June 23, 1977

Dr. Don W. Fawcett, President
American Society of Andrology
Department of Anatomy
Harvard Medical School
25 Shattuck Street
Boston, Mass. 02115

Dear Dr. Fawcett,

When I wrote to you last, I was concerned about the new journal "Archives of Andrology" and the consequences of three journals competing for manuscripts and readership in a relatively restricted area. Your letter of JUne 20 indicates that now we are facing the choice between three and four andrological journals.

I have serious reservations about the probability of all these journals maintaining good standards of quality and indeed surviving. However, the possibility of USA-based and ASA-controlled journal is certainly attractive. To me, the chances of securing enough subscriptions and receiving enough good manuscriptsto make this journal a success are extremely slim, but from the enthusiastic support of Williams and Wilkins I must conclude that my estimations may very well be wrong. If you are persuaded by the arguments of Drs. Rosemberg and Albert and by the offer of Williams and Wilkins that the "American Journal of Andrology" can become a viable and "respectable" periodical, than we should all help in starting this journal.

I am sorry if I did not go very much beyond re-iterating my original concerns.

With warmest regards,

Andrzej Bartke

American Society of Andrology

June 20, 1977

Dr. Andrzej Bartke
Worcester Foundation for Experimental Biology
222 Maple Avenue
Shrewsbury, Massachusetts 01545

Dear Andrzej:

I am writing to you as a member of the Council of the American Society of Andrology, to seek your advice on a matter of some urgency. The details are set forth in the enclosed memorandum from Dr. Eugenia Rosemberg, Chairperson of our Publication Committee.

In the period since organization of our Society and adoption of Andrologia as our official publication, very few of our members have submitted papers to the journal, and a number have expressed concern over the quality of this publication. It seems clear to me therefore that Andrologia is not adequately serving the interests of our membership.

Negotiations of the Comité Internationale d'Andrologie (CIDA) with a new publisher, Scriptor, for publication of an International Journal of Andrology have proceeded rather preciptously to an advanced stage. Since our representatives in the governance of CIDA were strong advocates of separation from Andrologia, it is regrettable that we cannot now follow up this initiative by giving wholehearted support to the proposed International Journal of Andrology which will be published by Scriptor under the sponsorship of CIDA. The unexpected advent of another journal, Archives of Andrology, unrelated to A.S.A. or CIDA complicates the problem and raises the question as to whether a field which until recently had no specialty journal can now support three competing publications. I am persuaded however, that (1) economic considerations, (2) the basic differences in policies of European and American journals, and (3) the problems involved in securing for the A.S.A. sufficient control over the standards and policies of a journal based in Europe, make it necessary to give serious consideration to an American Journal of Andrology, owned by the A.S.A. and published in this country.

I hope you will give serious consideration to this matter and let me have your advice as soon as possible. I am sensitive to the criticism

that the founding of the A.S.A. and its governance in its first two years has depended heavily upon the dedication and initiative of a relatively small group of enthusiastic proponents. In my experience, this is always true in the beginning of any new society. It is time now, however, to broaden the base of support for important decisions such as the one I now place before you. As the elected representatives of the membership, I hope to hear from all of you soon. We are all busy and would prefer to avoid an interim meeting of the Council. However, if there is substantial disagreement in your responses, or a generally expressed desire for discussion, I will call you together.

Sincerely,

Don W. Fawcett

Don W. Fawcett, M.D.
President

F/d
encs

Address: Department of Anatomy, Harvard Medical School
25 Shattuck Street, Boston, Massachusetts 02115

MEDICAL RESEARCH INSTITUTE OF WORCESTER, INC.

CLINICAL AFFILIATE OF THE WORCESTER CITY HOSPITAL

26 QUEEN STREET

WORCESTER, MASSACHUSETTS 01610

DIRECTOR OF RESEARCH:

EUGENIA ROSEMBERG, M. D.

756-1551 (AREA CODE 617)

June 14, 1977

COMMUNICATION

TO: Members of the Council, ASA.

