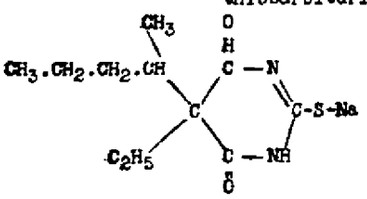
Nitrous Oxide (nitrogen monoxide, N_2O) USP

Ethylene (dimethylene, CH_2: CH_2) USP

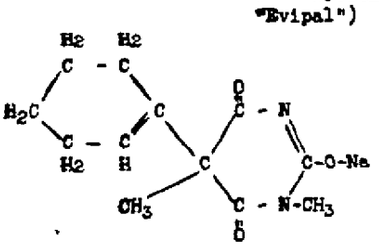
Cyclopropane (trimethylene, ) USP

B. Intravenous Anesthetics

Thiopental Sodium (Monosodium salt of 5-ethyl-5-(1-methylbutyl) thiobarbituric acid-"Pentothal") USP

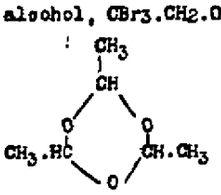


Hexobarbital Soluble (monosodium salt of 1,5 dimethyl-5 cyclohexenyl barbituric acid-"Evipal") NNR



C. Rectal Anesthetics

Tribromoethanol (tribromoethyl alcohol, $CBr_3.CH_2.OH$) USP

Paraldehyde (paracetaldehyde ) USP

9

11-29-48

(2)

Two main types of substances available for meas. clearance
(no reabsorption in tubules)

1. mannitol, inulin, creatinine, $Na_2S_2O_3$ ([illegible])

2. cleared completely by kidney (eliminated 100%) 4/11/50 [illegible]

{ p-aminohippuric acid
Diodrast (organic iodine cpd. contg. 51% Iodine)

→ 90-95% cleared.

anti diuretics — check secretion of H₂O in urine.
diuretics — ↑ " " " " "
some of
ethyl urea, xanthines & theophylline derivs & NaCl but
mostly are mercurials.

Specific Vasodilator (blood vessels)
1. CO_2 on brain & constricts blood vessels elsewhere in body.
2. possibly Khellin & Khellidin dilate coronary blood vessels more than they do elsewhere — relieve [illegible]
3. Cytochrome C (people would [illegible]) — but controlled tests failed to ↑ deficient blood flow in [illegible]
4. need vasodilators mostly in sclerosis of arteries.

Autonomic Pharmacology

chapter 3

1. Drug Characteristics (mimic accurately effects of [illegible])
2. amounts needed small (as small as $\frac{1}{1000}$ γ acetylcholine)
3. drugs display specific antagonisms
4. [illegible] problems parallel & intermix the problems of all pharmacology
also,
1. [illegible] of [illegible] in [illegible] — of [illegible]
2. [illegible] of [illegible]

(9

(U) 11-29-48

1 p.1 autonomic – regulate without any intervention
↳ opposite is voluntary or "somatic" nervous system

6/6/50 [illegible]

cranio – skull
sacral – lower part of spine

thoracic – lumbar
↳ exciting or [illegible]
[illegible]

both S + P$_{s}$ have ganglia at all [illegible] effects — [illegible] + [illegible].

Cannon – [illegible] ability to dilate blood vessels
[illegible] – [illegible]

Par 2

Sympathomimetic – coined by Sir Henry Dale + [illegible] [illegible] ([illegible])

[illegible] [illegible] really [illegible] sym. on S. – [illegible] S.m.S. [illegible]

[illegible] ⇌ parasym. [illegible] — [illegible]!

[illegible] [illegible]

(1) [illegible] does not [illegible] p.m.S.
[illegible] " " " Sym. on S.

→ [illegible]

(2) Sym. blocking agents – (? [illegible])
Parasym " " – atropine + [illegible]

(3) C.m.S. – [illegible]
P.S.m.S. – [illegible] closely related.

(4) [illegible] sufficiently similar to [illegible]

(5) [illegible] – [illegible] effects ( )

(6) How blocking agents are supposed to act ([illegible] a) [illegible]
antagonist [illegible] [illegible] receptor [illegible] agonist [illegible]
[illegible] receptor — [illegible]

C 9

(5) 11-29-47

P-5

Sk. [illegible] – [illegible]

eyeball – exophthalmic goiter ([illegible] goiter)

Dig. Glands

Secretion (of saliva)

Resp. tract

muscle (bronchial) S slightly < PS markedly >

Secretion (of fluid)
Constriction

Heart
as is

[illegible] heart – [illegible] involved [illegible]

Blood vessels
dilation [illegible]

* [illegible] all ready [illegible] to [illegible]

now to Sympathomimetic Drugs

(1) Schäfer & Oliver (at Oxford) – [illegible] in 18[illegible]
extracts
studied [illegible] adrenal glands – Study published in 1895
→ [illegible] action
of B.P.

(2) discovered in 1887 – Jap. chemist Nagai
from Chinese Source
[illegible] – [illegible] to [illegible]
Pharmacology [illegible]
[illegible]
ex. first
noted as true "mydriatic"

(3) Ephedrine – [illegible] of [illegible] – crude drug
So, could have had synthetic drug in place of natural drug
ago.
[illegible] [illegible]

(6) 11-[illegible]-48

Benzedrine – inferior to ephedrine in some respects

{ does not raise b.p. as markedly
{ does affect central nervous system more than ephedrine

→ but [illegible] good.

Tuamine – aliphatic
Naphazoline – histamine-like [illegible]
N.N.R. = non official

P3 (1) not potent
(2) N.D.
(3) Found naturally – formed by decarboxylation of tyrosine
→ thought for a while to be cause of essential hypertension
(4) not bought there
(5) according to recent reports is quite potent

OH groups → brief effects
(alkyl " ? → longer effects)

epinephrine – because of 2 OH rapidly oxidized in body
ephedrine – stable in body, less potent, & handled by diff enzyme systems than epinephrine

Uses of Sympathomimetic Drugs
1. greatest practical value – add to local anesthetic solution to delay its absorption into system – i.e., and vasoconstrictor effect to delay absorption into system & prolong effect — epinephrine the [illegible]

(9

6 11.29.48

v. Second use – to relax bronchial spasms (to relieve asthma) – Epinephrine will relax most bronchial spasms – except that after a while its effects become [illegible].

can [illegible] by mouth only as [illegible] – otherwise with [illegible]

Ephedrine – can take by mouth – but effects

trouble with both is that > heart beat & raises b.p.

So far have no drug which acts specifically on bronchial muscles & still have no bad effects & can take by mouth

3. decrease congestion of membranes of nose – Ephedrine.

too much in children (ephedrine in oil) → patchy pneumonia

[illegible] inhalation is [illegible]

use of Epinephrine inhalation may actually be due to decongestion similar to ephedrine inhalation ✓ in asthma

4. use effect on blood vessels in spinal anesthesia – to keep b.p. from falling too low.

ephedrine, neosynephrine, etc.

these

How drugs act

1. stimulate sympathetic [illegible] – but this is [illegible] for [illegible]

2. may alter fate of sympathin (destruction of) – not proved

3. most probably – drugs simply replace sympathin in combination with (unit) receptors

9

(8) 11-9-48

How Test Effects of these Drugs (Ephedrine, [illegible] ?)

1. Simplest (& best) — measure rise in B.P. of anesthetized animal or with ([illegible])

2. measure effect on isolated intestine → [illegible]
sympathetic — < intestinal activity

3. Effects on blood vessels - vasoconstriction
- inject drug into artery while ~~[illegible]~~ measuring plethysmograph vol.
→ measuring vol of arm or leg.

tachyphylaxis - loss of effect on > dose

[illegible] get fall

one of difficulties in testing these drugs.
How get around — keep doses down to minimum (& still get effect)
→ use intermittent injection - come in for short period.

4. Uterine muscle record (in vivo ?)
rat & cat - inhibited
rabbit - > ..

5. Bronchial muscle

6. Salivary gland of cat — very characteristic response in [illegible] of saliva.

next sympathetic blocking agents

11-22-49

2 Action of Drugs on Heart

Methods

1. Perfusion (one of oldest & best) – remove from animal's body (frog or ?) & continue to beat as perfused – use modified Ringer's Soln (balanced – isotonic NaCl in water + [illegible] KCl & [illegible] CaCl₂ (+ [illegible] buffer?))

[illegible] amount

2. Perfusion of mammalian Heart – used mainly for action of drugs on coronary artery – use Langendorf method

hydrostatic head = 50 mm Hg

use Heart of Rabbit, Guinea Pig, cat, dog

coronary blood flow

3. Heart Lung – method – [illegible] blood [illegible]

[illegible] 1, 2 & 3 [illegible] [illegible]

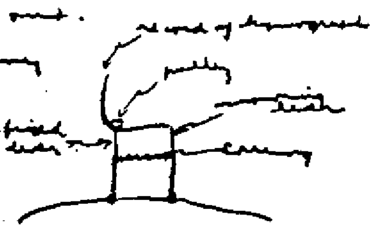
Semi - Quant method

1. EKG – [illegible] rate / type of heart beat / presence of block / [illegible] nature of contraction of muscle.

no info as to amount of blood put out.

Big advantage – no operation of any [illegible]

2. Myocardiograph – expose heart



3. Cardiometer – put heart inside glass or other rigid chamber

[illegible] to be [illegible]

C 9

11-22-48

4. Cut out papillary muscle – [illegible] in [illegible] ?
a [illegible] ?

→ most controllable of all of last four

5. [illegible] measurements of cardiac output

a – Fick principle – depends upon O_2 uptake of blood in passing through lungs.

