and Ag-AgCl electrodes were used in the determinations. One electrode was strapped on the lower abdomen above the symphysis pubis; the other, placed on or alongside the cervix. Using a chart speed of 1 inch in 2 minutes, records were taken for periods of 10–15 minutes. The results for the malignancies are shown in Table 1; for the nonmalignancies, in Table 2.

TABLE 1

MALIGNANCY

Case	Age	Diagnosis	Mv	
			Initial P.D.	Mean P.D.
SR	54	Metastatic vagina T	−6	−12
MK	94	Stage IV	−21	−27
SR	(Repeat)		−9	−9
RW	65	Stage IV	−27	−28
CB	63	Stage IV	−10	−11
MM	54	Stage II	−36	−33
MP	45	Stage IV	−30	−22
ET	63	Stage IV T	−36	−37
TD	53	Metastatic bladder Stage IV T	−45	−45
MM	54	Stage II T	−27	−27
CB	63	Stage IV	−10	−13
LJ	51	Fibroids–ovarian cyst Stage II	−3	−6
MD	63	Stage I	−21	−25
AS	54	Carcinoma of fundus	−3	−7

T = Treated

The cases were selected from patients on the gynecological service in Bellevue Hospital and number 30. It will be noted that all the cases of malignancy showed a marked negativity of the region of the cervix with respect to the symphysis. In these patients the diagnosis was confirmed by pathological examination.

TABLE 2

NONMALIGNANCY

Case	Age	Diagnosis	Mv	
			Initial P.D.	Mean P.D.
TM		Fibroids	+9	−3
SR	44	Fibroids	+33	+28
LB	32	Pap serous cyst Adenoma	+33	+27
AD	43	Bleeding fibroids	−24	−28
WD	22	I.D. abscess P.I.D.	+6	−12
TD	22	Cystic ovary	+16	+16
FL	22	Menorrhagia	+6	−3
EJ	27	Fibroids P.I.D.	+3	−3
BM	25	Salpingitis Menorrhagia	+30	+26
MJ	34	Salpingitis Fibroids	−6	−14
MB	57	Bleeding from estrogen withdrawal	+30	+30
MR	27	Pregnancy, 3 months	+6	−9
TW	28	Pregnancy with bleeding	+21	+17
ER	46	Amenorrhea	+30	+28
SE	35	Fibroids	+39	+35
MF	22	Condylomata	−21	−25
HL	28	Pregnancy, 5½ months Mild P.I.D. ovarian cyst	+24	+20

By contrast, the patients with nonmalignancy showed, under the same conditions, an almost uniform positivity of considerable magnitude in the region of the cervix. Three exceptions are to be noted, explanations for which require further study.

Treatment by X-ray therapy or by radium apparently does not affect the measurements.

The method employed in this study is obviously an adjunct to other diagnostic procedures, and in no sense should it be construed as a substitute for them. The study is being continued, and a full report will be made at a later date.

This preliminary account is offered in the hope that it will stimulate studies by others.

The Effect of Combining Sodium Benzoate With Oral Penicillins[1]

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Diodrast (*8*), para-aminohippuric acid (*1*, *6*), benzoic acid (*3*), and sodium benzoate (*2*) have been reported as effective in elevating and prolonging penicillin serum levels, possibly by competition for renal tubular excretion. Bronfenbrenner and Favour (*3*) obtained at least a 2-fold increase by combining benzoic acid orally with intramuscular injections of sodium penicillin. Bohls and co-workers (*2*), using a total dose of 8.4 grams of sodium benzoate orally and a mixture of aluminum potassium sulfate and penicillin intramuscularly, reported assayable serum levels 28 hours following a single 50,000-unit injection. These same authors made determinations on an oral tablet containing alum-precipitated penicillin and sodium benzoate. The published data show assayable levels in 6 out of 10 individuals 24 hours after a single 100,000-unit dose. Both groups of investigators used infected individuals as subjects.

During the course of studies on oral penicillin the authors examined several preparations in combination with sodium benzoate. The present communication deals primarily with the effects observed. The subjects were 10 healthy adults who, with one exception to be mentioned later, participated in the entire study. Neither the diet nor the fluid intake was restricted; but food and fluids were avoided for a minimum of 1½ hours before administration of penicillin. The compounds were tested at one-week intervals. In all instances the test dose was 100,000 units of penicillin either alone or together with 1.2 gram of sodium benzoate. Blood was collected ½, 1, 1½, 3, and 6 hours later for serum level determinations, which were carried out by the method of Randall, *et al.* (*9*) and controlled for antisubtilis factor as described by Chandler and co-workers (*4*).

[1] These studies were made possible by financial aid from Hynson, Wescott and Dunning, Inc., and Commercial Solvents Corporation.

