

THE EFFECTS OF PYRIDOXINE (VITAMIN B<sub>6</sub>) ON PERSISTENT ADOLESCENT ACNE<sup>1, 2</sup>NORMAN JOLLIFFE, M.D., LOUIS A. ROSENBLUM, M.D.,  
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The prominence of skin lesions in avitaminosis in experimental animals has stimulated the investigation of nutritional factors involved in dermatological conditions in man. The experimental deprivation of nicotinic acid, riboflavin and pyridoxine are followed by skin lesions in suitable animals which respond to the administration of the specific vitamin. It is thus seen that many of these experimental skin lesions are the result of deficiency in some fraction or fractions of the B-complex (1). In man the response of the skin and mucous membrane lesions of pellagra to the administration of adequate amounts of nicotinic acid is well known. Recently, skin lesions characterized by a nasolabial dermatitis and a cheilosis which respond promptly to treatment with riboflavin have been demonstrated as due to a deficiency of riboflavin (2). Gross (3) has recently reported the successful use of a crude liver extract and parenteral vitamin B-complex in the treatment of a group of patients who presented diverse cutaneous eruptions which although apparently non-specific in type did have in common a seborrheic diathesis. He states that he has been unable to duplicate the effect of the whole vitamin B-complex, as contained in yeast or liver, with pure nicotinic acid or riboflavin; pyridoxine was not used.

A specific dermatitis occurring in vitamin B<sub>6</sub> (pyridoxine) deficient rats has been described by Györgi (4) as "rat acrodynia." These lesions in the rat are seborrheic in nature and may be the analogue of certain seborrheic diseases in man. A further step in the comparative dermatology of vitamin B deficiencies has been made by Smith, Smith and Calloway (5). They produced, experimentally, sebaceous gland lesions in the rat by a diet deficient in the entire B<sub>2</sub>-complex. These lesions were cured or prevented by crude aqueous liver extracts, by autoclaved yeast or by a combination of riboflavin and pyridoxine. In the same report the authors also described a sebaceous gland syndrome frequently found associated with pellagra which they have termed "dyssebacia." This lesion is characterized by the presence of plugs of inspissated sebum projecting from the sebaceous follicles and responds readily to autoclaved yeast and crude extracts of liver. Thiamine, riboflavin and nicotinic acid were not nearly as effective as yeast and liver.

We have observed the presence of "dyssebacia" in many, though by no means in a majority, of patients with pellagra and ariboflavinosis and in many alcoholics without anatomic evidence of deficiency disease. The administration of

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<sup>2</sup> From the Student Health Service, New York University, New York, N. Y.

thiamine, nicotinic acid and riboflavin were without significant effect on the "dyssebacia" but there was usually a good result when the whole B-complex in the form of a good diet, and brewer's yeast or vegex or yeast concentrates was administered.

When pyridoxine became available in pure form, it therefore seemed logical to test its efficacy in subjects having adolescent acne. As a preliminary test, 10 subjects with persistent severe adolescent acne were selected. The subjects were freshmen university students selected at random as they presented themselves for their routine health examinations. Their ages varied from 17 to 23 years, and the duration of the acne was from one to seven years. Many of them had run the gamut of all the prevalent forms of therapy with only temporary or indifferent success. Physical examination and laboratory data were all essentially within normal limits. None presented recognized clinical evidence of deficiency of other members of the vitamin B-complex, and none had par-

TABLE 1  
*Treatment of acne with pyridoxine*

NO.	CASE	SEX	AGE	DURATION OF ACNE	DURATION OF OBSERVATION	EFFECTIVE DOSE	RESULTS
				<i>years</i>	<i>months</i>	<i>mg.</i>	
1	H. W.	M	17	4	11	50	Improved
2	F. F.	F	17	1	10	30	Improved
3	F. H.	M	23	7	5	50	Cleared
4	H. P.	M	18	3	1	20	Improved
5	M. L.	M	21	5	4	20	Improved
6	A. P.	M	17	6	3	50	Improved
7	E. I.	F	18	2	10	50	Cleared
8	V. K.	M	19	5	11	50	Cleared
9	H. F.	F	17	4	6	20	Improved
10	S. L.	M	18	2	1	50	Improved

ticular food idiosyncrasies, gastrointestinal diseases, or other conditions that would either increase the requirements or prevent absorption and utilization of the B-vitamins.