[illegible]

Eg

O_2 uptake – 250 cc/min

(1) (in [illegible]) venous blood – 15 vol% O_2

(2) (in [illegible]) arterial " – 20 " " "

(3) a.v. diff = 5 " " "

So $\frac{0.250}{0.05}$ l/min = 5 l/min

i.e., need to collect arterial & venous blood

only serious problem – collection of mixed venous blood

a. [illegible] put needle in rt. [illegible] of heart & collect ([illegible])

b. now intracardiac catheterization

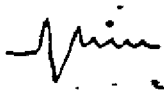
c. arterial blood – no real problem (composition of blood same in all arteries)

→ diff from venous blood

Last is method of choice

6. Ballistocardiograph – ideal from all standpoints except one — accuracy.

Flat bed (wood) on which patient lies – measure movement of bed ([illegible] or air transmission devices)



calibrate empirically ([illegible])

(3)

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6. [illegible] for [illegible] of normal [illegible] => formula ([illegible] for normal heart, but not abnormal [illegible])

any calibration method would

Disadvantage of Fick Principle is 10 min time required for assay.

D.C.G. is good because it measures each heart beat by itself — so good for very rapid & [illegible] drug methods.

7. Stewart (or Dye-Dilution) Principle — calc from color dilution (of arterial blood) — Has been used with dyestuffs & more recently NaCl (measure increased electrical conductivity)

8. Rosenthal – Kymograph (Temple U.) — [illegible] of movements of shadow of heart — measured [illegible] — very [illegible] method, very [illegible] & requires skilled [illegible]

9. Methods for measuring Cardiac Efficiency

Engineer method → amt of work done / amt of Energy

Energy used = O_2 used by heart muscle

(1) vol of cor. blood flow
(2) vol of A V Diff
& (1) × (2) = vol of blood flow

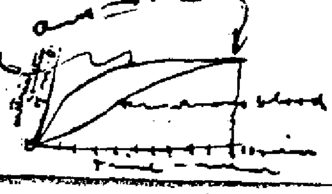
[illegible] recently [illegible] — now can measure in dogs & (in humans) in humans — made possible by introduction of catheter into coronary sinus (guided by fluoroscopic control)

For [illegible] measurement — Kety method

a. Pat inhales 15% nitrous oxide (too low for anesthesia)

b. [illegible] How much does taken up by heart muscle? ([illegible] solubility coeff of [illegible])

(in [illegible]) = 1.00 [illegible]



11-22-48

[illegible] to calculate $\frac{\text{No. O}}{\text{1 [illegible] time}}$ / A-V. diff

use integral AV diff

So can use in intact dog or man to measure mechanical efficiency of heart.

Results soon so far — can't control control period.

But action of drugs on Heart involves abnormal conditions

1. Digitalis has effect of nor. heart just opposite to that of diseased heart ⟶ decreases cardiac output, [illegible]

But for patients with heart disease (slow beats, decomp. etc) — a get increased output & easier breathing.

So that Dig. was studied before pharmacologists got hold of it.

2. Reason for "1" — Ernest Starling — great Eng. Physiologist.

— more the muscle is stretched the more blood is [illegible]
(within certain limits)
↳ at outside & [illegible] into ability to contract (like [illegible] rubber bands)

∴ Dig. shortens heart muscle to point where it is again efficient

in nor. heart go beyond limit.

3. What Dig. does
a. Increases output of failing (or decomp.) heart
b. Slows down heart rate
(1) > activity of cardio- [illegible] center
(2) nodular block bet auricles & ventricles
↓ [illegible]
greater than [illegible]

2. (c) auricular fibrillation — may be 400 to 600 or 1000 times/min — for auricular rate & then (some of them) get thru to ventricles & → rapid pulse beat ∴ pulse goes from 120 to 150 to 70 to 75, for ex. but the slowing is much less rapid & sometimes doesn't occur.

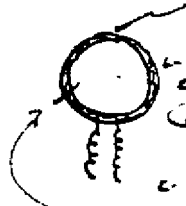
So, Dig most effective when
1. cardiac decompensation
+
2. auricular fibrillation

But Dig. does not remove auricular fibrillation but does make ventric. rate slower.

4. But Quinidine will alter auricular fibrillation
↳ and/or atebrine (recent)

50% of cases of auric fib. stopped by quinidine
(but use cautiously for already diseased heart as quinidine actually → depressant for heart muscle)

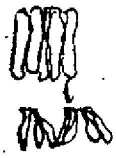
Explanation of How Quinidine & atebrine work in auric. fib.
↳ of Sir Thomas Lewis
↓ at least in this country



to block conduction of [illegible] but at [illegible] equally & [illegible] out.

[illegible] to set so-called circus movement
all started by refractory period of [illegible] [illegible] in heart muscle

So in Human Heart



again
1. block in muscle
2. refractory period is abnormally slow

11-22-47

6/4/50 [illegible]

[-1?] How do these drugs act on this phenomenon

1. Dig does not [illegible]
2. But Q prolongs refractory period & won't respond & fibrillation does not

---

[illegible]

Some Drugs which Notoriously ↑ Excitability of Heart muscle very markedly.

Ex. when Ventricles Fibrillate then get death (Fib. of Ventricle is irreversible & Fatal) — usual cause of death in electrocutions.

1. Chloroform (in low concen.) ↑ excitability of heart muscle & when get ↑ output then can get [pain, exercise, etc.] ventricular Fibrillation

Ex a. Tonsillectomy & removal adhesions on tonsil [by ?]
b. Packing of nose with adrenalin [get ↑ accelerated rate]
c. Same thing can happen under Benzol & also under cyclopropane anesthesia

---

[illegible] List page 2

A. 1. [illegible] & [illegible]

2. Xanthine drugs (Diuretics) — formerly used more than they are now
aminophylline used in coronary heart disease (acute coronary)
[illegible] aminophylline leads to lower O₂ content of blood. ↑ [illegible] coronary dilator may be all [illegible]

3. [illegible] — effects indistinguishable from those of Dig.

9

11-22-48

B / 1. use for extra systoles (extra beats) — [illegible] use in?

2. also [illegible] etc

3. Knott [illegible] heart muscle — [illegible] to stop ventricular fibrillation as desperate measure to stop ventric fibrillation

C 1. A-V block (auriculo-ventricular block)

2. ~~[illegible]~~ [illegible] muscle fibers themselves

(not on sheets) . [illegible] tendency now

For Congestive Heart Failure (because of [illegible] too little [illegible])

use organic mercurial to produce a profuse diuresis [illegible] — lose [illegible] fluid to account for extra work of heart muscle.

Congestive Heart Failure — too much fluid for heart to handle

D - ~~Pituitary Extract~~ produce strong constriction of coronary artery.

[illegible] 1. [illegible] pituitary [illegible] — [illegible] effect (e.g., as in contraction of uterus after child-birth to stop hemorrhage)

[illegible] idea is [illegible] for the [illegible] is.

2. Dilatation of heart muscle — Nitrites etc.

[illegible] (coronaries)

[illegible] (ethyl [illegible] formulae)

papaverine — opium alkaloid

[illegible] — [illegible] etc

all of above - [illegible] blood vessels [illegible] whole, [illegible] dilate coronaries

[illegible] principle — Drugs which dilate blood vessels [illegible] are [illegible] because of their [illegible] effect. giving rise to other side of [illegible].

C 9

(2)

11-22-47

Ex nitroglycerine – dilatory coronary arteries was only a small effect of > [illegible] of [illegible].

6/10/50 [illegible]

Action of Drugs on Peripheral circulation

[illegible] – Vol of blood [illegible] tends to keep at level only [illegible] Tonus of [illegible] is maintained – i.e. keep [illegible] [illegible] [illegible] level

otherwise get anoxia – for brain

For Heart – coronary insufficiency → angina pectoris [illegible] from heart to [illegible]

For coronary occlusion – Heart muscle will degenerate & get infarction.

For skeletal muscle – can get bad enough in legs to get gangrene.

For Kidney – recent evidence – when blood supply is insuff get substances produced which [illegible] & maintain hi b.p.

Treatment procedure

1. > blood supply – attention to patient & physician has only limited therapeutic value.

Difficulty – vasodilator drugs act too profoundly.

Only epinephrine ([illegible]) are constrictors elsewhere & dilator to coronaries.

note (sclerosis – organic ~~[illegible]~~ hardening of blood vessels) attributed to →

Methods for measuring Vol of blood flowing thru individual. Tissues of all part of body – to find out how output is distributed.

1. In animals a most direct way, put in some sort of flowmeter & pass blood thru & then back to body.

usual dilemma – precision of meas. vs. departure from normals

[illegible] – R. [illegible] [illegible] for diff t°

2. Thermocouples

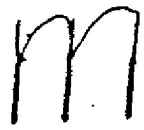
[illegible] – [illegible] flow & t° <. [illegible] heat gradient bet skin & blood. [illegible] > blood t° [illegible] ([illegible] skin is [illegible])

(9) 11-22-48

But must measure in const. Temp Room & activity of subject
{not chiromotors' neurocalometer}

6/6/50

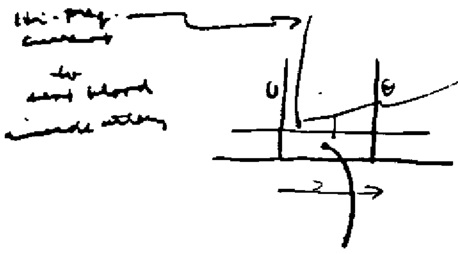
Thermopile / no. of junctions



Can use only for direction of extent of

2. Variation on "1"

Thermothermocouple 'Rhine' in Germany
→ only doesn't really do what it should



a (1) warmer than (2) & at warmer than thermocouple

Difficulty here - could not control Hi freq. current + other difficulties.

Rhine say can't use in building with steel framework - need wood.

3. Mayo Clinic - use Heating Heater to heat blood directly.

But all of "1" & "2" give same conclusion - diff in t° at two junctions depends on many ~~junctions~~ conditions; think diff = 'blood t°'

perm. method → methods in use to calibrate thermothermocouple.

Form 101

PHILADELPHIA GENERAL HOSPITAL

HEART STATION

Name_____ Dept._____ Date_____ No._____

Last Name First

(7)

(6) 11/15/90 12-15-47

p. 5 — a-4 [illegible] — can actually cure malaria — but can be toxic — so not yet released.

