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APR 10 1943

Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Treatment of Hypertension

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Published for the General Staff Meeting each week
during the school year, October to June, inclusive.

Financed by the Citizens Aid Society,
Alumni and Friends.

William A. O'Brien, M.D.

I. LAST WEEK

Date: April 2, 1943
Place: Recreation Room,
Powell Hall
Time: 12:15 - 1:20 p.m.
Program: "Medical Aspects of Chemical
Warfare"
L. W. Foker
 Discussion
Harold Diehl

Attendance: 99

Gertrude Gunn,
Record Librarian

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II. MEETINGS1. ANATOMY SEMINAR

Saturday, April 10 at
11:30 a.m. in room 226, Institute of
Anatomy.

"Recent Studies on the Trigeminal Nerve"

A. T. Rasmussen

"Pathological Effect of Radiant Energy
Upon the Eye"

J. P. Wendland

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2. SPRING QUARTER STAFF-MEETINGS

Apr. 16	Medicine	C. J. Watson
Apr. 30	Obstetrics and Gynecology	John McKelvey
May 7	Orthopedics	Wallace Cole
May 14	Pediatric Psychiatry	Irvine McQuarrie
May 21	Surgery	O. H. Wangensteen
May 28	Physical Therapy	Miland Knapp
June 4	Laboratory Service	Gerald T. Evans
June 11	Anesthesiology	Ralph Knight

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III. CONGRATULATIONS

Baby boy to Dr. and Mrs. Disney Litow
February 21, 1943.

Baby girl to Dr. and Mrs. Ernst
Strakosch, March 17, 1943.

Baby boy to Dr. and Mrs. Wallace
Armstrong, March 24, 1943.

Baby girl to Dr. and Mrs. Schelessmon
March 31, 1943.

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IV. OFFICE REMOVAL

EDWARD C. MAEDER, M.D.
announces the removal of his offices to

Suite 948 Medical Arts Building
Minneapolis, Minnesota
After April 1, 1943

Practice limited to Obstetrics and Gynecology	By appointment Tel.: Atlantic 7564
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V. COMMUNICABLE DISEASES

Course for public health nurses
will be given at Center for Continuation
Study, Thursday, Friday, and Saturday,
April 15, 16, 17, 1943. Faculty will
include Kenneth F. Maxcey, head of depart-
ment of epidemiology, Johns Hopkins
School of Hygiene and Public Health, Bal-
timore, former head of department of pre-
ventive medicine and public health, Univer-
sity of Minnesota, and Medical School and
Health Department representatives Breslow,
Chesley, Cuckler, Eklund, Feldman,
Flancher, Freeman, Hill, Hoffbauer, Irvine,
Knapp, Lynch, Marcley, Nolte, Nyquist,
O'Brien, Pearce, Platou, Ricard, Riley,
Spink, Wert, Whittaker, and others.

Subjects: Water and food infections,
tuberculosis, venereal diseases, measles,
scarlet fever, virus infections, meningi-
tis, influenza, pertussis, undulant fever,
poliomyelitis, parasitic diseases, skin
infections, serum therapy, chemotherapy,
pneumonia, administrative practices, local
and global problems. Tuition \$5.

VI. TREATMENT OF HYPERTENSION

J. S. Blumenthal
Macnider Wetherby

It must be apparent to most of us that the methods of treatment of hypertension available to us today are unsatisfactory as far as reduction in blood pressure is concerned. Treatment medically is much the same as that in use 25 years ago,^{1,2} and the failure to change is certainly not due to its efficiency. Time after time we see the diagnosis of hypertension made and the notation immediately thereafter "no cardiac decompensation, no therapy indicated." The average patient with high blood pressure is told to go home and "take it easy." If he is at all apprehensive or has some symptoms of hypertension, he is given large amounts of phenobarbital to help him "take it easy." We then sit back and await the sequelae of the condition---cerebral accident in 19%, renal failure in 9%, myocardial failure and coronary disease in 61%.³ If the patient develops cardiac

failure, we eagerly digitalize him, realizing that here at least we have a condition in which adequate therapy will be of unquestioned benefit. If a cerebral accident ensues, we assure the patient or his relatives that if he recovers from the initial attack, he will, no doubt, regain a large proportion of the faculties he has lost--and he will then surely "take it easier." I do not believe this is too harsh a resumé of the present medical treatment of high blood pressure in the average case.

PREVALENCE OF HYPERTENSION AND PROGNOSIS

Another factor that needs emphasis is that hypertension is a common and a serious condition. Dr. Wetherby, in a study of 20,000 patients in our own department, gives what seems to me, some very interesting and even startling figures. At the age of 40 to 49--17% of the men and 35% of the women in this group had systolic blood pressure above 140 and 28% of men and 38% of women had a diastolic blood pressure of above 90mm. of mercury. (Table I)

Table I

The Percentage of Cases above Certain Blood Pressure Levels for
Men and Women in the Total Out-Patient Group

Percentage Over	40-49 Years Men	40-49 Years Women	50-59 Years Men	50-59 Years Women	60-69 Years Men	60-69 Years Women	70-Years and Over Men	70-Years and Over Women
Systolic Blood Pressure								
140 mm.	16.64	34.71	29.05	55.89	44.60	70.06	55.75	74.89
150 mm.	8.66	22.63	16.87	40.04	30.37	53.88	41.85	61.24
160 mm.	5.37	14.84	12.03	27.52	22.30	42.36	28.90	50.77
180 mm.	2.59	6.06	4.46	13.02	8.76	24.55	14.84	26.97
220 mm.	.95	2.91	1.51	6.58	4.25	11.40	5.84	10.47
Diastolic Blood Pressure								
90 mm.	28.38	38.23	33.37	50.39	40.01	53.90	42.33	51.42
100 mm.	9.63	14.45	13.77	24.77	17.79	28.06	20.69	30.79

The mortality from hypertension has been estimated in the United States at from 250,000 to 375,000 deaths annually.⁴ About one-fourth of all deaths past 50 years of life is referable to hypertension⁵--2 to 3 times the number of cancer deaths. Keith, Wagener, and Barker⁶ have shown that the mortality varies from 30% to 98% in a period of 4 years depending on the degree of hypertension. Among persons with a systolic blood pressure of 170 mm. of mercury, insurance statistics show a relation of actual to expected mortality of 219.6 to 100; with a systolic blood pressure of 200 the actual mortality is to the expected as 827.5 is to 100.^{7,8} Many physicians are misled by the occasional patient that survives many years; for while hypertension is compatible with longevity⁹ it is not conducive to it. Hypertension is a serious disease and fatal within a relatively short period of time.