FROM: Dr. Eugenia Rosemberg, Chairman, Publication Committee, ASA.

THROUGH: Dr. Don W. Fawcett, President, ASA.

On March 15, 1977, I presented the Report of the Publication Committee to the ASA Council in which I indicated that our membership was not satisfied with our Journal, i.e.: Andrologia. At that time, I informed the ASA Council that CIDA was prepared to sever relationships with Grosse-Verlag and was ready to seek another Publisher. I indicated that, if this was going to be the case, it was envisaged that the cost for a future CIDA Journal was to be increased over the price charged for Andrologia.

On March 24, 1977, Dr. Steinberger informed me that by action of the ASA Council, I have been directed to investigate possibilities for our Society with respect to the publication of its own Journal. This implied that it was also necessary to investigate the directions to be taken by CIDA with respect to the publication of their proposed new Journal.

As you know, Dr. Steinberger and myself are Members of the Executive Council of CIDA and, therefore, participated at their Meeting which took place in L'Aquila, Italy, April 21, 1977. It was then unanimously agreed not to renew the contract with Grosse-Verlag which expires December 31, 1977. Dr. Eliasson, President of CIDA, reported that contacts had been made with Scriptor in Denmark, the firm that publishes Acta Endocrinologica. The preliminary contract proposal received from Scriptor was also presented. Various names were proposed for the position of Chief-Editor of the new Journal to be called the "International Journal of Andrology" (IJA). It was decided that the Chief-Editor should be a person from the U.S.A., and that Dr. Aakvaag from Norway was to be the Managing Editor. It was also decided that the present members of the Editorial Board of Andrologia, i.e.: Associate Editors and Members of the Board, were to be contacted to determine if they wished to serve the new Journal.

While the search for a Chief-Editor was to be conducted in the U.S.A., by Drs. Steinberger and Rosemberg, Dr. Rosemberg volunteered for the position of Acting Chief-Editor of the IJA for a period of only 6 months. Dr. Rosemberg was given the following mission: 1) to consult with people in the U.S.A., including Dr. Fawcett, President of the ASA, in order to identify the individual who could accept the job of Chief-Editor of the proposed IJA; 2) as Acting Chief-Editor, to consider the organization of the Editorial Board.

During the period May 1, 1977 to June 6, 1977, Dr. Fawcett approached Dr. Alexander Albert, who is a member of the Publication Committee of the ASA, in order to find out if he would be willing to accept the job of Chief-Editor of the IJA. Also, during that period, I received various communications from Dr. Eliasson, who had continued the negotiations with Scriptor, and with Dr. Aakvaag. It became obvious that Dr. Eliasson was very eager to finalize the contract with Scriptor and organize an Editorial Board, identifying a Chief-Editor within a short period of time, as their intention is to start the IJA in January 1978.

I met with Dr. Albert and various members of the Publication Committee of the ASA in Chicago at the time of the Meeting of the Endocrine Society June 7-10, 1977. The contract proposal submitted by Scriptor, and the informational material received from Dr. Eliasson and Dr. Aakvaag were extensively reviewed. It was considered that their Table of Organization was extremely complicated. The intricate relationships described by Dr. Aakvaag as "preliminary job descriptions", as well as their Table of Organization, were unrealistic as <u>each issue</u> was to be set up by the Managing Editor and not by the Chief-Editor. The Editorial Office was apparently being utilized as a "high class secretarial office". Moreover, the terms of the Scriptor Contract as well as the financial aspects were considered to be unfavorable to CIDA. Specifically they indicated a price of <u>$60 for members</u> for 6 issues per year equivalent to 1,000 pages. This was thought to be extremely high for the members of the ASA. There were other considerations relating to their time-table, which was not acceptable, as well as lack of realistic provisions with respect to the expenses of Chief Editor's office and Editorial Board, etc.