CCFU — work on [illegible] (not [illegible])

also Rhesus monkeys (closest type of malaria to that of man)

ultimate exp. on man (fed. pen. at Joliet, Ill.)

really definitive exp. — perfect & complete control.

actually value of this work during war did not relate [illegible] to malaria as to that of [illegible] finding of [illegible] systems)

2nd Hr. p. 5

VI. Bacteria

Pasteur — nearly [illegible] by French [illegible].

1st [illegible] of

antiseptic era of surgery ("[illegible]")
[illegible] of D. Hayes [illegible] — [illegible] of phenol — [illegible]
[illegible].

now

aseptic era — masks, [illegible] etc. [illegible] sterilized etc.
so [illegible] infection of wounds [illegible] — healing by 1st [illegible]

4. H_2O_2 [illegible]
[illegible] food
[illegible] — local applications

5. NaOCl — [illegible] of W.W. I.
[illegible] — [illegible] of water [illegible]
I_2 — used too strong — dilute tinct. [illegible].

6. [illegible] — used for [illegible] infections

8. Surface active agents

9. [illegible] — [illegible] of W.W. I [illegible] out.

11 miscellaneous

12-13-48.

p. 6

B Systemic A A agents
(some of most brilliant chapters)

Testing of all Drugs (systematically) produced at German Dye Works.

Fourneau's paper at Dusseldorf
Results on Streptozon (now called Prontosil — and others)
Treat Elliot Roosevelt's [illegible]

Deutsche med. Woch. Feb. 1935 (Hundreds of patients)
Really tried first on patients

Sulfanilamide - excreted in urine - [illegible] really [illegible] important

French Work

still one of most valuable but
[illegible] methemoglobin (cyanosis) in [illegible]
and doesn't [illegible] liver.

Sulfapyridine
Whitby & Baker (British [illegible]) - 1st effective chemotherapeutic agent in pneumonia - but [illegible] vomiting - now discarded!!

Sulfathiazole - [illegible] spectrum of usefulness
but is also one of most toxic
[illegible]

B. 1

a b, & c.

Sulfa - [illegible]

1. [illegible] of maintaining steady blood [illegible]
2. [illegible] for determining sulfa [illegible] in blood [illegible]

9

(6)

12-13-48

d
e } not abs. in intest. tract.
f } better than d in this respect.

g not antagonized by p.a.b. acid
while a, b, c are ∴ most useful in [illegible] for
infected wound!

a b c used in t.b. & in [illegible], particularly g.
& f

activity in sulfonamides etc was finished for
Fleming & (Florey) had difficulty in convincing
[illegible] manufacturers.

Now [illegible] back to S. & [illegible] & develop both
S & antibiotics.

1. [illegible]
2. [illegible]

Sulfonamides (peculiarities & [illegible])

1. When used in human medicine they are bacteriostatic & not bactericidal & not bacteriophidal
(in [illegible] in which can be used)

2. "Log phase" in their action. bacteriostatic action not exerted immediately.

3. compete with bacteria for some essential metabolite which is necessary for the proliferation of the bacteria
with enzyme system in the bacteria
[illegible] p.a.b. acid
Explanation of log phase.
Similar forms of explanation - not really so, [illegible] see on dehydrog. enzyme system.
[illegible] - act by competitive inhibition.

C 9

①

12-20-48

6/6/50 [illegible]

antibiotic – anti(microbial agent) (anti)
– bio (biological origin)

[illegible]

1. extreme potency
2. hi-specificity
3. extremely low [illegible]specificity

development (& history) of antibiotics

1. [illegible] [illegible] interested
2. [illegible] to situation where [illegible] lucky accident occurs
3. [illegible] for [illegible] in nature : [illegible].

Pasteur – How come organisms do not grow (with [illegible] rate of propagation)

1. anthrax bacilli in soil disappear in few weeks
2. [illegible] something in air [illegible] which destroy pathogenic organisms

1899 – [illegible] & (Loew?)
bacillus Pyocyaneus secrete [illegible] which is toxic to ?

1928 – Fleming's Famous Contamination
↳ ([illegible] [illegible] [illegible] of [illegible])

med. officer in W.W.I. – heavy [illegible] losses due to infected wounds
[illegible] of [illegible] almost [illegible]

1930 – [illegible] produced by leucocytes
Lysozyme – product of animal cells
↳ proteolytic enzyme

1928 – [illegible] [illegible] of
↳ clear space on petri dish culture contam by air borne mold
to cultivated [illegible] mold → penicillin notatum
yellow extract
[illegible] in England
one of few that → [illegible] toxic substance

but no [illegible] sulfonamides → 1000s

but Fleming [illegible] [illegible]
1. found out that penicillin killed [illegible] in [illegible] but not influenza bacillus
to [illegible] to sep. i.b. from [illegible] [illegible]

C 9

©

Guest (Sir) Howard Florey (new Zealander) 12-20-48

1. War coming
2. Tried (Ehrlich, [illegible]) [illegible] & finally penicillin
3. Got [illegible] (Fleming [illegible])
4. 1st patient – member of Oxford Police Force – fell off bike
   [illegible] penicillin – got febrile reaction (pyrogens)
   [illegible] from urine – no longer toxic
   [illegible] & purified by [illegible] Oxford Police Force.
5. July 1941 A.N. Richards U of P. chairman of med research of O.S.R.D.
   Florey [illegible] for R.
   1. decided on [illegible]
   2. [illegible] discovered (in Peoria) that [illegible] liquor [illegible] 10 x yield
   3. called in manufacturers (Abbott, [illegible], [illegible], Pfizer)
6. also discovered P ([illegible]) on [illegible] (or irradiation)
7. Penicillin has been produced synthetically (by [illegible])
   [illegible] in synthesis still [illegible]
   consequent efforts unsuccessful
8. [illegible] still grown on synthetic culture media under aseptic conditions – [illegible].
   [illegible]
   [illegible] off solvent by distillation & freezing
   most penicillin now produced in Penicillin G.
   = benzyl penicillin
   (most effective in syphilis

Superior of [illegible] sulfonamides?
1. superiority [illegible] is bactericidal & not merely bacteriostatic
2. Toxicity of P is much lower than that of sulfonamides
3. none of toxicity reactions of P are very severe – unpleasant but not dangerous
4. broader spectrum of activity – closest approach in
   effective streptococcus
   gonococcus
   etc.
5. acts more rapidly – no lag phase
6. not rendered inactive by presence of pus & tissue exudates

⑥

12-20-48

4/6/50 MB

Disadvantages

1. changing [illegible] culture method of [illegible]
2. Difficult to store & [illegible] well
3. Doesn't work as well by mouth — absorbed as rapidly as is excreted by kidney
   ↳ acid destroy
4. [illegible] system [illegible] & is destroyed by penicillinase
5. produces local irritation (i.e., added procaine)
   ↳ [illegible], etc.

6. Retention — Caronamide → competes with P for renal excretion mechanism —

Inherent Disadvantages

7. People are developing sensitivities (rash, asthma
8. Bacteria may become resistant
   [illegible] in course of time { population become sensitive / bacteria become resistant

9. Useless against ~~[illegible]~~ dangerous organisms
   a. Gram neg. Rods of Typhoid bacillus
   b. Influenza Bacillus
   c. acid fast organisms (?) — Tubercular bacillus & Leper bacillus

Techniques for [illegible]

1. Paper chromatography
2. Craig's [illegible]-current [illegible].
3. growth of [illegible] mycology
   ↳ Selman Waksman at Rutgers
   → (1944) Streptomycin

Discovered as result of patient & painstaking search.

[illegible] — and Substance

Streptomycin — basic substance — [illegible] as HCl or Sulfate

and only to Penicillin.

[illegible] of S — acts on Typhoid colon Rods (Tubercular bacillus, Leper bacillus, Influenza)

(4) 12-20-48

4/4/51
gib

- retained better than P
  & used as blocking agent

vs. Strepto

1. Toxicity much like penicillin
   plus action on auditory nerve → { equilibration apparatus / auditory " / permanent in animals }

2. development of resistant bacterial strains

   meningococci { → strepto & all sulfonamides → (and S) / inject → (sulfonamides) a → S / → cured (Toxic) }

   Cures tubercle bacilli infection
   (but must give continuously at first)
   but resistance to tubercle bacilli is temporary
   (wait 4 or 5 weeks & give again)
   → limited to acute tuberculosis
   (galloping)

   1st effective remedy for { tuberculosis meningitis / [illegible] }

2nd Hr

Bacitracin (named after the little girl named Tracy) (from whom)

discovered by Frank Meleney (surgeon of N.Y.) (Presbyterian Hosp.)
searched for antibiotic that would do for heavily infected wounds what maggots did for the osteomyelitis
initially grown in culture which used in T.
synthesis (mechanism) of bacitracin similar to that of Strepto

- spore forming rod
- Has wider spectrum (includes gram negative bacilli)
- Not inhibited by penicillinase
- Not effective in depth & [illegible]

(5)

10-21-48

4/6/50 [illegible]

Excreted much less slowly than P
more stable in solution & solid form than P

Disadvan.
1. lge doses → albuminuria (kidney injury)
   & [illegible] also → liver injury
2. If persist in giving drug albumin may disappear.
3. Q quantity Prodn.
   (Reluctance of manufs.)
   → big investment
   C.S.C. are going in
4. Rockefeller Instit (have identified several chemical components. Merck)

Effective
1. Penicillin resistant strains
2. vs. amoebic dysentery
3. Real place in local treat. of infections
   { Wounds
   { oral places (mouth)

Substances in Part III.
1. aureomycin (Duomycin) - see chart
2. chloromycetin (Recently in Life mag)
   see chart
3. aerosporin (Polymyxin)
   (Brit) (American)
   w. [illegible] appeared 3 days apart - Done independently
   Have done more work.
   pertussis - whooping cough
   Great Treatment
   toxicity > strepto but need lower dose
4. Tyrothricin - Fairly old - 1939 - Used only locally on infected wounds
   Too toxic otherwise

(6) 12-20-48

[illegible] (wide open fields for)
agents that can be used locally as well as systemically.

need
1. effective
2. nontoxic
3. kind of desired activity
4. can be produced in quantity, practically

crazy not at all hopeful about synthesis of the actual ingredients
other
chemists – really 3 diff [illegible] of [illegible]
known previously

wide open fields
1. Virus diseases – aureomycin effective vs. Virus Pneumonia.