It has, at times, been stated that hypertension per se may have little influence on the development of arteriosclerosis¹⁰ and that the injurious effect on the vascular system may be due to a hypothetical noxious substance which causes hypertension; but most of us will agree, I believe, that "all pathologic changes in the disease can reasonably be explained as resulting directly from mechanical effects of a persistent elevated arterial tension acting on a vulnerable vascular system."¹¹

LEVEL OF HYPERTENSION

There has been a great deal of diversity of opinion regarding the exact level at which we should consider a patient as having hypertension. More recently, general opinion has tended to place the normal blood pressure at lower levels. Where 30 years ago, Janeway and others regarded 160 systolic and 100 diastolic as hypertension, we now regard 140 and 90 as more nearly the true levels; and many would place it lower. The old rule of thumb of 100 plus the age is grossly inaccurate and if cases of hypertension are excluded, it would seem that blood pressure rises very little with advancing age.^{12,13} The study made in 1939 by the

Joint Committee of the Association of Life Insurance Directors and Actuaries Society of America¹⁴ shows that levels above 140 systolic and 90 diastolic are abnormal at any age. For persons over 40, systolic blood pressure 35 to 44 mm. in excess increases expected mortality two and one half times; and increased mortality is in direct proportion to the increased blood pressure. It would be reasonable to assume that even a moderate persistent reduction should retard degenerative processes.

HYPOTENSIVE DRUGS

It is with these facts in mind that Dr. Wetherby and I decided to try some of the so-called hypotensive drugs in a hypertension clinic. We realized as do you, that many men have agreed with Mosenthal¹⁵ when he recently summarized the effects of common methods of medical treatment of human hypertension with the statement "there are no means by which an elevated blood pressure can be appreciably and persistently lowered." We also realized, however, that some very capable observers have at times reported encouraging results with some drugs--the list is long--among them pentothal sodium, pentobarbital sodium, choralosane, nitrites, mannitol hexanitrate, viscum album, allium sativum (garlic extract), extract of watermelon seed, sodium bromide, veratrum viride, acetyl choline, choline chloride, sodium chloride, nicotinic acid, biotin (Vitamin H) and the cyanates.¹⁵

Various diets have been tried but with no apparent effect. Orgonotherapy in the form of pancreatic, liver and of course, kidney extract has been used. The very multiplicity of therapy speaks for itself; but most encouraging reports have come in the use of the cyanates and most recently, renal extract. In our present series we have used vitamin A in 20 cases and potassium thiocyanate in 70 cases.

VITAMIN A
IN THE TREATMENT OF HYPERTENSION

(With Dr. Wetherby)

At times hypovitaminosis of several of the vitamins has been reported as a possible factor in the causation of hypertension. There has been very little substantiating evidence but vast quantities of vitamins have been sold on this basis. Juan Govea Peña and M. Villaverde^{16,17,18} of Cuba have recently reported on the use of Vitamin A in large doses in hypertension. They rationalize this treatment by citing the work of Herfort¹⁹ who states that Vitamin A exercises a stimulating effect upon the internal and external secretions of the pancreas. They then state that assuming that these secretions contain hypotensive hormones, vitamin A would then exercise the same hypotensive action indirectly by exciting production of such hormones. These authors then further report that they have studied the content of vitamin A and total carotinoids in the blood of chronic arterial hypertensives and have found a low content of this vitamin. Sixty five cases are reported as being treated. The dose was 180,000 international units daily for 2 weeks followed by maintenance dose of 90,000 international units daily. A drop in blood pressure was noted as long as the medication was continued. The hypotensive action of this medication was then declared to have been "not only undeniable but remarkable." Only 4 out of 65 cases and these of malignant hypertension, were not benefited.

This report is on the result of the use of vitamin A in large doses in 20 cases of hypertension followed at the University of Minnesota. These patients were not selected. They were taken consecutively. Their chief complaints were headache, dizziness, and dyspnea on exertion. They were not decompensated. No marked coronary diseases were included in this series. These cases were given capsules containing 50,000 international units of vitamin A each. 200,000 international units of vitamin A were given daily. This dosage was continued for 20 weeks and followed by a maintenance dose

of 100,000 international units daily. The average period of treatment was 8 weeks. There were 6 males and 14 females. Ages varied from 31 to 69 years. The average period of known hypertension was 7½ years. In all cases, many blood pressure readings were taken to get an average and all readings were taken under similar circumstances before and after treatment. Subjectively, 6 patients said they felt better but this improvement had no apparent relation to the blood pressure. The trend of readings as shown in the table, did not give evidence of any action on blood pressure whatsoever. Our findings did not corroborate the reported hypotensive action of vitamin A.

The systolic blood pressure determination of these 20 hypertensive patients after treatment was of a higher average in 11 cases and lower in 9 cases. The diastolic blood pressure was of a higher average in 9 cases, lower in 8 cases and the same in 3 cases. There was no striking evidence of any changes in blood pressure following therapy other than the usual variations in readings. (Table II.)