Treatment with pyridoxine was instituted as follows:

Each subject was directed to take a 10 mg. tablet of pyridoxine<sup>3</sup> five times a day for the first three days then to continue with two tablets a day. The patients were instructed to continue any form of local therapy that they were using at the time the pyridoxine regimen was instituted, but no new procedure was permitted. The subjects were observed at weekly intervals and the dosage of pyridoxine was increased if necessary. Table 1 summarizes the pertinent data and the therapeutic results in these 10 patients. In three of the subjects (Nos. 3, 7, 8) the acne lesions cleared completely, while all the others noted varying degrees of improvement during the administration of the pyridoxine. One effect observed in practically all the cases, irrespective of degree of improvement

<sup>3</sup> Supplied through the courtesy of Merck & Co., Inc., Rahway, N. J.

of the acne, was a decrease in oiliness of the skin. Generally it took seven to ten days of continued administration of the effective dose of vitamin B<sub>6</sub> to obtain definite improvement; although in one case (No. 8), remissions or exacerbations could be observed in as short a time as three days. In six of the ten cases the effective dose was found to be 50 mg. daily in divided doses. Administration of more than 50 mg. daily, in those subjects who were improved, but not entirely relieved did not cause further improvement. Maintenance of improvement, on discontinuing pyridoxine was observed in four (Nos. 2, 4, 5, 9) subjects. The remaining 6 subjects, all of whom exhibited relapses on discontinuing pyridoxine, had remissions on again instituting pyridoxine therapy. In those subjects who did not relapse on discontinuing pyridoxine, it is open to doubt if the apparent improvement was due to pyridoxine.

In view of these apparent good results in some subjects having adolescent acne it was decided to perform a controlled study on a larger group of university students having persistent adolescent acne. This second controlled experiment was carried out with subjects chosen from the same group of freshmen university

TABLE 2  
*Summary of results in second (controlled) study treatment group*

RESULT	PYRIDOXINE		CONTROL	
	NUMBER	PER CENT	NUMBER	PER CENT
Cleared.....	9	24	0	0
Improved.....	19	57	7	20
Unchanged.....	6	16	19	54
Dropped out.....	3	8	9	26
Total.....	37		35	

students as the preliminary study and in addition students from other classes with persistent acne who requested treatment. In all, 72 subjects were available. The ages varied from 16 to 29 years with the duration of acne from 1 to 10 years. As in the first study many of these subjects had tried many different forms of local and systemic treatment with notable lack of success. As these subjects presented themselves they were alternately placed in either the group that was to receive pyridoxine or in a group that was given tablets of starch and sugar similar in size and appearance to the pyridoxine tablets. None of the subjects presented any anatomical evidence of deficiency of thiamine, riboflavin, or nicotinic acid, nor were there any with gastrointestinal diseases or other conditions known to affect the requirement or utilization of the members of the vitamin B-complex.

The initial dosage of pyridoxine was 25 mg. twice daily, and this was increased as necessary to 250 mg. (50 mg. five times daily) in several of the subjects before definite improvement or actual clearing of the lesions could be obtained.

Table 2 summarizes the results of treating 37 subjects with pyridoxine as compared to the results in 35 control subjects. In the pyridoxine treated group

there were 9 (24.3%) whose acne completely cleared, 19 (51.5%) who showed definite improvement and 6 who exhibited no change whatsoever. On the other hand, in the control series, there were none whose acne cleared, only 7 (20%) that experienced some degree of improvement and 19 whose acne remained unchanged. It is of some significance that 9 in the controlled group dropped out, while only 3 discontinued treatment with pyridoxine.

In three of the control subjects whose condition remained unchanged after 4, 6, and 7 months treatment respectively, the pyridoxine tablets were substituted for the placebo tablets without the subjects' knowledge. Administration of the pyridoxine produced complete clearing of the acne lesions in one and three months time in two of the subjects, with maintenance of the improvement as long as the pyridoxine was continued. These subjects also reported a considerable decrease in oiliness of their skins, a phenomenon which had also been noted in 13 of the treated group.

#### DISCUSSION

The effectiveness of pyridoxine would appear at a first glance to indicate that certain cases of acne have a nutritional factor in their etiology. The stage at which the nutritional deficiency might manifest itself is probably in the secondary phase of the acne complex, where the hyperactive sebaceous gland becomes the seat of an inflammatory process. Evidence suggesting the value of the B-vitamins in acne may be found in the prevalent use of yeast and in crude liver extract. Sutton (6) in 1928 observed improvement in acne cases when he fed his patients diets high in liver. In 1939 Marshall (7) in reporting the use of a parenteral liver extract in acne suggested that probably a specific skin factor, "S" was present in the liver extracts. In further experiments (8) he found that boiling or autoclaving his liver extracts would not destroy the antidermatitic effects. Such treatment of liver extract destroyed the thiamine and possibly some of the riboflavin, but nicotinic acid and pyridoxine remained because of their heat stability. In a comprehensive analysis of the acne complex Stokes and Sternberg (9) have reviewed the results of vitamin therapy in acne and conclude that large doses are necessary and that the results with high potency yeast extracts plus liver extracts and iron have been worthwhile.

Any explanation of the role of pyridoxine in clearing the acne lesions in some subjects, must, at this time, be speculative. If the primary seborrheic process is considered the human homologue of rat acrodynia, then we may consider the action of pyridoxine as one of substitution, and acne may, at least in a number of instances, be considered as a pyridoxine deficiency disease in man.