2. use to control infections in animals & plants

3. possibility of therapy of this type in neoplastic disease (cancer)
→ undesired cells
really off in future.
but something favorable in long outcome.

omitted type areas
1. Insecticides – Rodenticides
2. poisonings
3. Biochemical background of drug actions.

Task of testing drugs is usually more difficult than that of producing them
also for task of explaining what they do.

Trends
1. Biochemical basis of Drug Actions
a. [illegible] pharmacological action
particularly on some basis other than trial & error
up till recently unsuccessful
in attempt on

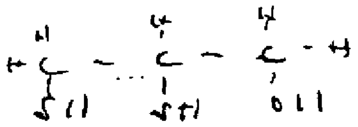
6/6/50 [illegible]

12-20-47

BAL (British anti Lewisite) → contains As

4|6|50
820

dimercaptopropanol



built by Peters & colleagues at Oxford

SH combines with glutathione which is vulnerable

could be opening of new era - calling shot beforehand & having it come true

used for Cd & Pb poisoning as well & brilliantly as As.

∴ if can find out more about other cell mechanisms than we now know, then we could lead to work effectively

---

cf Results on enzyme systems involved in action of malaria on cells
& parasites.

Like all pure science -
∴ can't tell what will happen (Results unpredictable)
∴ dividends can be very high.

---

clinical pharmacology
methods for quant. study of drug action in man.

great financial support
U.S. P.H.S.
Rockefeller
Army
Private patient out front door & we prize

1. cardiac output
2. blood vol.
3. rate of oxygen satn.
4. cerebral blood flow
5. renal " " in kidney disease

many methods developed during war & are now in use here.

for Dempsey - push nutrition Research

18 Res.
10 tech.
2 [illegible]
[illegible]) & clinicians

(7)

10-20-48

6/6/50

Rural [illegible] - setting up objectives & appraising results.

Screening of new [illegible]

[illegible] of activity between chemist & biologists

Better done in industr. labs - better done than in [illegible] work in [illegible] labs.

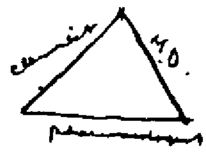
major problem is that of personnel.

Formerly - Toxicity Studies (industrial)

[illegible] NH

[illegible]

Lebanon (Schmidt's Home Town) - [illegible] NH



equilateral Δ

Excellent example of pooling of resources.

next [illegible] see expansion of effort (& financial [illegible])

[illegible]

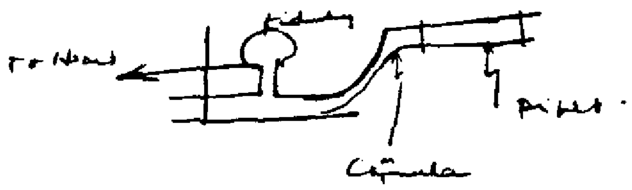
①

11-29-48

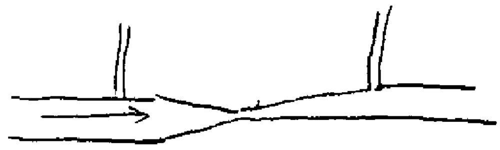
Methods for blood flow (all [illegible])

1. [illegible] Stromuhr (for measuring venous flow)

4/11/50 [illegible]



2. Venturi [illegible]

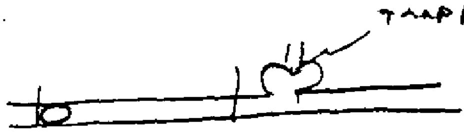


also, will do [illegible]

3. Rotameter — do not account for high viscosity factor

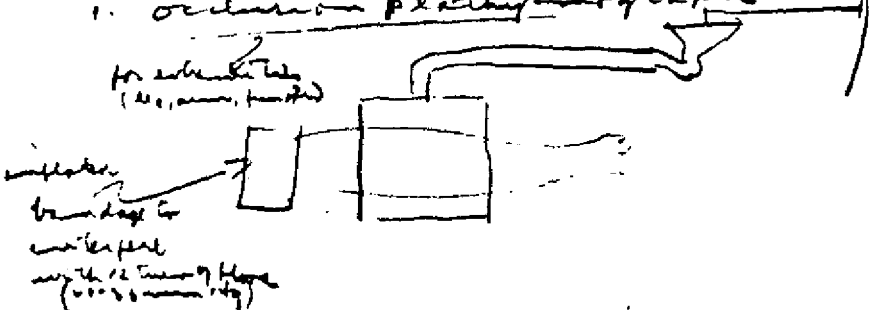
4. Orifice plate meter

5. Bubble flow meter — at least some low viscosity factor



Methods for man, [illegible], and [illegible]

1. occlusion plethysmograph

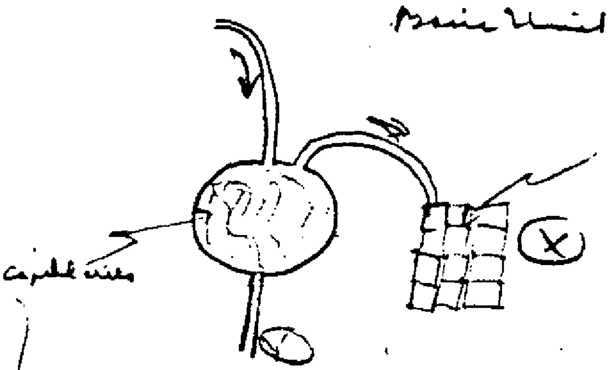


2. Kety's method — N_2O mixed venous blood.

used successfully so far for only brain & heart — [illegible] of circulation.

3. Clearance methods (2) (for Kidney) 11·29·47

Basic Unit of Kidney Function



→ dialysis (into glomerular space) protein free filtrate

output 100 - 120 cc /min of glomerular filtrate

all but 1 to 2 cc /min is reabsorbed

↓

finished urine (av. rate)

Secretion in urine (Y)

Reabsorption in blood stream (X)

Ex glucose normally reabsorbed

creatinine excreted in urine 100%

no of basic units - 2,000,000 in normal kidney

ie, now clearance method

conc. in blood × vol of blood

= conc in urine × vol of urine

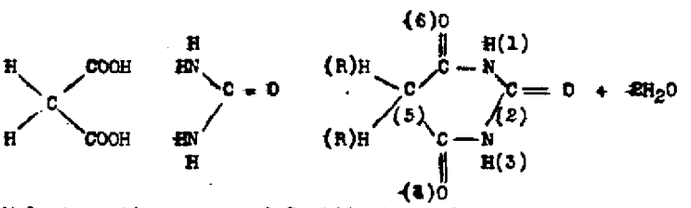
vol of blood = only unknown factor

$$C = \frac{U(\text{urine conc}) \times V(\text{urine vol})}{P(\text{conc in blood})} = \frac{UV}{P}$$

→ really P for Plasma

D. Simple Sedatives (to be taken by mouth to combat insomnia and restlessness not associated with severe pain)

1. Derivatives of Barbituric Acid



Malonic acid + urea ⟶ Barbituric acid

Hundreds of derivatives have been made and tested: 4 are in USP, 13 in NNR. Most important difference among these is in duration of action:

Long acting (more than 8 hours)

Barbital (diethyl barbituric acid-"Veronal")	USP
Phenobarbital (phenyl-ethyl barb. acid-"Luminal")	USP
Alurate (allylisopropyl " ")	NNR

Intermediate (6-8 hours) NNR

Amytal (isoamyl-ethyl " ")	NNR
Neonal (n-butyl-ethyl " ")	NNR
Dial (allyl-allyl " ")	NNR
Ipral (isopropyl ethyl " ")	NNR
Nostal (B-bromallyl isopropyl " ")	NNR
Sandoptal (allyl-isobutyl " ")	NNR

Short (4-6 hours)

Pentobarbital (metylbutyl ethyl barb. acid) ("Nembutal")	USP
Phanodorn (cyclohexenyl-ethyl " ")	NNR
Ortal (n-hexyl ethyl " ")	NNR
Seconal (allyl-methylbutyl " ")	NNR
Vinbarbital (methylbutenyl-ethyl " ")	NNR

Ultra-short (less than 1 hour)

Thiopental ("Pentothal" - see above)	USP
Hexobarbital ("Evipal" - see above)	NNR

2. Derivatives of Ethyl Alcohol

Alcohol (C_2H_5OH)	USP
Diluted alcohol (about 49% C_2H_5OH)	USP
Spiritus Frumenti (whiskey-about 50% C_2H_5OH)	NF
Spiritus Vini Vitis (Brandy " " ")	NF
Tribromoethanol ($CBr_3.CH_2OH$ - see above)	USP
Chloral Hydrate (Trichloracetaldehyde, $Cl_3C.CH(OH)_2$)	USP
Chlorobutanol (Trichlortertiary butanol-"chloretone") $Cl_3C.C(CH_3)_2.OH$	USP
Paraldehyde (paracetaldehyde-see above)	USP
Chloralose (chloral + glucose)	NO

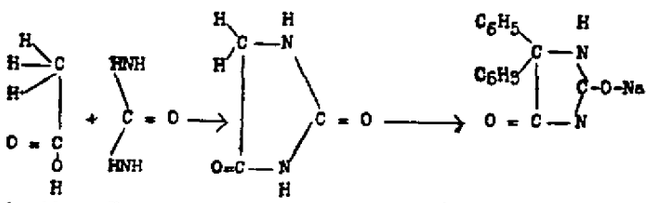
3. Sulfones, urethanes, carbamides - seldom used now.