Table II

No.	Name	Before Treatment		After Treatment		Change	
		Average Systolic Blood Pressure	Average Diastolic Blood Pressure	Average Systolic Blood Pressure	Average Diastolic Blood Pressure	Systolic Blood Pressure	Diastolic Blood Pressure
1		174	110	177	114	+ 3	+ 4
2		158	107	134	80	- 24	- 27
3		179	101	161	91	- 18	- 10
4		163	106	188	115	+ 25	+ 9
5		196	119	213	118	+ 17	- 1
6		240	136	229	133	- 11	- 3
7		233	116	250	130	+ 17	+ 14
8		198	122	211	123	+ 13	+ 1
9		212	116	216	113	+ 4	- 3
10		198	100	201	101	+ 3	+ 1
11		170	110	171	111	+ 1	+ 1
12		190	102	177	94	- 13	- 8
13		210	105	206	109	- 4	+ 4
14		235	97	229	120	- 6	+ 23
15		170	104	172	103	+ 2	+ 1
16		206	108	199	108	- 7	- 0
17		130	118	177	100	- 3	- 18
18		203	110	205	110	+ 2	+ 0
19		242	127	239	129	+ 3	+ 2
20		200	110	206	110	+ 6	+ 0

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SUMMARY ON THE USE OF VITAMIN A

Vitamin A in doses up to 200,000 international units daily for 2 weeks followed by 100,000 international units daily for 6 to 12 weeks did not have any significant effect on the blood pressure determination of 20 hypertensive patients.

POTASSIUM THIOCYANATE

Sulphocyanic acid is a synonym of thiocyanic acid, rhodan acid, sulphocyanates, sulphacyanids, thiocyanates, thiocyanids, rhodanates or rhodanids. The acid is unstable but the compounds are. It forms a large number of salts and has chemical relationship with various complex organic compounds especially the purine group. The alkaline salts potassium, sodium, ammonium are most usually used. They are white crystalline substances saline in taste and very soluble in water and alcohol. Solutions turn to brilliant dark red by the addition of excess mercuric

chloride. These changes do not take place if the mixture is markedly alkaline. This characteristic forms a very sensitive test--the reaction being well noted even in 1 to 100,000 solution of the cyanates. Normal saliva yields this reaction as do gastric juices and tears. The mode of fumatation may be the result of katabolism of sulphur containing proteins. The urine of persons taking cyanates turns a dark red on addition of ferric chloride which is only slightly different from the cherry red of diacetic acid.

PHARMACOLOGY OF THE CYANATES

Claude Bernard²⁰ in 1857 first reported the pharmacological observations on these drugs. Ingested cyanates are excreted by the kidneys and in the urine very slowly. The urine is negative only 2 to 3 weeks after stopping the drug, suggesting accumulation in the system. They are also excreted in the saliva where

they persist after the urine is free. The cyanates pass thru unchanged and are not transformed into deadly hydrocyanic acid. Prolonged administration in animals of sublethal doses produces no harmful effects. In large doses, they are a powerful poison acting directly on the muscle, and in very large doses causes immediate cessation of heart action. In doses not immediately fatal, they cause marked diarrhea and intense stimulation of the motor cells of the cord, as in tetanus; and corrosion and hemorrhage of the gastric mucosa. The effect is due to the sulphonic radical and the lethal dose in a 70 kg man would be 15 to 30 gm. at one dose though this varies greatly.

POTASSIUM THIOCYANATE IN HYPERTENSION

Pauli²¹ in 1903, noted that blood pressure was reduced with use of cyanates. He also remarked about the sedative action on pain, of the drug and its possible action of removing Calcareous deposits in arteries. LeRoy²² in 1908, thought the cyanates had a solvent and eliminative action on the earthy salts and advanced their use on this basis in degenerative conditions for eliminating calcareous deposits. Since that time many investigators have reported on the use of the cyanates in hypertension. (See Table III). A great advance in the treatment of hypertension with cyanates is the determination of blood cyanates

Table III

Clinical Reports

Author	Average Dose	No. of Cases	Results
Nichols ²⁸	5 grains three times daily	12	Effective in reducing blood pressure tho with unpleasant side effects
Gager ²⁹	1½ grains 3 times daily	35	Blood pressure reduced in 32
Smith and Rudolf ³⁰	2½ grains twice daily to 5 grains 3 times daily	72	Response satisfactory in 61 cases
Palmer, Silver & White ³¹	1½ grains 3 times daily	59	42% of the results were favorable
Logefoil ³²	5 grains 3 times daily	24	Blood pressure reduced in 21 cases
Fineberg ³³	1½ to 5 grains 3 times daily	58	37% of the cases showed a decline in blood pressure with smaller dose; with larger dose, 57% exhibited decline in blood pressure but with toxic signs
Maguire ³⁴	1½ grains 3 times daily	4	Blood pressure lowered and condition improved in all 4
Borg ³⁵	2 to 10 grains 3 times daily	24	22 patients showed a decrease in systolic pressure but toxicity common
Salisbury ³⁶	1½ grains 3 times daily	88	Satisfactory results observed in 90% of cases
Ayman ³⁷	1½ to 3 grains 3 to 5 times daily	26	Large doses produced marked decreases in blood pressure but toxicity noted; small doses ineffective
Goldring & Chasis ³⁸	2½ to 25 grains daily	50	Effective in 31% of the patients but larger doses usually give toxic effects

Table III (Continued)

<u>Clinical Reports</u>			
Author	Average Dose	No. of Cases	Results
Palmer ³⁹	1½ to 5 grains one to three times daily	35	Blood pressure reduced in 31%
Bolotin ⁴⁰	1½ to 5 grains 3 times daily	99	Improvement in 68.8% of women and 23.5% of men
Barker ²⁵	5 grains daily	246	Over a ten-year period roughly 47½% have responded to thiocyanate therapy. 76% benefited
Griffith & Lindauer ⁴¹	5 to 15 grains daily	16	Improvement in 10 cases
Massie, Ethridge & O'Hare ⁴²	3 to 12 grains daily	14	Lowering of blood pressure in every case; 12 patients reported marked symptomatic improvement
Doles ⁴³	2 to 7½ grains daily	300	Blood pressure lowered only in cases with macrocytosis
Doles ⁴⁴	2 to 7½ grains daily	10	Patients having macrocytosis showed satisfactory falls in blood pressure
Robinson & O'Hare ⁴⁵	3 grains 2 to 3 times daily	75	Average drops of 40 mm. systolic and 20 mm. diastolic occurred in 63% of the patients
William & William ⁴⁶	6 grains daily	6	6 fatal cases reported. Blood cyanate level of 15 to 20 mg. is critical

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concentration. Studies show a great individual variation in the absorption of the drug.²⁵ In 1929, a simple technic as described by Schreiber,²⁴ for determination of cyanates in blood was modified so that adequate control of dosage could be obtained.