Many investigators, however, believe disturbances in lipid metabolism, either primary or associated with endocrine changes, to be an etiologic factor in acne. Sutton (10) in a recent communication has postulated that acne vulgaris is a metabolic disease dependent on a defect in the ability of the patient to metabolize the dietary lipoids and resulting in the collection of oily material in the sebaceous glands with the inciting of a pustular lipoidosis. Hormonal influence in the production of acne vulgaris has received an enthusiastic reception particularly

with reference to therapy. However, the results of controlled experiments have been reviewed by Stokes and Sternberg (8) who conclude that the results of controlled experiments have been disappointing. Hamilton (11) has experimentally produced acne in male castrates by administration of testosterone. This observation plus the great prevalence of acne in the adolescent, at which time the blood of the male and probably the female is subjected to an increased amount of testosterone probably indicates that this substance plays some role in the high incidence of acne at puberty. Puberty is also a period when other hormonal changes and imbalances may operate to produce a disturbance in seborrheal function which precedes the acne lesion. Sutton (10) believes that the endocrine imbalance operates through a deficiency of thyroid secretion and its control of lipemia. But this does not explain the persistence of acne vulgaris well past the adolescent period and in the absence of clinical or laboratory signs of endocrine dysfunction. To explain this we must consider disturbances of sebaceous function, interference with epithelial resistance to infection and disturbances in lipid metabolism as factors in persistent post-adolescent acne. Vitamin intake or assimilation and utilization are important because of the well known role of members of the vitamin B-complex in the health of epithelial structures.

Physiologically the functions of pyridoxine may be connected with the utilization of unsaturated fatty acid since Birch (12) has demonstrated that apparently two factors, pyridoxine and a factor that is fat soluble and found in the fatty acid fraction of maize oil are concerned in the production and cure of the acrodynia-like dermatitis of rats. It is suggested that the physiological function of pyridoxine is connected with utilization of the unsaturated fatty acids. On this basis, then, pyridoxine might function through its corrective action on a deranged fatty acid or lipid metabolism, although this would not invalidate the concept of a direct physiological action of pyridoxine on the activity of the sebaceous apparatus of the skin. In support of this second suggested mechanism is the marked action of the pyridoxine in reducing the oiliness of the skin, even though the effect on the acne lesions per se may not have been remarkable.

#### CONCLUSIONS

1. The oral administration of pyridoxine (vitamin B<sub>6</sub>) was effective in improving the skin of some patients with persistent post-adolescent acne vulgaris.
2. In many of the subjects treated with pyridoxine a marked reduction in the oiliness of the skin, even in some case to the point of actual dryness and scaling, was noted. This occurred independent of the effect on the acne.
3. The effective oral doses varied from 50 to 250 mg. daily in divided doses.

#### REFERENCES

- (1) SULLIVAN, M., AND NICHOLLS, J.: The nutritional approach to experimental dermatology. *J. Invest. Dermat.*, **3**: 309, (Aug.) 1940.
- (2) (a) SEBRELL, W. H., AND BUTLER, R. E.: Riboflavin deficiency in man; preliminary note. *Pub. Health Rep.*, **53**: 2282, (Dec. 30) 1938.  
(b) JOLLIFFE, N., FEIN, H. D., AND ROSENBLUM, L. A.: Riboflavin deficiency in man. *New England J. M.*, **221**: 921, (June) 1939.

- (3) GROSS, P.: Non-pellagrous eruptions due to deficiency of Vitamin B complex. *Arch. Dermat. & Syph.*, **43**: 504, (March) 1941.
- (4) GYÖRGI, P., AND ECKARDT, R. E.: Further investigation on Vitamin B<sub>6</sub> and related factors of the Vitamin B<sub>2</sub> complex in rats. *Biochem. J.*, **34**: 1143, (Sept.) 1940.
- (5) SMITH, S. G., SMITH, D. T., AND CALLOWAY, J. L.: Dysfunction of the sebaceous glands associated with pellagra. *J. Invest. Dermat.*, **4**: 23, (Feb.) 1941.
- (6) SUTTON, R. L.: Liver diet in acne vulgaris and in furunculosis. *Arch. Dermat. & Syph.*, **18**: 887, (Dec.) 1928.
- (7) MARSHALL, W.: Probable "S" factor in the treatment of acne vulgaris with liver extract. *M. World* **57**: 101, 1939.
- (8) MARSHALL, W.: Further studies with treated liver extract therapy for acne vulgaris. *J. Invest. Dermat.*, **2**: 205, (Aug.) 1939.
- (9) STOKES, J. H., AND STERNBERG, T. H.: A factor analysis of the acne complex with therapeutic comment. *Arch. Dermat. & Syph.*, **40**: 345, (Sept.) 1939.
- (10) SUTTON, R. L.: Acne vulgaris. *J. Missouri State M. A.*, **38**: 50, (Feb.) 1941.
- (11) HAMILTON, J. B.: Male hormone substance: A prime factor in acne. *J. Clin. Endocrin.*, **1**: 570, (July) 1941.
- (12) BIRCH, T. W.: The relation between Vitamin B<sub>6</sub> and the unsaturated fatty acid factor. *J. Biol. Chem.*, **124**: 775, (Aug.) 1938.