E. Anticonvulsants

General anesthetics in anesthetic concentration

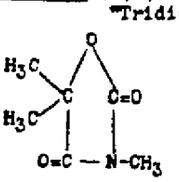
Barbiturates (especially phenobarbital for chronic use, thiopental for acute emergency)

Bromides (Na, K, NH_4, Ca)	USP
Diphenyl hydantoin sodium	USP



Acetic Acid — Urea — Hydantoin — ("Dilantin," Phenytoin).

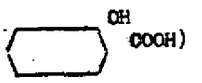
Trimethadione (3,5,5-trimethyloxazolidine-2,4-dione-"Tridione")	NNR

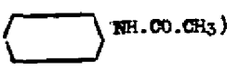


F. Analgesics

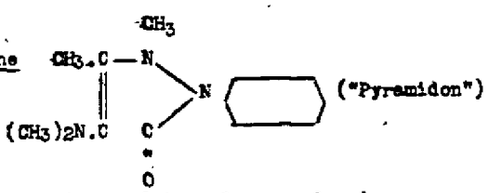
1. With effects on cerebral and smooth muscle functions - morphine, codeine, etc. USP

2. With antipyretic effects

Derivatives of salicylic acid (O-hydroxy benzoic acid,  USP

Acetanilid (acetylaniline,  USP

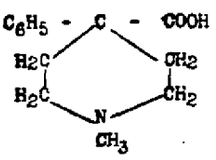
Acetophenetidine,  USP

Aminopyrine  ("Pyramidon") USP

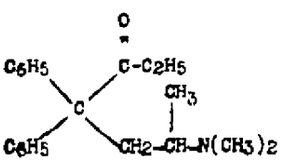
(Dimethylamino dimethyl benzyl pyrazolone)

3. With antispasmodic (atropine-like) effects

Meperidine (1-methyl-4-phenyl-piperidine-4-carboxylic acid. Isonipecaine, pethidine, "Demerol", "Dolantin") NNR



"Amidone" (1,1-diphenyl-1-(dimethylaminoisapropyl)-butanone-2) "Methadon" NO



G. Miscellaneous central nervous depressants

Scopolamine Hydrobromide USP

Apomorphine Hydrochloride USP

Bulbocapnine NO

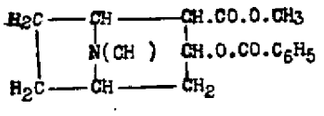
Magnesium salts (only when injected)

Cannabis (Marihuana, Hashish)

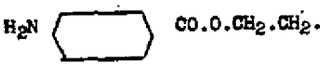
DRUGS USED MAINLY FOR THEIR EFFECTS ON THE PERIPHERAL NERVOUS SYSTEM

A. Local anesthetics

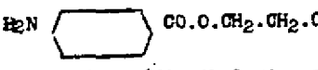
Cocaine (benzoyl methylecgonine) USP



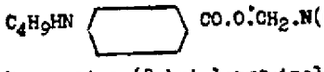
Procaine (diethylamino-ethyl ester of para-aminobenzoic acid) USP
("Novacaine")



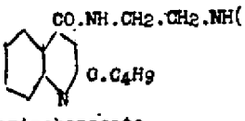
Butacaine (dibutyl aminopropyl ester of para-aminobenzoic acid) USP
("Butyn")



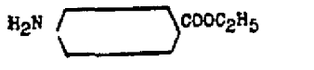
Tetracaine (dimethylamino-ester of butylpara-aminobenzoic acid) USP
("Pontocaine")



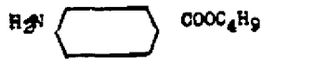
Nupercaine (2-butyloxycinoline carboxylic acid-diethyl- MNR
ethylenediamidiamide)



Ethylaminobenzoate USP
("Benzocaine")



Butylaminobenzoate USP
("Butesin")



B. Specific neuromyal blocking agents

Curare and derivatives NO
("intocostrin", curarine, d-tubocurarine)

Erythrina derivatives (B-erythroidine) — NO

Quinine methochloride and ethochloride — NO
Large doses of choline, acetylcholine, nicotine and strychnine.

Quarternary alkyl derivatives of NH_4 — NO

II. Stimulants of Nervous System

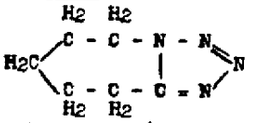
1. Convulsants (analeptics)

Strychnine — USP

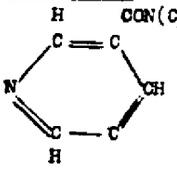
Caffeine and congeners — USP

Picrotoxin ($C_{30}H_{34}O_{13}$) — USP

Metrazol (pentamethylene tetrazole - "Cardiazol", Leptazol) — NNR



Nikethamide (diethyl nicotimamide, "Coramine") — NNR



Lobeline (alpha lobeline) — NO

2. Antiourarizing agents

Physostigmine (Eserine) — USP

Neostigmine ("Prostigmine") — USP

REPRESENTATIVE DRUGS AFFECTING CIRCULATION

I. Drugs acting predominantly on the nerve mechanisms that control the circulation.

A. In the Central Nervous System

1. Centers regulating heart rate.

Cardioaccelerator center stimulation - only as part of generalized stimulation of centers controlling sympathetic nervous activity by convulsant (analeptic) drugs. None used primarily for central cardioaccelerator stimulation.

Cardioaccelerator center depression - only as part of generalized depression of these centers by narcotic drugs. None used primarily for this purpose.

Cardioinhibitory center stimulation - important effect of digitalis group and veratrum alkaloids (see below); action due largely or entirely to reflexes aroused by drug in heart or lungs.

Cardioinhibitory center depression - only as part of generalized depression by narcotic.

Reciprocal innervation between cardioaccelerator and cardioinhibitory centers: increased activity of one automatically produces decreased activity of the other.

2. Centers regulating tone of blood vessels.

Vasoconstrictor center stimulation and depression like cardioaccelerator with which it is closely associated. Rise in blood pressure following analeptic (other than ephedrine-benzedrine type) is one of most favorable signs, fall in blood pressure following a narcotic one of most unfavorable.

Vasodilator center (or centers) - no important drug actions recognized.

B. In the Blood vessels

1. Pressure-sensitive nerve receptors in carotid sinuses and aortic arch - no drug actions known. Nerves can be inactivated by local anesthetics.

2. Chemo-sensitive nerve receptors in carotid and aortic bodies - stimulated by: - (a) inhibitors of oxidations like cyanides and sulfides; (b) nicotinic agents like nicotine, lobeline, choline derivatives etc.; (c) miscellaneous agents like papaverine, aminophylline, K+ salts etc. Depressed by excess nicotine, lobeline or choline derivatives. Nerves same as from pressoreceptors of carotid sinuses and aortic arch.

3. Sympathetic and parasympathetic ganglia (see Autonomic Pharmacology) stimulated by small doses of nicotine, lobeline, choline etc, depressed or paralyzed by larger doses. Usual effect is vasoconstriction and rise in blood pressure followed by vasodilatation and fall.

4. Sympathetic nerve endings stimulated by sympathomimetic agents (epinephrine, ephedrine, amphetamine, neosynephrine, paredrine, etc., etc.), paralyzed by sympathetic blocking agents, (ergotoxine, ergotamine, priscol, dibenamine etc.)

5. Parasympathetic nerve endings stimulated by muscarinic agents (muscarine, choline derivatives, physostigmine, neostigmine etc.), paralyzed by atropine and derivatives (scopolamine, homotropine, syntropan etc.)

6. Special nerve receptors in heart (perhaps also in liver) when stimulated by digitalis group reflexly produce increased activity of cardioinhibitory and vomiting centers.

7. Special nerve receptors in coronary and pulmonary circulations when stimulated by veratrum alkaloids reflexly produce slowing of heart, dilatation of blood vessels and inhibition of respiration.

8. (Uncertain but probable) - receptors in muscles reflexly produce increased heart rate and blood pressure during muscular exercise.

II. Drugs acting predominantly on the heart.
   A. Stimulation of contractility of heart muscle -
      1. Digitalis group: USP - digitalis, digitoxin, digoxin, lanotoside C, ouabain, strophanthin, NNR - digalen, digifolin, digilanid, digipoten, digitan, digitol, gitalin, scillaren.
      2. Xanthine derivatives - caffeine, theophylline, aminophyllin.
      3. Barium ions (purely toxic).
   B. Depression of contractility of heart muscle
      1. Quinine and (particularly) quinidine; atebrine.
      2. Narcotic drugs (particularly chloroform).
      3. Potassium ions.
   C. Interference with conduction of cardiac impulse.
      1. Between auricles and ventricles - digitalis group.
      2. Among muscle fibers - quinine and quinidine.
   D. Changes in coronary circulation
      1. Constriction - posterior pituitary extract and its pressor component (pitressin).
      2. Dilatation - nitrites (ethyl, amyl, sodium), nitrates (glyceryl, mannitol etc.), xanthine derivatives (caffeine, theobromine, theophylline), choline derivatives (acetylcholine, mecholyl, carbachol, urecholine), papaverine, nikethamide, epinephrine and other sympathomimetics, etc.
      3. Changes in cardiac work (increased by epinephrine group, xanthines, nikethamide; decreased by vasodilator drugs or any fall in blood pressure).

Chemotherapy 12-13-48

(definition - OK)

Ideal - [illegible] to tissues of parasite & no effect on tissues of host.

Chemotherapy - recently associated with [illegible], [illegible] of [illegible] in [illegible].

p. 1

I. oldest type - (older [illegible] older than man - intestinal parasites)
(common, [illegible] - [illegible] - [illegible])

A. (a) & (b) for [illegible]
(f) proteolytic enzymes - digest tissues of parasites

way they act
- a - [illegible]
- b - [illegible] so as to cause [illegible] around

to get them to loosen their hold

[illegible] + cathartics [illegible]

Synthetic products (used [illegible] for [illegible] for [illegible])

a -

b -

c -

d. [illegible] parasites [illegible] but not [illegible]

Idea - selective action (drug [illegible] [illegible])

B - [illegible] - [illegible] to live cleanly

C - Amoeba

amoebic dysentery - not [illegible] common [illegible] but [illegible] [illegible]. [illegible] infected [illegible] others. Difficult to wipe out completely.