TEST FOR BLOOD CYANATE CONCENTRATION

(Pour 5 cc. of 10% trichloroacetic acid in a test tube, add 5 c.c. serum or plasma. Shake. Allow to stand 10 minutes, filter. Measure 5 c.c. filtrate, add 1 c.c. 10% ferric nitrate. Mix and read in a colorimeter with the standard solution set at 20 mm. choosing that standard which most nearly matches the unknown.)

Barker reporting on the use of potassium thiocyanate over a period of 10 years states a blood cyanate concentration of 8 to 12 mg. per hundred c.c. of blood will give the best sustained symptomatic relief and improvement in blood pressure without endangering the patient.²⁵

Caviness, Bell and Satterfield²⁶ in 1941 using the Evelyn Photo-Electric Colorimeter with filter of wave length 440 mu and some modifications in technique report very interesting though as yet unconfirmed findings. Using 241 persons in 2 institutions under controlled conditions of diet, activity and environment, they found blood concentrations of sulphocyanates in normal individuals who

had not taken any drug to be 50,000 times that of the nitrites; and to vary from 0.31 mg. to 2.55 mg. per 100 c.c. of blood. The average level was 1.20 mg. per cent. This concentration did not vary from week to week in 29 persons on whom this was done. The mean variation was 0.14 mg. per cent with initial concentrations from .36 mg. to 2.04 mg. per cent. On further investigation, they also found that the blood sulphocyanates, as they tested for them, varied in inverse proportion to the blood pressure. They concluded that the sulphocyanates are the most important natural depressor substances in the blood. If confirmed this would, of course, be extremely important.

There have been many reports on the toxicity of the cyanates, most of them before adequate control was used. The Council of Therapy of the American Medical Association in 1929 condemned the use of the cyanates and again in 1940 repeated that their use was dangerous.²⁷ The toxic symptoms are reported as weakness, depression, aphasia, anorexia, disorientation, anemia, dermatitis, and even death.^{37,46,38}

In almost all serious cases the blood cyanate level was allowed to rise above 12 mg. per cent or was not observed.

The dosage given by the many investigators have varied but usually began with $1\frac{1}{2}$ to 6 grains with a gradual increase in dosage until either there was a satisfactory fall in blood pressure, toxicity developed, or no results were obtained in doses as high as twenty-five grains daily. (Table III)

As shown in this table, the results have varied. Thus Nichols reports the drug effective but with unpleasant toxic effects in doses of 15 grains a day. Gager reports reduced blood pressure in 32 out of 35 cases on a daily dose of $4\frac{1}{2}$ grains. Smith and Rudolf show a satisfactory response in 61 out of 72 cases with a dosage of 5 to 15 grains daily. Iogefcil reports 21 out of 24 cases of hypertension as having blood pressure reduced. Fineberg reports 37% of cases showing a decline in blood pressure with $1\frac{1}{2}$ grains of potassium thiocyanate 3 times

a day and 57% with doses up to 15 grains a day but the larger doses gave toxic effects. Borg's work showed 22 of 24 patients with a lowered blood pressure on 2 to 10 grains 3 times a day but toxicity was frequent. Saleeby reports 90% satisfactory results in 88 patients. Ayman concluded in a study of 26 cases that large doses (15 grains daily) produced marked decrease in blood pressure but toxicity resulted; while small doses were not effective. Barker gives the most comprehensive and prolonged study and he reports 246 cases observed over a period of ten years. Of these, $47\frac{1}{2}\%$ have responded to thiocyanate therapy while 76% have benefited if he includes those with relief of symptoms and only minor reduction in blood pressure. William and William report on 6 fatal cases with dosage of 6 grains daily but with a cyanate level above 15 mg. per 100 c.c. of blood. These authors have judged satisfactory results as being a reduction of 10 to 15% in average systolic and diastolic blood pressure readings or an average drop in diastolic blood pressure of 20 mm. of mercury and an average drop in systolic blood pressure of 40 mm. of mercury.

Table IV

Report on Use of Potassium Thiocyanate
in 70 Cases of Hypertension

Number of patients	70
Males	18
Females	52
Period of known hypertension	2 months to 12 years
Average period of known hypertension	5.4 years

Seventy cases of hypertension were treated with potassium thiocyanate for periods ranging from 3 to 18 months. They were all ambulatory patients. As shown in Table IV, the ages varied from 18 to 78 years. There were 18 males and

52 females. The known period of hypertension was 2 months to 12 years with an average of 5.4 years duration. Major complicating diseases were diabetes in 3, arthritis in 10, hypoplasia of right kidney in 1, hydronephrosis in 2, evidence of hypertensive or coronary heart disease in 31. Other complications were glaucoma, skin cancer, obesity, cervical polyp, fibroids. Two had had bilateral sympathectomies. Systolic blood pressures taken after a period of rest ranged from 148 to 268 mm. of mercury with a mean of 192. Diastolic pressure ranged from 88 to 160 with a mean of 112. These patients were not selected except that no cases of decompensation, marked coronary, or renal damage were included. The great majority of them had had the usual treatment of hypertension including sedation, attempt at social adjustments, rest, cardiovascular support, vasodilators, etc.