The authors gratefully acknowledge the technical assistance of Catherine C. Dietz and Cecelia Chemerda.

The crystalline sodium salt[2] used in these studies was reconstituted in water from the dried state. The aluminum salts[3] were received as unbuffered tablets with and without sodium benzoate. The alum-precipitated, penicillin-sodium benzoate tablet is identical with that reported on by Bohls and co-workers (*2*). The crystalline potassium penicillin was contained in gelatin capsules[2] and, when indicated, was taken at the same time as, but separately from, the sodium benzoate tablets.

TABLE 1

AVERAGE SERUM CONCENTRATION IN UNITS/ML.

Penicillin salt	Hours following administration (100,000 units)					
	½	1	1½	3	6	Average
Sodium	0.038	0.018	0.012	0.003	*	0.014
Aluminum	.009	.015	.015	.006	*	.009
Aluminum + sodium benzoate	.078	.101	.090	.027	.003	.060
Alum-ppt. + sodium benzoate	.054	.094	.094	.027	.003	.054
Potassium	.050	.040	.021	.009	*	.024
Potassium + sodium benzoate	.100	.136	.062	.024	.012	.067

* No assayable level with any of the 10 subjects.

The average serum concentrations for the 10 subjects appear in Table 1. To facilitate comparisons, the over-all averages for each preparation are also presented. In the absence of sodium benzoate none of the penicillin salts produced an average level above 0.05 unit/ml. or an assayable level at 6 hours. In contrast, the simultaneous administration of sodium benzoate resulted in maximum averages approximating or exceeding 0.1 unit/ml. and, in some instances, assayable levels at 6 hours.

The striking variation in individual response deserves emphasis. When averages were computed from the levels produced by each subject for all six preparations, it was found that the figures ranged from .009 to .073, an 8-fold difference. One subject did not show a single assayable level when the benzoate salt was omitted. In contrast, another subject accounted for all of the 6-hour levels recorded in Table 1. In passing, it should be mentioned that a subject who produced relatively high levels with one preparation also did so with the remaining preparations. Similarly, the "poor absorbers" remained relatively low, regardless of the preparation being employed. Because individuals vary markedly in their ability to absorb orally administered penicillin, the indiscriminate use of any one such preparation is not justified until it can be demonstrated that none of a large number of test subjects fails to develop therapeutically effective serum levels.

The inaccuracy of serum penicillin determinations has been repeatedly emphasized by the authors cited earlier. Although the alum-precipitated, penicillin-benzoate tablet included in the present study is apparently identical with that employed by Bohls and co-workers (*2*), the high and prolonged levels reported by those authors were not seen. As an explanation for the discrepancy it should be pointed out that their subjects were infected persons who might be expected to show higher levels than normal individuals and who are reputed to produce larger amounts of antisubtilis factor (*5*). Certain of the prolonged levels reported by Bohls could have been due to antisubtilis factor which was apparently not taken into consideration. With respect to the present study, however, no instance of complete inhibition was observed in the clarase controls.

The present authors were impressed by the need of close inspection of the tests for evidence of growth. The test organism (*Bacillus subtilis*, N.R.R.L. # 558) usually developed in broth (2 per cent tryptose extract) as a sediment with some diffuse turbidity rather than as a pellicle. Careful observation often revealed a small amount of sedimented growth or a faint turbidity. Final readings were made after 21–24 hours incubation, and the levels were frequently lower than those recorded 5 hours earlier. Therefore, a standardized incubation time is desirable.

The ability of sodium benzoate to increase and prolong serum levels appears to be established. The choice of a dose of 1.2 gram/100,000 units, as employed in the present study, was purely arbitrary. In view of the relatively innocuous nature of this compound (*7*), the value of using larger amounts in combination with oral penicillin should be determined.

One subject in the present study developed a reaction which was attributed to penicillin sensitization. Fifteen minutes after the administration of the third compound urticaria appeared, followed later by edema. No other untoward effects were noted.

[2] Kindly supplied by Dr. L. W. Smith, of Commercial Solvents Corporation.

[3] Kindly supplied by Dr. Roger Reid, of Hynson, Wescott and Dunning.

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Action of Thiamine Applied Directly to the Cerebral Cortex

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It is generally claimed that vitamin B_1 (thiamine) exerts influence on the nervous functions. This assumption is based more on data obtained from deficiency states than on an effective action of thiamine on the specific functions of the nervous system. Indeed, it has been verified that this vitamin presents no typical or characteristic pharmacological effect on normal animals. Large doses by the intravenous route are tolerated, showing only discrete reactions in the blood pressure or urinary excretion (*7*, *12*). Death occurs by respiratory failure (*12*).

On the other hand, there is some experimental evidence indicating a possible association of thiamine with acetylcholine in the processes of nervous excitation. Binet and Minz (*3*) have