After careful consideration of the above, Dr. Albert indicated that he was not interested in the position of Chief-Editor of the IJA. Moreover, it became evident that it was practically impossible to find a person in the U.S.A., who would be interested in the position, and that under the conditions established by CIDA, the IJA was not suitable for ASA members.

While attending the Endocrine Meeting, Dr. Albert suggested that, as Members of the ASA Publication Committee, we meet with Mr. Hoover, Vice President for Periodicals, Williams and Wilkins Company, in order to investigate possibilities for the ASA. Enclosed please find, for your consideration, a summary of Williams and Wilkins proposal.

The important points are the following:

1) There is no doubt about the ability of Williams and Wilkins to produce a first-class Journal.

2) According to their preliminary discussions, the price for Members will be $25 compared to $60 quoted for the IJA for the same number of issues and total number of pages per year or, compared to a price of $40 which we are presently paying for Andrologia.

3) The ASA will not invest any monies to initiate this Journal and, when the initial investment will be met, the ASA will receive 50% of the net profits.

4) The ASA will have absolute control over Editorial policies.

5) The management of the Journal will be in the hands of the ASA Council through the Publication Committee.

As of June 13, 1977, I have resigned as Acting Chief-Editor of the IJA, and suggested to Dr. Eliasson that, because we cannot find a person in the U.S.A. who will accept the job of Chief-Editor of the IJA, Dr. Aakvaag be named to that position.

Although, the possibility exists that in 1978 three (3) Andrology Journals will be published in Europe, i.e.: Andrologia, Archives of Andrology (Chief-Editor Dr. Saad Hafez), and the International Journal of Andrology, the various Members of the Publication Committee of the ASA who discussed the matter in Chicago believe that, with a strong Editor and Editorial Board, the ASA will be able to offer the membership an excellent Journal and, therefore, contribute to rapid increase in the number of scientists joining our Society.

Dr. Fawcett and myself would be very appreciative if you could communicate with us as soon as possible sending your comments regarding the contents of this communication. More specifically, we would like to know if you will be in favor of an ASA Journal with Williams and Wilkins as a possible Publisher.

As a final note, I have contacted another Publisher, Geron-X. However, as Geron-X uses the photo off-set method, Dr. Fawcett does not think that this publisher will be suitable for the ASA.

MEDICAL RESEARCH INSTITUTE OF WORCESTER, INC.

CLINICAL AFFILIATE OF THE WORCESTER CITY HOSPITAL

26 QUEEN STREET

WORCESTER, MASSACHUSETTS 01610

DIRECTOR OF RESEARCH:

EUGENIA ROSEMBERG, M. D.

756-1551 (AREA CODE 617)

June 15, 1977

COMMUNICATION

TO: Members of Council, ASA.

FROM: Dr. Eugenia Rosemberg, Chairman, Publication Committee, ASA.

THROUGH: Dr. Don W. Fawcett, President, ASA.

Preliminary Information Concerning a Contract Proposal received from Williams and Wilkins Company

Reference: Publication of an ASA Journal to be called "American Journal of Andrology"

1- Ownership: the Journal belongs to ASA.

2- The publisher, Williams and Wilkins, will publish the Journal at his own risk until all incurred expenses will be covered. Thereafter, ASA will receive 50% of net profits.

3- The publisher includes, as part of the initial investment, some financial help for the Editorial Office, the amount to be determined in consultation with ASA Officials.

4- It is assumed that during the first year of operations a maximum of 1,000 pages will be published in six (6) issues. With a calculation of 800 subscribers derived from a theoretical number of 300(+) ASA members, and 500 library subscriptions, the price of each volume (6 issues per year) including postage was considered feasible as follows:

Members (USA and overseas)	$25.00
Non-members	$50.00
Libraries	$60.00

Extra postage of $5 to be charged to non-members from overseas.

5- The owner, ASA, appoints the Chief Editor and Editorial Board and establishes the scientific standards of the Journal and Editorial policies.