They were all followed under the same conditions as the 20 vitamin A group and with the same technique. Phenolsulphophthalein, blood urea nitrogen, and urine concentration and dilution was done on all cases in addition to the usual laboratory studies. Intravenous pyelograms were done with genito-urinary consultation on all cases with the least reason to warrant study from that angle. All cases were given the drug even if kidney function was poor but the dose was smaller and the patients were followed more closely as the blood cyanate concentration increased very rapidly in the patients with poor kidney function. Most had electrocardiograms and orthodiagrams.

METHOD OF ADMINISTRATION

The initial dose was 3 grains of potassium thiocyanate by mouth once daily. This dose was continued for 1 week. At the end of that time the blood cyanate concentration and blood pressure was determined. This procedure was done every week or two. If a sharp drop in blood pressure occurred or if toxic symptoms or severe weakness developed, the dosage was decreased. If the blood cyanate level

had not reached 12 mg. per cent, if no blood pressure drop occurred and if no signs of toxicity were present, the dose was increased by 3 grains daily every week or 2 until a drop did take place, the blood cyanate level did reach 12 mg. per cent or really toxic symptoms developed. When the symptoms, blood pressure, dosage and blood cyanate level had been correlated to the best results possible, the patient was observed at 1 to 3 month intervals. A level higher than 12 mg. per cent was lowered by decreasing the dose of the drug until the level was less. An attempt was made to keep the cyanate level as low as possible compatible with the well-being of the patient and lowering of the blood pressure. Tolerance to the drug had not developed.

RESULTS OF TREATMENT WITH POTASSIUM THIOCYANATE

Table V

Subjective Results

Number of Patients	70
Number of patients with symptoms of hypertension	58
Number of patients improved symptomatically	43
Number of patients who developed a rash	2
Number of patients with diarrhea and nausea	2
Number of patients with vomiting	1

Of the 70 patients treated with potassium thiocyanate, 58 had symptoms usually associated with hypertension; headaches, dizziness, weakness, tinnitus. Of these 58, 43 felt much better while under treatment. Too rapid a reduction in blood pressure often produced a marked feeling of weakness but for a few weeks only. Two developed a rash about the neck but this disappeared on withdrawal of the drug. Two had a severe diarrhea which ceased on reducing dosage. One had vomiting which ceased when potassium thiocyanate was stopped but on giving phenobarbital, the drug was resumed with no

further difficulty resulting.

Table VI

Objective Results

	Before KCNS	After KCNS	
Systolic blood pressure range	148-268	118-250	
Average systolic blood pressure	192	156	
Diastolic blood pressure range	88-160	70-148	
Average diastolic blood pressure	112	96	
Number of patients			70
Number of patients with reduction of systolic and diastolic blood pressure of 15%			32
Number of patients with reduction of systolic and diastolic blood pressure of 10%			15

Taking the effect of thiocyanate on the whole series, the systolic blood pressure in this group dropped from a range of 148-to-268 mm. of mercury to 118-to-250; the diastolic from a range of 88-to-160 to 70-to-148 mm.; and the average systolic blood pressure dropped from 192 to 156 mm. of mercury. In judging improvement in blood pressure an aver-

age reduction of 15% or more in the average of systolic and diastolic blood pressure for the period before thiocyanate was started was considered good. A reduction of 10% or more was considered fair. On this basis, good response was obtained in 32 patients and fair in 15 patients.

Table VII

Blood Cyanates and Dosage

Range of Dose Daily	Average Dose Daily	Range of Blood Cyanate Level	Average Blood Cyanate Maintained
3 to 18 grains	7.2 grains	2.5 mg. to 11.6 mg.	6.9

The optimum blood cyanate level varied a great deal in different individuals and often in the same person at different times. This level ranged from as low as 2.5 mg. to 11.6 mg. per cent. The average of the group, judging on the basis of subjective and objective response in those who gave a satisfactory result, was 6.9 mg. per 100 c.c. of blood. Dosage varied a great deal and often in the same patient at different times ranging from 3 grains every other day to 18 grains daily. The average daily dose was 7.2 grains. Blood counts, urinalysis,

and electrocardiograms showed no significant changes during treatment with this dosage.

Table VIII

Control Cases Given A Placebo

Number of patients (10)

	Before KCNS	After KCNS	On PLACEBO	On Repeating KCNS
Range in systolic blood pressure	158-230	118-180	148-220	126-184
Range in diastolic blood pressure	88-132	70-100	88-112	78-102
Average systolic blood pressure	208	152	190	156
Average diastolic blood pressure	108	88	98	92

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On 10 patients who gave response to treatment, placebos were given after a period of stabilization. Beyond change to the placebo, no other change was made in any procedure of treatment. Blood pressures were taken under the same conditions as during treatment with potassium thiocyanate. The range in blood pressure of this group before any potassium thiocyanate had been given was 158 to 230 systolic and 88 to 132 diastolic with an average of 208 systolic and 108 diastolic. After treatment with potassium thiocyanate, the range was systolic blood pressure 118 to 180 and diastolic blood pressure 70 to 100 with an average of 152 systolic and 88 diastolic. Placebos were then given for 4 to 8 weeks. The blood pressure ranged then from 148 to 220 systolic and 88 to 112 diastolic with an average of 190 systolic and 98 diastolic. At the end of the 4 to 8 week period, potassium thiocyanate was again started with the same dosage as last given. This resulted in a range of blood pressure with an average of 156 systolic and 92 diastolic blood pressure. The blood pressure tended to remain lower than before treating even after the blood cyanates were reported as only a trace or none at all.

