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Influence of Arginine on Oligospermia.

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Shettles observed that oligospermia, occurring in men fed an arginine-deficient diet, was relieved when arginine was returned to the diet.[1] Since the therapeutic approaches to oligospermia have been unsatisfactory, it appeared that arginine might prove helpful in clinical cases of oligospermia.

The present report is an account of observations made in this laboratory on 23 patients with oligospermia. Eighteen received large amounts of pure arginine and minimal quantities of lysine, pyridoxine, and tryptophane as supplements to their usual diet. Five patients received no specific therapy.

Methods. A complete medical history and physical examination in each of the 23 patients studied failed to reveal any known etiological factors contributing to the oligospermia. Thirteen had received previous hormonal therapy which failed to influence their low sperm counts. Ten men whose oligospermia was discovered during the present study had received no previous therapy.

The patients' semen was examined every 4 weeks for volume, sperm-motility, and concentration of spermatozoa according to the method of Macomber and Saunders.[2] The specimens were obtained by masturbation or coitus interruptus after the patients had abstained from intercourse for 4-5 days.

After the semen specimens were studied from 1-3 months, the patients ingested daily, as uncoated tablets, 1.8-2.7 g arginine and 40-60 mg each of lysine, pyridoxine and tryptophane in addition to their usual diet.† Therapy lasted for 8 months and terminated after that interval in most cases because the sperm concentration had not risen significantly.

Table I summarizes the results of the study and includes pertinent clinical data as well as the sperm counts observed.

Group I includes 5 patients who were studied before, during, and after amino acid therapy. The initial sperm count of these men averaged 12.9 million per cc. One month later, just prior to the amino acid therapy, the average concentration was 11.2 million per cc. After 8 months of treatment, the average sperm count had increased to 47.0 million per cc. The amino acids were then discontinued and 8 months later, the sperm counts averaged 28.1 million per cc. Although these patients received much larger quantities of arginine than Shettles' subjects, their sperm counts did not increase rapidly or to normal levels as Shettles observed in his arginine-deprived men.[1] One patient in our group developed a normal count (100 million per cc) during treatment, but conception did not occur.

The 7 patients in Group II demonstrated a drop in sperm count (from 26.0 to 12.4 million per cc) in the 3-month pretreatment period. After taking arginine for 7 months, these men had an average sperm count of 21.8 million per cc. Since the sperm concentration under arginine did not even attain the initially low levels, it appears that the response noted was not significant. None of these patients' wives became pregnant during the study.

* The department is in part supported by the Michael Reese Research Foundation.

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† The amino acids were generously supplied by Dr. Clair Folsome, Ortho Research Foundation, Raritan, N.J.

TABLE I.
Summary of Results.

Group	No. of pts.	Age	Infertility (years)	Arginine treatment (mo.)	Conceptions	Sperm counts ($\times 10^6$ per cc)			
						Initial	Pretreatment	At end of treatment	Final after treatment discontinued
I	5	35	5.4	8	0	12.9 (4-22)	11.2 (0-18)	47 (15-100)	28.1 (7-45)
II	7	34	4.0	7	0	26.0 (0-75)	12.4 (0-30)	21.8 (0-70)	—
III	6	32	4.1	8.8	0	—	17.3 (5-46)	26.4 (1.5-57)	—
IV	5	36	5.5	—	2	20.3 (0-35.5)	40.2 (0-104)	—	—

The numbers indicate the averages for the group. The numbers in parentheses indicate the ranges observed.

The oligospermia of the 6 patients in Group III had been present 1.5-9 years. They received arginine after the first semenalysis in this laboratory, and 8 months later the average sperm count had risen to 26.4 million per cc from the initially recorded 17.3 million per cc. No pregnancies occurred in this group during the study.

The sperm counts of the 5 men in Group IV rose during the period prior to contemplated therapy. These patients did not receive the amino acids, since the spontaneous increase in sperm concentration might have been interpreted as a direct result of treatment. In the average 3-month period of study, the sperm counts of these men rose from an average of 20.3 to 40.2 million per cc. The wives of two of the patients with low counts became pregnant in this period. Although one patient attained a sperm count of 140 million per cc, conception did not occur.

Discussion. Arginine (with small amounts of lysine, pyridoxine, and tryptophane) did not solve the primary problem of the 18 treated infertile patients in this study. The increase in sperm counts of the untreated control group was as great as that of the treated group. None of the wives of the treated subjects became pregnant during the study, while 2 pregnancies occurred among the couples of the untreated group.

All the patients in this series gave a history of adequate protein intake. Shettles' studies on the beneficial effects of arginine on oligospermia were carried out on men and animals who became oligospermic on an arginine-deficient diet and then returned to normal status in a few weeks with the addition of arginine to the deficient diet.[1] In view of the results obtained in the present study, it appears that the beneficial action of arginine on impaired spermatogenesis is specific for oligospermia due to arginine deficiency. Its use for this purpose should be reserved for patients with oligospermia who exhibit or give the history of a deficient intake of arginine.

Summary. 1. Eighteen infertile men with oligospermia received 1.8-2.7 g of arginine

and minimal amounts of lysine, pyridoxine, and tryptophane in tablet form for 8 months.

2. The tendency for sperm concentration to increase was as great in the untreated group as in the treated groups.

3. Although no pregnancies occurred in the treated groups, 2 pregnancies were recorded among the wives of 2 of the control subjects.

4. It appears that amino acid therapy for oligospermia should be reserved for those patients who exhibit or give the history of inadequate protein intake.

The author wishes to acknowledge with thanks, the aid and encouragement of Dr. R. Levine, Director of the Department of Metabolism and Endocrinology, in this work. Dr. A. Koff was most cooperative in referring patients for study.

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Effect of Para-Aminobenzoic Acid on Fever and Joint Pains of Acute Rheumatic Fever.

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Para-aminobenzoic acid has been shown to be beneficial in the treatment of the rickettsial group of diseases.[1-4] With the idea in mind that acute rheumatic fever shows a vasculitis[5] which is similar in some respects to that produced by the rickettsial diseases, and that both diseases are again similar in that they may be aggravated by the use of the sulfonamides,[6-8] para-aminobenzoic acid has been used experimentally to determine what effect, if any, it would produce on the fever and joint pains of acute rheumatic fever. There is one report[9] in which it was used to sustain the salicylate level in the blood, and in which case the para-aminobenzoic acid, when used alone, apparently exerted no effect for the time during which it was administered.

Material and Procedure. Nine patients in which the diagnosis conformed to accepted criteria[10] have been given the drug. These were all colored children ranging in age from 6 to 12 years. Eight of them had joint pains. In some cases they were mild and in others they were severe to the point of incapacitation. Sickle cell anemia was carefully excluded in each instance.

Para-aminobenzoic acid powder was used and an immediate dose of 3-4 g was given, followed by a maintenance dose of 1-3 g given at 2-3-hour intervals. Blood levels were taken within an hour of the administration of the drug. Alkalis were given to prevent the development of acidosis. Salicylates, penicillin, and sulfonamides were withheld, except prior to the establishment of a definite diagnosis, or when they were necessary

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