6- In January 1978, Williams and Wilkins will replace Lippincott as publishers of the J. of Clinical Endocr. and Endocrinology. For the management of the ASA journal relating to financial arrangements between owner (ASA) and publisher, Williams and Wilkins suggested to follow the Endocrine Society system in that, the Publication Committee acts as the Manager for the Journals. Of course, the Publication Committee reports and receives directives from the Council of the Society.

7- All advertisements to appear in the Journal will be procured by Williams and Wilkins, will have to be cleared by ASA (Publication Committee?)

8- Williams and Wilkins will publish subsidized Supplements.

HIGHLIGHTS IN ANDROLOGY

Published by
The Publication Committee
American Society of Andrology

Volume 2, Number 1
February, 1979

This publication is intended to provide members of the American Society of Andrology with a better access to the Society's current activities and with a forum for opinions and questions. In addition, the HIGHLIGHTS IN ANDROLOGY provides summaries of advances in basic and clinical sciences related to Andrology.

FROM THE PUBLICATION COMMITTEE

We look forward to seeing each of you March 13-16 in Houston, Texas for the Fourth Annual American Society of Andrology Meeting and Postgraduate Course.

EVALUATION OF SEMEN UTILIZING CERVICAL MUCUS PENETRATION TESTS

The assessment of semen is best performed by semen analysis which includes volume, pH, liquefaction time, sperm count, sperm motility, quality of the motility, and sperm morphology. The evaluation of sperm-cervical mucus interaction complements the semen analysis. Specific infertility factors may be revealed by the latter. Elstein[1] described the various functions of cervical secretions as follows: (a) transmission of sperm at or near the time of ovulation and interference with entry at all other times; (b) protection of sperm from the hostile environment of the vagina and from being phagocytized; (c) supplementing the energy requirements of sperm; (d) filtering of abnormal and poorly motile sperm and selectively facilitating actively motile sperm of normal shape into the upper genital tract at the time of estrogen dominance; (e) serving as a possible reservoir of sperm; and (f) providing a likely site where the process for the possible capacitation of sperm takes place.

One can also evaluate the pre-ovulatory cervical mucus by pH determination, character (abundant, glossy, transparent with low viscosity), spinnbarkeit, fern pattern, and the absence of leukocytes on microscopic examination.

Sims-Huhner Postcoital Test [2,3]: This is the best known and most widely used method to determine cervical mucus sperm penetration. It should be performed 24 to 36 hours prior to expected ovulation, after 2 days of coital abstinence, and 2 hours after intercourse. Unfortunately, there is a lack of uniformity in the performance of this examination and a wide variation in the interpretation of the results due to a lack of specific criteria for quantitation. Moghissi[4] emphasized similar discrepancies in 1972.

As a screening test, however, the postcoital examination does help the clinician to evaluate the cervical factor and to rule out infection and possible immunologic problems (the absence of immotile or

agglutinated speratozoa). The number of motile spermatozoa and the type of motility can be assessed and should be documented.

The value of the postcoital test has been questioned by Kovacs et al.[5] who stated that there was no importance in the number of spermatozoa per high power field, that if spermatozoa are seen the test confirms the couple's coital technique and anatomical normality, that the finding of necrospermia was debatable, and that the quality and the quantity of mucus did not correlate with sperm counts or motility seen on semen analyses.

Therefore, the postcoital test does provide information on the couple's coital technique, the quality and physical properties of the cervical mucus, and the quality of the spermatozoa found in that specific cervical mucus.

Fractional Postcoital Test (Davajan and Kunitake[6]): Tredway et al.[7] compared the fractional postcoital test to the semen analysis and found that when there were more than 15 motile sperm per high power field at the internal cervical os level the sperm count was usually greater than 20 million spermatozoa per ml. However, they concluded that even though 5 motile sperm per high power field were considered normal for the fractional postcoital test, semen analysis was still necessary to evaluate fertility potential.