CASE REPORTS

Case I. (Chart I) . . . , a 62-year old white male was first seen October 10, 1941 with a history of hypertension of 8 years duration. Blood urea nitrogen, phenolsulphophthalein, urine concentration and dilution, electrocardiograms and blood cell counts within normal limits. Only symptom of hypertension was severe headache. Blood pressure ranged from 170 to 200 systolic and 96 to 110 diastolic with an average of 180 systolic and 102 diastolic. Thiocyanate begun on December 30, 1941 controlled the headache and a dose of 6 grains maintained a lowered blood pressure averaging 131.2 systolic and 85.8 diastolic on a dosage of 6 grains of potassium thiocyanate and a blood cyanate level averaging 3.4 mg. per cent.

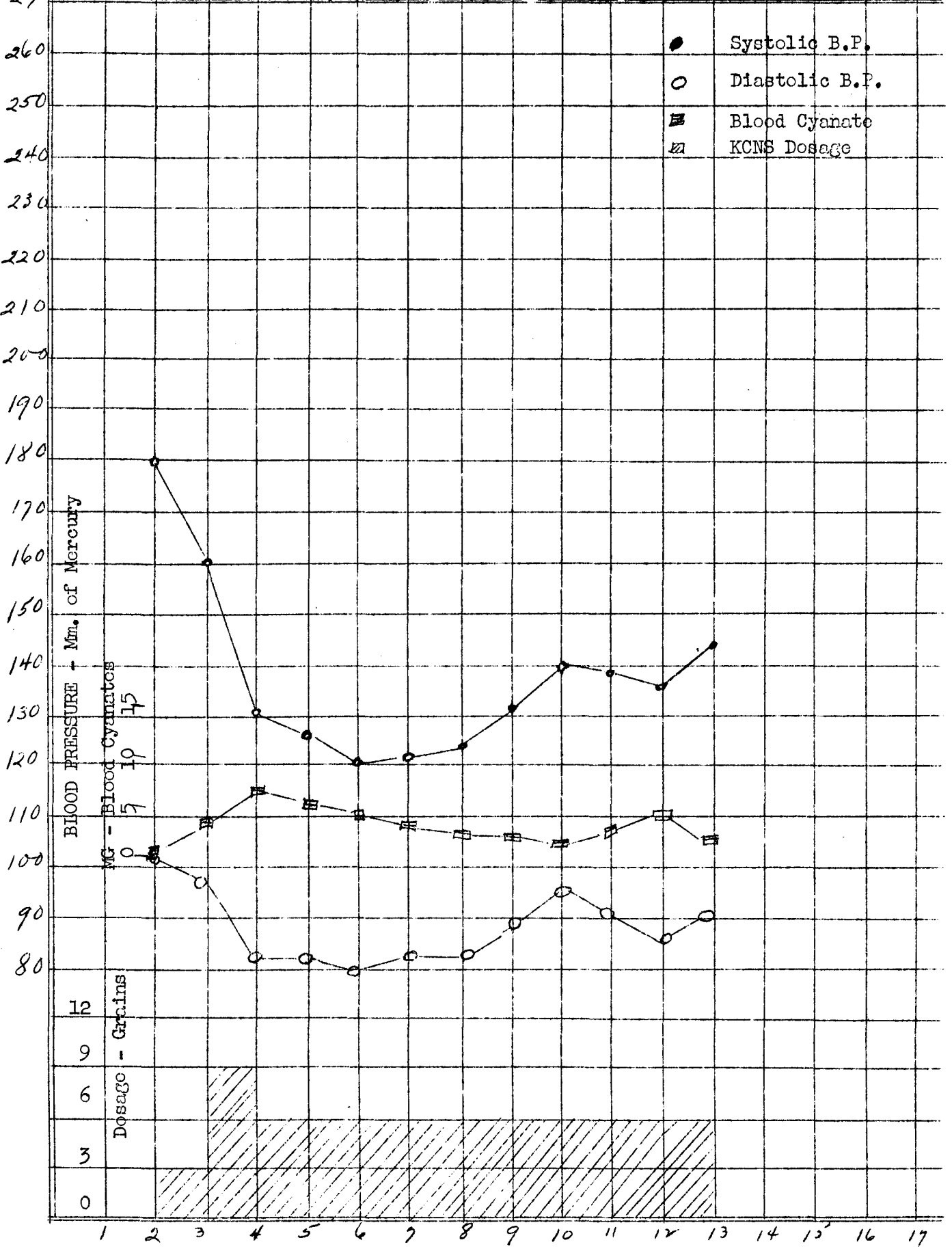
Case II (Chart II) . . . , a . . . year old female, was first seen May 20, 1942 with a history of hypertension of 2 years known duration and no hypertensive symptoms. Laboratory routine tests were within normal limits. Blood pressure before treatment ranged from 210 to 232 systolic and 108 to 120 diastolic with an average of 224 systolic and 112 diastolic. Potassium thiocyanate was started July 2, 1942. On a dose of 6 grains, the blood pressure dropped to an average of 168 systolic and 91 diastolic on an average does of 6 grains and a blood cyanate level averaging 9.8 mg. per 100 c.c. of blood.