Two main categories of treatment

a - Iodine [illegible] - taken by mouth
b - arsenic " ; [illegible]

[illegible] (Kittens) for controllable [illegible] [illegible]

(2) 12-13-48

Carbarsone — no As in I
used for cutaneous in So. America (Africa) to produce something in dysentery infections
best for [illegible] curing amoebic dysentery but others best for other types

amoeba → absence of [illegible].

II Treatment of Syphilis

Spirochaeta pallida (formerly)

Treponema pallidum

Related biologically to trypanosome which causes African sleeping sickness.

Italians called it French disease & ~~Italians~~ French called it Italian Disease

used Hg in treatment. → till 1910.

As drugs — need 6 week treatment

penicillin — 1 day (or a 4 day) treatment

best argument for penicillin — seems to be most effective

Syph — really need 10 yrs. period of obs.

bacitracin used on syph.

---

org. As — due to Ehrlich

(1) methylene blue — [illegible] in nerve cells.
also on "toxophore" & "actophore" group theory
actually C & group were [illegible] for [illegible] trypanosomiasis (colonization of Africa)
actually 606 is [illegible] effective so
[illegible] with [illegible] with NaOH or Na_2CO_3 → di Na salt.

12-13-48

as di [illegible] [illegible] rapid fatality. [illegible] ([illegible] 9.14)

So [illegible] 300+ [illegible] ⇒ [illegible]

(1) no [illegible]

(2) [illegible] by [illegible] — [illegible] medicinal [illegible]

Thought at first that needed reduced [illegible] [illegible]

but Tatum & group (Wisc.) found they needed smaller quant on account of favorable therapeutic ratio. So got "[illegible]"

used also for [illegible] [illegible] drip by 1 drop

[illegible] — used in neurological complications

(paresis etc.
→ [illegible] than penicillin alone.

i. [illegible] [illegible]

[illegible] [illegible] completely satisfactory. probably [illegible] [illegible] part in this country

Found as originator [illegible] [illegible]
[illegible] of [illegible] — [illegible] [illegible] [illegible] body [illegible]

---

malaria

1st effective agent

Cinchona bark — brought back by one of Spanish [illegible] [illegible].
→ Cinchona tree — produced curing body — [illegible] by [illegible]. Columbia

Quinine (legend of [illegible] & Water)
→ [illegible] out of S.A. — [illegible] mostly in Dutch East Indies.

atabrine — really potentially German product
→ put together (U.S.A.) [illegible] subsequent [illegible] toxicity than quinine & [illegible] Q → [illegible] to parasites

Received [illegible]

(Name of Contributor)

(Address) Field Sketch

(Name of Special Agent)

To Be Returned Yes ( ) No (x)

Description: Item #10 material from [illegible] cabinet in basement of [illegible]

File No. 157-4107-1B-12(1)

SAC, PHILADELPHIA

July 7, 1950

T. SCOTT MILLER, SA

HARRY GOLD, was.,
ESPIONAGE - R

65-4307-1B 12 (1) Folder No. 10

The above material was shown to GOLD on June 24, 1950 at which time GOLD explained the material therein.

The application for employment with the Sun Oil Company GOLD stated, he obtained in 1948 with the idea of seeking employment with this company. He said that he never filled out the application.

GOLD said MORRELL E. DOUGHERTY on behalf of GOLD, called up JOHN ASHENFELTER of the Sun Oil Company in August 1948 and told ASHENFELTER that GOLD would be in to see him relative to a position. GOLD said he did go to see ASHENFELTER but that the meeting was very unsatisfactory inasmuch as there were so many interruptions and it was suggested that another meeting be held but since the position at the Philadelphia General Hospital was about to materialize at that time, GOLD never followed through with the Sun Oil employment.

The material marked "#1" GOLD stated, were notes in his handwriting on literature searches for EDDY QUICK who owned the Peacock Gold Leaf Company, in which building the Laboratory of A. BROTHMAN and Associates is located.

The last 8 pages of notes GOLD stated were notes on work at Abe Brothman and Associates relative to the Diol process. Some of this material is not in the handwriting of GOLD.

TSM:ERC
65-4307

SUN OIL COMPANY

APPLICATION FOR EMPLOYMENT

ANSWER ALL QUESTIONS COMPLETELY IN YOUR OWN HANDWRITING. USE (X) IN SQUARES PROVIDED

Date _____

Referred by _____

FOR PERSONNEL DEPARTMENT USE ONLY				
1	2	3	4	5

Remarks:

FOR POSITION AS

SOCIAL SECURITY No.

OTHER POSITIONS FOR WHICH YOU ARE QUALIFIED

NAME (First) (Middle) (Last)

ADDRESS (Street No.) (Street) (Apt. No.)

(City) (State) (Telephone No.) (Years of Residence in this locality)

IN CASE OF ACCIDENT NOTIFY (Name) (Relationship)

(Address) (Telephone)

MARITAL STATUS

Single ☐
Married ☐
Widow ☐
Widower ☐
Divorced ☐
Separated ☐

NOTE: IT IS ESSENTIAL THAT THE AGE DATA BE ACCURATELY INSERTED.

AGE _____

DATE OF BIRTH (Mo.)_____ (Day)_____ (Year)_____

HEIGHT_____ WEIGHT_____ SEX _____

OWN HOME ☐ RENT HOME ☐

ROOM ☐ LIVE WITH RELATIVES ☐

NUMBER OF DEPENDENTS

Under 16	Over 16	Relationship

Were you ever employed by Sun Oil Company Yes ☐ No ☐ If yes, Where?

Why did you leave?

Are you related to anyone now employed by Sun Oil Company Yes ☐ No ☐

If yes,— Name	Department	Relationship

DESCRIBE ANY MILITARY TRAINING YOU HAVE HAD

Entry DATE OF Discharge

Honorable ☐ Dishonorable ☐

EDUCATION

		CIRCLE LAST YEAR COMPLETED	YEAR GRADUATED	DEGREES	STANDING IN CLASS
PRIMARY SCHOOLING High School ☐ or Prep School ☐		5 6 7 8 9 10 11 12			
COLLEGE OR UNIVERSITY	Day School ☐ Night School ☐	1 2 3 4 5 6 7			
OTHER	Day School ☐ Night School ☐	1 2 3 4			

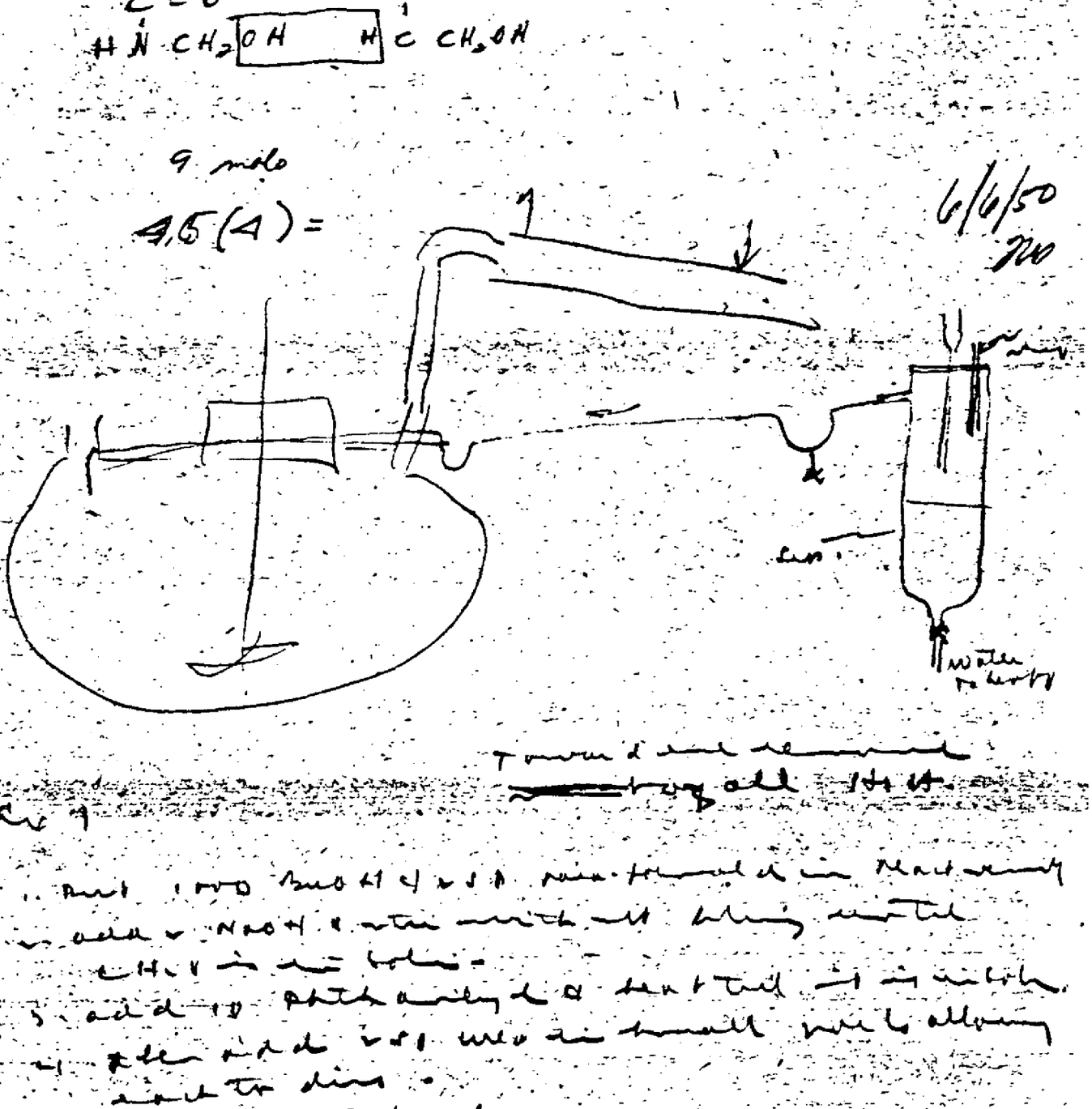
Chemical Abstracts
EASTON, PA.