Capillary Cervical Mucus Sperm Penetration Test: Kremer,[8] in 1965, described this practical, simple office procedure which measures the distance spermatozoa travel in a column of cervical mucus, the spermatozoal density at various levels, the character of spermatozoal motility, and the viability of the spermatozoa in the cervical mucus based upon length of exposure.

Cross matching of semen and cervical mucus specimens can be accomplished to determine which sample is causing lack of sperm-cervical mucus penetration (wife's cervical mucus versus husband's spermatozoa, donor's cervical mucus versus husband's spermatozoa, wife's cervical mucus versus donor's spermatozoa, and donor's cervical mucus versus donor's spermatozoa[9]).

Sperm-Cervical Mucus Contact Test: In 1976, Kremer and Jager[10] reported this clinically useful procedure to differentiate immunologic from non-immunologic sperm agglutination: if sperm antibodies are present, either in the semen sample or in the cervical mucus, the motile spermatozoa with forward progression became stationary with a shaking type of motility pattern as soon as contact between the sperm and cervical mucus occurred.

This simple, in vitro office procedure, wherein the spermatozoal activity in the sperm-cervical mixture is compared to the motility of the spermatozoa alone, was used by Morgan and his co-workers[11] for "crossed hostility testing." They found that the sperm-cervical mucus contact test, in conjunction with the postcoital test, was a good screening test for immunologic causes of infertility. It was helpful in distinguishing whether poor sperm penetration of the cervical mucus was due to a problem in the husband, the wife, or both. A good correlation was obtained with the finding of agglutinating or immobilizing sperm antibodies in men and poor sperm cervical mucus penetration: high titers of these antibodies prevented spermatozoa from invading the cervical mucus effectively, even though the spermatozoa appeared normal on semen analysis.

Comments: Proper controls are mandatory for the evaluation of sperm-cervical mucus penetration tests. Donor semen and donor cervical mucus must be readily available. Human cervical mucus can be stored at 4° Celsius for a few days. Bovine cervical mucus can be substituted for human cervical mucus and can be stored in the frozen state without altering its viscoelastic properties or its permeability to spermatozoa.[12]

Sperm-cervical mucus penetration tests are adjuncts to semen analyses. They cannot replace a properly performed semen analysis, but can reveal a potential problem in a particular couple's infertile state and may pinpoint the defect in either the male or the female.

REFERENCES

1. Elstein, M.: Functions and physical properties of mucus in the female genital tract. Br Med Bull 34: 83-88, 1978.
2. Sims, J.M.: *Clinical Notes on Uterine Surgery with Special Reference to the Sterile Conditions*. New York, Wood, 1966.
3. Huhner, M.: *Sterility in the Male and Female and Its Treatment*. New York, Robman, 1913.
4. Moghissi, K.S.: Current Perspectives: The function of the cervix in infertility. Fertil Steril 23: 295-306, 1972.
5. Kovacs, G.T., Newman, G.B., and Henson, G.L.: The postcoital test: what is normal? Br Med J 1: 818, 1978.
6. Davajan, V. and Kunitake, G.M.: Fractional in-vivo and in-vitro examination of postcoital cervical mucus in the human. Fertil Steril 20: 197, 1969.

7. Tredway, D.R., Buchanan, G.C., and Drake, T.S.: Comparison of the fractional postcoital test and semen analysis. Am J Obstst Gynecol 130: 647, 1978.

8. Kremer, J.: A simple sperm penetration test. Int J Fertil 10: 209, 1965.

9. Ansbacher, R., Keung-Yeung, K., and Behrman, S.J.: Clinical significance of sperm antibodies in infertile couples. Fertil Steril 24: 305-308, 1973.

10. Kremer, J. and Jager, S.: The sperm-cervical mucus contact test: A preliminary report. Fertil Steril 27: 335, 1976.

11. Morgan, H., Hendry, W.F., Stedronska, J., Chamberlain, G.V.P., and Dewhurst, C.J.: Sperm/cervical-mucus crossed hostility testing and antisperm antibodies in the husband. Lancet 1: 1228-1230, 1977.