CASE I

CHART I

1943

1942 12/30 1/22 2/5 2/19 3/5 4/26 5/7 8/11 10/27 12/3 3/4 3/23



BLOOD PRESSURE - Mm. of Mercury

MG - Blood Cyanates

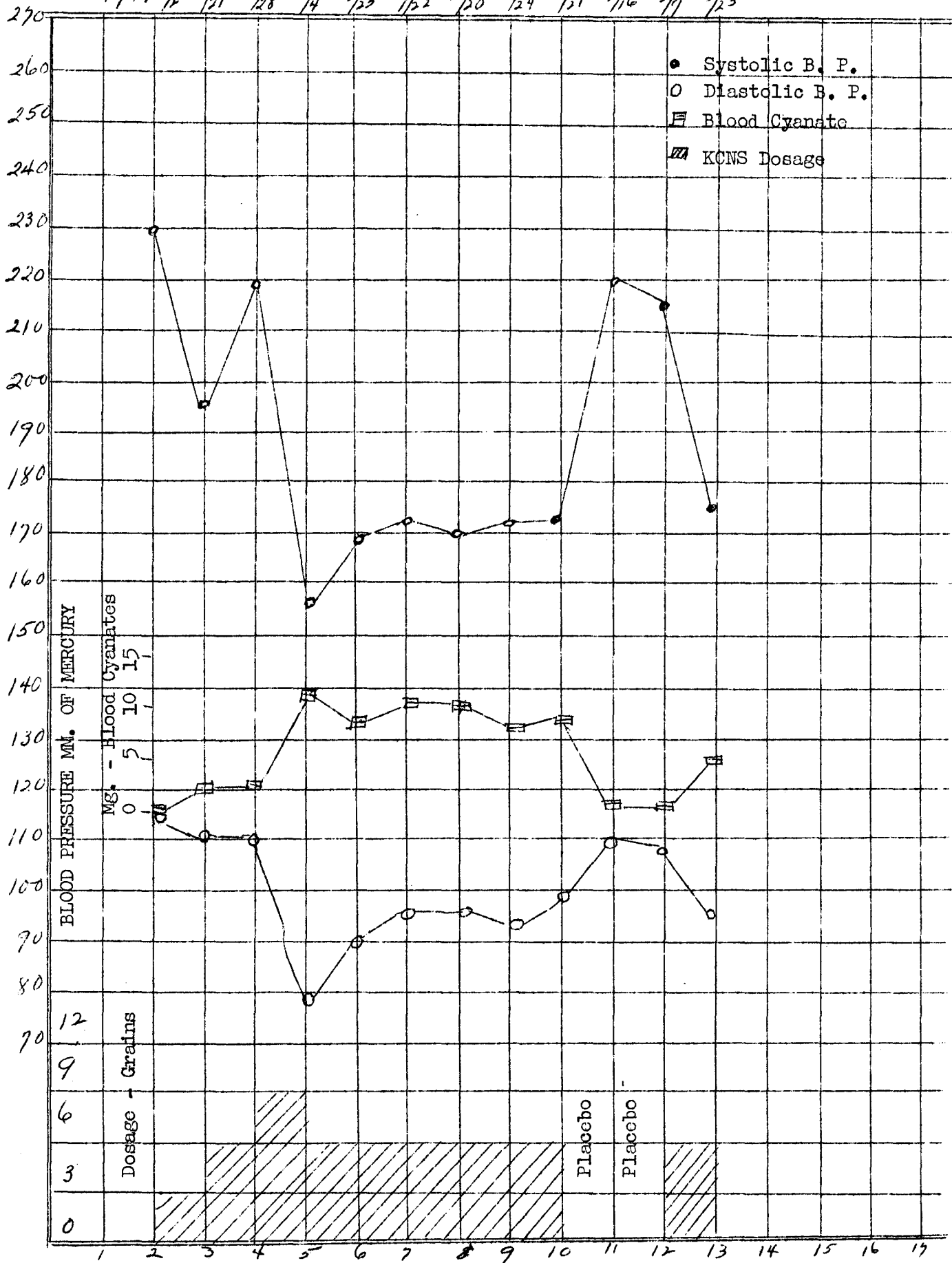
Dosage - Grains

12
9
6
3
0

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

CASE II CHART II

1942 7/12 7/21 7/28 8/4 8/25 9/22 10/20 11/24 1943 1/21 2/16 3/7 3/23



On January 21, 1943 a placebo was given. On February 16th the systolic blood pressure rose from 172 to 220 and the diastolic from 98 to 110 while the blood cyanates were 1.1 mg. per cent. On March 9, 1943 the systolic blood pressure was 216 and the diastolic was 108 and blood cyanates a trace. On this date potassium thiocyanate was again started with 6 grains and on March 23, 1943 the systolic blood pressure was 174, the diastolic blood pressure was 94 and the blood cyanates 5.5 mg. per cent.

COMMENT

Assuming that it is desirable to reduce the blood pressure in hypertensive patients in order to lessen the dangers of cardiac failure, cerebral hemorrhage, and uremia, it is reasonable to believe that any drug that will do so even if moderately or even if only for limited periods, will tend to prolong life. Whether potassium thiocyanate will prolong life in hypertensive people is, of course, the factor that needs more prolonged intensive study. I believe that in potassium thiocyanate, we have a valuable drug in attempting to obtain this end. It is toxic and should only be given under strict supervision and careful laboratory check. Under these circumstances, it is safe but it should only be given to cooperative patients. As in all chronic diseases where medication is used over prolonged periods, it is very difficult to keep patients on treatment especially if they have no symptoms, are feeling better, and at the same time must report at relatively frequent intervals to get blood tests. It is possible, though admittedly difficult, to do this by impressing the patient with the importance of trying to reduce the pressure to avoid the usual hypertensive risks.

SUMMARY

1. Vitamin A had no effect in 20 cases of hypertension.
2. Potassium thiocyanate in 70 cases, resulted in 15% reduction in blood pressure in 32 cases and 10% in 15 cases.

3. Potassium thiocyanate gave symptomatic relief in 43 of 58 patients with hypertension symptoms.
4. Potassium thiocyanate should be used only under strict laboratory supervision and only in cooperative patients.
5. The blood cyanate level should not exceed 12 mg. per cent.
6. The question of the ability of this drug to prolong life in hypertension patients needs more intensive study and control groups over a long period of time.

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VII. GOSSIP

The following extract from a letter from Jerry Hilger to Larry Boies is so good that we are duplicating it for you.