ENTERED AS SECOND CLASS
MATTER AT EASTON, PA.

GOLD, HARRY
6625 KINDRED ST
PHILADELPHIA 24 PA

1 wt plasticizer TCP [illegible] phos
comparison [illegible]
film would harden to [illegible] act [illegible]
film after several days at r.t.

also 18 min at 140°C
150°C for 1 hr → di-H. [illegible]


Water

(12)

U.S. 2,191,957 Feb. 27, 1940

Donald C. Edgar and Paul Robinson (to Du Pont)

Improved Urea Formaldehyde Resinous

Composition (for Decorative and Protec-

tive Films)

4/4/50

~~T. 6~~

$\frac{370}{30}$

$$\frac{1600\,(0.37)}{30} = 19.7$$

1971 1800 CHO

199 NaHCO3

pH 7.6 NaOH

9.0

ata 96 hrs.

wt. 20-30%

Cutting began 12-24 hrs

96 hrs at solid

Filter & Dry

38%

all 1600

100 Tolue

75 approved at

15

to

6/4/80 9/10

Permeability of Films
to H_2S

6/6/50

C.A. 21-30 (1927-1936)

29, 4247[9] unimolecular films on glass ✓ng.

25, 4749[8] soly in various solvents to ✓ng.

C.A. 31 (1937)

3987[4] permeability of skin to ✓ng

C.A. 32 (1938)

nothing

C.A. 33 (1939)

nothing

C.A. 34 (1940)

7123[5] Testing coating resistance to ✓ng

C.A. 35 (1941)

6610[9] permeability of skin to ✓ng

C.A. 36 (1942)

5107[2] abs. by amberlite IR-4 for removal of Group II ions. ✓ng.

amine-formaldehyde type resin

C.A. 37 (1943)

✓ 1206[2] stability of varnishes and resins against.

(2)

Remissibility

C.A. 37 (cont'd)

p 740' } wood preservative impregnants
p 741' } and [illegible]

C.A. 38 (1944)

nothing

4/4/50
[illegible]

C.A. 39 (1945)

nothing

C.A. 40 (1946)

nothing

C.A. 37, 1206[2] (1943) 6/II/50 gmp

Hydroisolation materials, org. Dielektriki, Trudy Vsesoyuz. Elektrotekh. Inst. 1940, no. 37, p. 82-99; Khim. Referat. Zhur. 1940, no. 12, p. 76

M. F. Ryskalova

Stability of resins and varnishes against various chemical substances.

R. investigated the behavior of varnishes from various synthetic condensed and polymerized resins, esters, celluloses, bitumens and natural resins in H_2S, CO_2, SO_2, SO_3, NO_2 and HCl vapors. Films from alkyd varnishes, albertol, asphalt, and combination films from varnish 1154 plus alkylphenol oil-sol. resin or albertol withstood best the action of H_2S.

2-29-49

Tarnishing

CA 21 - 30 (1927 - 1936) 6/6/50 JM

✓ 30, 860[9] of gilt ink in contact with paper

27, p 1606[8] prevention of ✓ m.g. oxide coating

24, p 3492[2] by coating metals (pr.) ✓ m g. lanolin + oxidized oil

✓ 24, p 502[3] pr. of electroplated articles

25, p 2532[6] pr. of Mg ✓ m g. H2SO4 treat.

27, p 595[5] pr. of metal articles ✓ use Ca acetate to impregnate cloth

✓ 30, 7246[9] of metals

✓ 27, p 4675[3]

26, p 3478[8] of Ag ✓ m.g.

28, p 3542[6] of Ag ✓ m.g. Ag_2CrO_4 coating

✓ 29, 2127[6] of Ag

29, p 3075[31] of Ag ✓ m.g. chromic and ...

27, p 1606[3] of Ag + alloys ✓ m g. treat surface with HCl, NH4Cl ...

28, p 1654[4] of Ag + alloys ✓ m g. electrodep of ...

✓ 24, p 5119[7] compn for pr. Ag

29, p 1183[2] compn for pr. Ag ✓ m g. with CaCl2 (pr 100) + CuSO4 (pr 1.5)

(2)

Tarnishing 6/6/50 JW 12-23-47

21, P2175.[2] of Ag, etc. [illegible] ZnOAc [illegible] for [illegible]

28, 7170[6] of Ag or silverware [illegible] electrodeposition

✓ 28, P2485[6] of silverware, [illegible] for [illegible] oneida patent

28, P2862[3,4] of silverware [illegible] for [illegible] [illegible] also [illegible]

29, P8394[3] of Ag [illegible] by [illegible] [illegible] by Ag

27, 3340[9] cloth for [illegible] Ag [illegible] ZnOAc [illegible] Ag salts

27, P4692[7] cloth for [illegible] Ag [illegible] PbOAc

29, P4858[1] cloth for [illegible] Ag [illegible] Ag [illegible]

25, P1958[2] receptacle for [illegible] Ag [illegible] PbOAc treat.

26, P2834[3] receptacle for [illegible] Ag [illegible] PbOAc

27, P1478[5] receptacle for [illegible] Ag [illegible] PbOAc.

24, P4129[3] [illegible] Ag, [illegible] for [illegible] [illegible] Ag [illegible]

✓ 27, 2922[7] of Ag [illegible]

25, 5652[9] of Ag by S [illegible] [illegible] Ag & S

24, P3207[8] Ag resist to tarnishing [illegible] with Cu, Ni, or I (oneida)

23, P4081[3] Ag resist to [illegible] [illegible] of Hg [illegible] (oneida)

25, P177[9] Ag resist to [illegible] oneida [illegible]

✓ 24, 6027[7] [illegible]

C.A. 27, 29227 (1933)   6/6/50 JM

Oberflächentechnik 10, 93-4 (1933)

H. Reinhardt

Protection against Tarnishing of Ag

Caused by H_2S or S-contg. cpds. means by use of (among others) Zapon lacquer or similar varnishes

See orig. article

C.A. 24, 5119 (1930) 6/6/50 [illegible]

U.S. 1,773,702 Aug. 19, 1930

R. O. Bailey & Wm. S. Murray (to Oneida Community Ltd)

Rendering silverware resistant to tarnish

Polish with mixt of kerosene and lampblack contg Iodine and free from tarnish producing ingredients.

See orig Patent

C.A. 29, 2127[b] (1935) 6/6/50 JM

Mitt. Forschungsinstitut Probieramt Edelmetalle 8, 61-7, 77-84, 105-12 (1934/35)

C. Raub

Tarnishing of Ag and its Prevention

Only one that applies here is the first one — "coating with a transparent lacquer, zaponize" — to make the surface resistant to S compounds.

See orig. article

C.A. <u>30</u>, 7246⁹ (1936) 6/4/50 gro

Seifensieder-Ztg <u>63</u>, 374-5 (1936)

Josef Augustin

<u>new</u> <u>preservation</u> <u>methods</u>

Recent improvements in methods for (among other things) preventing tarnish on metal surfaces.

<u>orig</u> <u>article</u>

C.A. 24, 3023 (1930)

6/4/50
JM

Brit. 309,339 June 7, 1927

H.A. [illegible] & B.F.G. [illegible]

Prevention of Tarnishing of Electroplated articles

S. & G. dip the article into a soln of celluloid & soap in AmOAc and heat at 32°C for 1-4 hrs.

C.A. 30, 760 (1936)

Pulp Paper Can. 36, 609-13 (1935)

O. J. Schierholz

4/4/50

Tarnishing of Gilt Inks

Gilt inks of bronze powder type — used to decorate wallpapers — tarnish due to absorption of SO_2 from mill air (produced by papermaker's alum). S. says this is an extremely delicate test for SO_2. Prevented by treating paper with $NaHCO_3$ prior to gilding.

6/6/50 MO

A. 27, 46753 (1933)

June 20, 1933

— 333, 430

C. Thurber and R. H. Schultz (to The Oneida Community Ltd)

$CuSO_4$ is added to paper pulp to precipitate the S in an inactive form. The paper formed does not tarnish well metals such as Ag or other

-A 24, 6027 (1930) — 1/16/50 JM

...ink J. I, no. 75, 47 (1938)

Taird - Arone - Palmer

Tarnished metal tissue (Fabrics)

gives non-tarnish lacquer formula,

see orig article (missing from files of Eng. Soc. Library)

C.A. 32, 9122 (1938)

Trans. Faraday Soc. 34, 905-14 (1938)

T.P. Hoar and L.E. Price 4/6/50 gm

Electrochem. Interpretation of Wagner's Theory of Tarnishing

Regard metal surface undergoing tarnishing as current producing cell with the metal/film and film/atmosphere surfaces as anode and cathode resp., the film being both the electrolyte and the external circuit.

C.A. 32, 8345[6] (1938) 4/4/50 JRD

Z. physik. Chem. B 40, 455-75 (1938)

cf. C.A. 30, 5165[2]

Carl Wagner and Carl Grunewald

Theory of the Tarnishing Process III

w. a measured rate of oxidation

of Cu, Ni and Ni-Au alloys

see orig articles

Tarnishing

6/4/50

C.A. 32 (1938)

✓ 8345[6] of metals

8343[1] of Ag & Au alloys ✓ in q. oxide films with small cation radii (around 70,000 [illegible]).

4506[8] Ag plate proofing ✓ in q. alloys with Rh.

✓ 9022[7] Theory

Tetrahedron

6/6/50 700

CA 34 (1940)

4045° of Ag and into penetration V=4. Ft. at d(1,0,0) Ft.