"The foggy docks in England with the roofs blown off and several thousand debarking troops milling about in the murk laden like burros and topped by their inverted kettles makes a memorable picture. But by the time one has hiked through the perfectly opaque English countryside half the ensuing night, been confronted with messy brussel sprouts and a raw mutton pattie for a 6 a.m. arrival breakfast, and climbed under four dirty blankets with overcoat, shoes and all-- by that time the novelty is gone, and getting it all down on paper becomes unimportant. And that seems to be characteristic of all our wartime moves--from the time we coasted past a pretty dim Statue of Liberty in a ferry, right up to and including now. It's interesting but it isn't romantic. It's acceptable, but it is no substitute for being at home. It's ninety-nine per cent waiting. Where the other one per cent is, is still a matter of conjecture to us. We think we are hot on the trail.

England in war or peace should be a nose and throat paradise. I don't believe I've ever seen such a high percentage of personnel afflicted with upper respiratory infections as we had there. The weather and living conditions effectively counteracted all the simple treatment one could apply. By the time one wave of bugs wore itself out, another took over. It was a nuisance. It proved too, that whereas the abdominal surgeon or tropical disease man may have long periods of idleness the nose and throat man always has something to do wherever he is.

By devious shananigans I contrived a two weeks detached leave and went to the English maxillo-facial center south of London. In that two weeks I squeezed in enough maxillary surgery and plastic procedure to compensate me for all the idle months in England. They had an amazing wealth of material from civilian casualties, R.A.F., and R.C.A.F. The men were excellent--Sir Harold Gilles, McIndoe, Kelsey-Frye, and their cohorts. In three years they have discarded a great many old

fetishes and leaned heavily on common sense. I had the run of the place including all the back records--each with serial photographs appended. Tea times and a few "gin times" I spent in question and answer sessions. I read their book and the records in the evenings and questioned by day. The two weeks were filled with a backlog of surgery that had piled up during McIndoe's absence and most days were field days. I have a notebook we can go over when I get back.

I was setting the stage for a visit to Negus and company when the strategy of somebody in authority took us out of England and back into the North Atlantic. The which, incidentally, is a hell of a place to be. The water is 2° from freezing, the waves are 40 and 50 feet high, and the Lord was exceeding kind. Among other things, I was amazed to find what a sensitive labyrinth I have. The trips have been interesting. We haven't had sense enough to be afraid yet. We are not warriors--we are still peaceable citizens. The sight of an empty life boat or deck cargo floating past was always cause for much reflection, and the jutting masts and funnels of a smashed hulk always brought a silent conjecture as to how many were down there. Perhaps if some day we have to jump into a ditch, we'll get mad at the enemy. So far he is an intangible something.

We got down to Mother Earth here in Africa--I've been sleeping on it for the past two weeks; up until then I had a cot. The infections have all cleared up. We are all tan and dirty. It has been a wholly pleasant change from England. There were no regrets on leaving the latter. The people were fine--the weather was execrable. The first few days here the sun was a source of constant amazement and comment. My domicile is a pup tent on the lee side of a large thorn scrub located roughly on the top of a rocky hill. I can't remember when I last ate out of anything but a tin mess kit, or sat down on anything but a rock to do it. The esthetic values of a straddle trench are now well known to the whole group. I am become amazingly adept at washing, shaving, and laundering in my inverted steel helmet.

I've cracked the ice in it on more than one morning. In England the shower water was hot and the shed so cold you became enveloped in a cloud of your own steam as you stepped from under the stream. Here the air and water are equally cold. However, the weather has moderated considerably in the while we have been here, and the insect population is noticeably on the increase. Several large, armour-clad beetle-like creatures have attempted to share my bed roll with me the last couple of nights.

The group is admirably congenial, and I am sure will do good work when given the chance. We seem to see that chance coming soon. Karl is fine, a source of unending humor as you would guess. We are all tough and quite durable. I'm fifteen pounds lighter than I was way back when, and never felt better. Since I can't be home anyway, this sort of life would be my first choice. I thrive on it. My shrunken waistline has resulted in unnumbered pleats and gathers in my trousers, but the fit of our clothes has ceased to concern us."

Gaylord W. Anderson, Major Medical Corps, United States Army, Head of the Department of Preventive Medicine and Public Health, University of Minnesota, has been assigned by the Surgeon-General to direct the Medical Intelligence Division. This service was described in the January 1943 issue of The Reader's Digest, from an article in Colliers. The article states in part: "No matter to what remote region our fighting men go, they are being protected against local diseases, thanks to the research of the army's Medical Intelligence Division.

When we sent soldiers to Trinidad, where 70 per cent of the population in certain arid regions suffers from malaria, Medical Intelligence was prepared. It knew that a local variety of malaria-carrying mosquito breeds in the water cup of an air plant that attaches itself to immortelle trees planted to furnish shade for cocoa groves. Medical officers dispatched troops to cut down the trees and air plants - and malaria was greatly reduced.

Becoming interested in geographical medicine two years ago, the army began collecting health facts from all available sources. The files tell of poisonous sea snakes in the Persian Gulf, and of South Pacific clams as big as meat platters which can grab a swimmer's foot with a bear-trap grasp. In the Burmese jungle are leeches so voracious that they produce anemia in a short time. Yanking them off leaves their heads under the skin, and an infection results.

Scorpions are a problem in North Africa. Liking a warm place to spend the night, these poisonous creatures crawl into shoes just taken off - and sting when the owner puts them on in the morning.

As soon as plans for moving troops overseas are made, requests for data come to Medical Intelligence and an officer is assigned to assemble all available information. His report will contain data on local health officers, if any; on sanitation, sewage disposal, water supply; on buildings which might serve as hospitals, and information on specific diseases and dangerous pests.

No fact is too small to be included in Medical Intelligence data if it bears on the health and well-being of troops. One report contained the story of a crab, found in certain Pacific islands, which lives on coconuts. Opening the nut, it eats part of the meat and leaves the rest. Rotted coconuts form an ideal breeding place for flies which spread dysentery, typhoid and other diseases. Instructed in advance how to conquer this evil, medical officers had the coconut palms cut down, thus destroying the crabs' source of food.

Such information collected by Medical Intelligence spells the difference between an army ready for action and one ready for the hospital."

Congratulations - - Gaylord!