2603° Ramin for Pt. of Ag; V=4. Ft. at d(1,1,1) Ft.

Tarnishing   6/6/50 JWD

CA 35 (1941)

1009^{4} of lacquered brass articles ✓ing due to TCE hydrolysis

3037^{9} by paper or printing ink ✓ing

✓ P 1756^{2} pr. of brass + Ag.

P 431^{1} pr of Ag alloys ✓ing coat with Be

P 4292^{9} pr of Ag + Ag alloys ✓ing coat with Be

7919^{3} resist. of dental Ag alloys ✓ing

Tarnishing [illegible]

4/4/50
[illegible]

.36 (1942)

67592 Crystal orientation in [illegible]

5759 effect of static field of [illegible] on a steel [illegible] [illegible]

27942 theory of [illegible]

4424 theory of [illegible]

(2)

C.A. 35, 1756[3] (1941) 6/4/51 ms.

4. Remove HOH by distillation, adding more BuOH if necessary, until the soln. is anhydrous.

5. Filter the lacquer.

Then, prepare an alkyd resin thus

6. Heat { pthalic anhydride 127 parts; glycerin 90 parts; castor oil 190 parts } till a suitable viscosity is reached. This resin is compatible with the lacquer and is suitable for a plasticizing agent.

7. For use, mix

40 parts melamine lacquer

60 parts alkyd resin

and cut with BuOH to a viscosity suitable for spraying. Spray to get a thin continuous film & dry at 150°C for 15 mins. Film is not only tarnish resistant, but does not burn or soften (under a lighted cigarette).

Jamming

C-A-37 (1943)

V. 23327 of ground installation, prior.

[illegible]

Terminating

C.A. 29 (1945)

nothing

6/6/50

Tanning [illegible]

6/10/50 [illegible]

C.A. 42 (1946)

✓ 2653[4] of Aq, [illegible] in [illegible]

p 4342[1], p 4654[3] } of Aq [illegible], [illegible] ✓ m.q. [illegible]

CA 40, 2653[4] (1946)

Industrial Finishing 22, no. 4, 27-8, 30, 32, 34, 36, 38, 40 (1946)

4/4/50

Gilbert C. Close

Synthetics in Industrial Finishing

Characteristics & uses of urea resins and of the two general types of phenolic resins are noted. The softer varieties of acrylic resins are sometimes used as base coats for textiles and in rubber lacquers. One specific use is to prevent odor from rubber application finishing. Chlorinated rubber and its uses are included in the discussion.

C.A. 37, 2332 (1943)

6/4/52 gp

U.S. 2,305,504

Dec 1, 1942.

Cornelius J. Regan (To DuPont)

Rendering metal powders Tarnish Resistant

Particles of a lamellar disintegrated brown powder or the like are coated with a partially polymerized urea-formaldehyde — aliphatic monohydric alc. condensation product by polishing at an elevated temp. not exceeding 145° F.

Orig. Patent applied Aug. 14, 1941

1. Soap brown powders used by stamping operations are extensively used in the manufacture of imitation gold transfer leaf as well as in bookbinding and general embossing work, of particular importance is high tarnish resistance.

2. Invention provides a metallic powder of unusual brilliancy and tarnish-resistance. A further object is a process producing powders of greater commercial value, without sacrificing the brightness,

C O

(2)

C.A. 37, 2335 (1943) cont'd 4/4/50

hiding power, or leafing characteristics of the powder. also, can use existing commercial eqt.

3. Describes usual method of preparing bronze powders:

a. stamping → small miniature plates

b. separation of finer particles → lowering finally a small average size. The at any point in the process the powder represents a composite of of a great variety of sizes.

c- Polishing operation to take care of:

(1) clumps of plates

(2) crumpled particles

(3) improving brilliancy and hiding power of particles.

(4) Improve leafing of powder (i.e., tendency of powder to float + leaf). This is accomplished by adding a small amt of a waxy material such as stearic acid, palmitic acid, candelilla wax, carnauba

(2) cont'd 6/6/50 JP

A 37, 23327 (1943)

wax and similar materials during the polishing operation. The type of agent is dependent on the use to which the powder is to be put.

4. R. has now found that by treating the powder during the polishing procedure with a small amount of a partially polymerized resinous urea-formaldehyde condensation product dissolved in an organic solvent vehicle, are placed in a conventional polishing drum and polishing carried out until the said condensation product is uniformly distributed over the surface of the metallic powder. The final stages of the resin condensation occur during the polishing operation and probably continue for a short period thereafter.

5. Example

coarse → fine (F, D, B, A and AA)

a. 50 lbs. of B-grade are put into a conventional stationary polishing drum with

C.A. 37, 2332 (1943) cont'd 6/4/50 JD

corrugated interior walls, equipped with soft brushes which rotate axially in contact with the inner wall of the drum.

b- The brushes are started and the powder is polished dry from 6 to 12 hrs. During this cycle the brilliancy of the powder increases, and the clumps of particles are broken up.

c- The second stage polishing (which can be conducted at any time following the dry polishing) is accomplished by loading a polishing drum with 50 lbs of the powder from "b" and then (1) allowing the brushes to run for 30 mins (or until the mass has warmed appreciably and all the clumps are broken up) a temp of 145°F is reached.

(2) 4 ounces of partially condensed urea formaldehyde resin solution are then added and the polishing process continued for 90

C.A. 37, 2332 (1943) (E) cont'd

minutes, with the temp. in the drum averaging 125°F (but should not appreciably exceed this figure). The powder at the end of this treatment has a slightly greasy feel but this disappears in a few hrs. The treated powder is very brilliant, far surpassing that secured by prior practice, a result which is probably due to a combination of

(1) dry polishing

(2) the reducing action of the free formaldehyde in the resin soln.

(3) the chemical action of the acid phosphate catalyst.

In addition to the high initial brilliance, the powder has an unusual and markedly superior resistance to tarnishing on exposure to conditions which quickly tarnish the ordinary commercial grade of stearic acid polished powder. It has also been found that the resin treated powder is particularly

C.A. 37, 2332 (1947) cont'd (6) 4/6/53 RB

adapted for use in gold transfer
leaf where tarnish resistance is
particularly important.
The resistance of the coating was
9- further tested by attempts to
extract the resin with the best known
solvents for the urea-formaldehyde
resins. The conc. of resin added
was 0.3% but it was possible to
extract only 0.0109%.
h- A suitable resin soln. is of the
type described by Edgar and
Robinson in U.S. Patent 2,191,957,
wherein a monohydric alcohol is
used as a suitable modifying
agent to produce stable partially
polymerized resin solns. adapted
for coating purposes and readily
baked (125°F - baking?) to a
tough hard film. A resin pre-
pared according to Example II
of E. and R. but in which
n-butyl alcohol was substituted

C.A. 37, 2332[7] (1943) cont'd 6/6/50
JW

for isobutyl alcohol and butyl acid phosphate was substituted for the phthalic anhydride catalyst constitutes a satisfactory material. The resin soln. contained 60% total solids by wt. Further,

i - The urea - formaldehyde condensation products are particularly adapted for use here as they are

(1) light in color

(2) easily prepared

(3) stable and easily handled

j - The use of aliphatic alcohols in the synthesis is of great importance because it has been found to be impossible to polish bronze powders in the presence of appreciable amts. of water. There are available commercial types of partially polymerized urea-formaldehyde resins in which water is used as the carrier but these are unsatisfactory here also.

C ● O ●

C. A. 37, 2332 (1943) cont'd 6/6/50 JJO

(1) Similarly, emulsions of partially polymerized urea-formaldehyde resins are unsatisfactory due to the water phase present.

(2) Mechanical dispersions or suspensions of solid partially polymerized urea-formaldehyde resins in organic liquids in which the resins are insoluble are also unsatisfactory, as it is impossible to obtain a satisfactory distribution of the resin during the polishing.

It is important, therefore, that the urea-formaldehyde complex used (1) represent an incompletely polymerized material

(2) be in the form of a solution in a volatile organic liquid (n-BuOH is preferred though n-PrOH can be used; EtOH leads to inferior water resistance and amyl, hexyl and octyl alcohols show slower drying characteristics).

Partial or complete substitution of the urea may be made by using

(9)

C.A. 37, 2332[7] (1943) cont'd 6/6/50 JW

the substituted ureas such as alkyl, aryl, or acyl ureas. The selection of the completely satisfactory resin soln. can be determined only by the appearance of the treated bronze powder. Excessive amounts of formaldehyde tend to dull the powder and excessive amts. of acidic catalysts tend to pit and corrode the powder.

It is advantageous to use sufficient urea-formaldehyde resin to completely and uniformly coat the disintegrated powders. The amount of resin used varies with the fineness of the powder and so the optimum quantity will vary from grade to grade — insufficient resin leads to poor tarnish resistance; and excessive amounts interfere with the polishing operation, causing clumping or sticking together of the particles and it becomes impossible to handle the powder. In general, satisfactory results have been obtained

C-A. 37, 3332 (1943) cont'd 6/6/50 gm

over the range of various bronze powders by the use of between 0.1% and 0.5% by wt. of solid treating resin.

m. other resins, both natural and synthetic have been evaluated in comparison with the urea-formaldehyde type. These include:

(1) alkyd resins
(2) phenol-formaldehyde
(3) vinyl resins
(4) cumar
(5) damar
(6) rosin
(7) ester resins

The majority of these failed to markedly improve the tarnish resistance of the treated powder. None of the resins tested equalled the urea-formaldehyde type.

o- Can use method for Sn, Ni and Ag powders.

p- modification. Note

(11)

6/6/50 JD

C A 37, 2332? (1943).

(1) If the powder is not removed from the polishing drum b (or that it cools), the treating soln may be added directly at the completion of the dry polishing cycle.

(2) In some cases (though as a rule the preliminary dry polishing is preferable for best results) the dry polishing step may be eliminated entirely and the resin solution added at the start of the polishing operation.

3. R has 10 claims.