12. Blandau, R.J., Gaddum-Rosse, P., and Lee, W.I.: Letter to the Editor. Fertil Steril 29: 707, 1978.

The opinions or assertions contained herein are the private views of the author and are not to be construed as reflecting the views of the Department of the Army or the Department of Defense.

RUDI ANSBACHER, M.D., M.S.
COLONEL, MC, USA F.A.C.O.G.
Department of Obstetrics and Gynecology
Letterman Army Medical Center
Presidio of San Francisco, California 94129

SPERM ANTIBODIES AND INFERTILITY

Despite the abundance of data showing a higher incidence of antisperm antibodies in infertile patients, there is no agreement on the causative role of these antibodies in inducing sterility. Because so little information is available, it is difficult for clinicians to determine which immunological test to order and how to interpret the results.

Antisperm antibodies are usually classified into three types on the basis of their detection by different types of tests: sperm-agglutinating, sperm-immobilizing, and those revealed by immunofluorescence (1). The gelatin agglutination test (GAT), developed by Kibrick et al., is the most widely used assay for sperm-agglutinating antibodies. Different dilutions of test serum are added to motile sperm in a gelatin solution. After the sperm have been incubated, agglutination is observed macroscopically as suspended clumps. More recently, Friberg has developed a tray agglutination test (TAT) that requires an inverted microscope. The advantages of this new assay are (a) that only small quantities of spermatozoa are necessary and (b) that the type of agglutination (head-to-head, head-to-tail, mixed) can be observed. These two tests are the most valid and repeatable of the agglutination tests developed to date.

In men, sperm-agglutinating antibodies are often associated with some obstruction of the duct system and are commonly of the tail-to-tail type (2). After vasectomy, about 50% of male develop antisperm antibodies. Spermatozoa in the ejaculates of men with antibodies often, but not always, show agglutination.

The sperm-immobilization test, developed by Isojima and co-workers (1), is the second main assay used for the detection of antisperm antibodies. This test entails comparison of sperm motility in the presence of test serum (possible containing antisperm antibodies) plus complement to sperm motility in control (antibody negative) serum plus complement. In the presence of complement, antibodies result in sperm death). Spermatozoa from males with circulating sperm-immobilizing antibodies demonstrate a reduced ability to penetrate cervical mucus (3,4).

Assays involving immunofluorescence can aid in the localization of antibodies on the spermatozoon. Most commonly, investigators use an indirect fluorescence method in which they incubate sperm smears with the serum to be tested and then with a fluorescent-labeled antibody such as anti-IgG or anti-IgM.

Antitail antibodies are more commonly seen in men considered to be infertile than in women. Few antisperm antibodies of the IgA class have been observed in sera from either men or women. Some sera from young children and virgin females contain antibodies which react with sperm antigens as revealed by immunofluorescence (5) and these antibodies are referred to as "natural antibodies." Their occurrence can be explained by similarities between some bacterial and sperm antigens which may occur becuase they both contain similar enzymes for cell penetration. However, antibodies to some parts of the spermatozoon are rarely found unless some insult has occurred; these are referred to as "immune antibodies."

For circulating antibodies to be a factor in fertility regulation, they must come in contact with spermatozoa. The antibodies discussed here which are detected in the circulation probably do not affect spermatogenesis because of an effective, efficient blood-testis barrier that sequesters sperm antigens from lymphoid tissue. However, antibodies are found in semen, presumably via prostatic secretions. Co-workers and I recently conducted studies to see whether antisperm antibodies in semen can affect sperm motility, fertilizing ability, and longevity; we observed that spermatozoa exposed to antisperm antibodies were unable to penetrate cervical mucus (4).

If antibodies can reduce fertility, how can clinicans adequately evaluate the situation? A cervical mucus penetration test (4) can be an easy and useful initial assay. Serum or seminal plasma antisperm antibody tests are best done by workers experienced with the techniques, particularly the sperm-agglutination test; because it is a qualitative test, it must be performed with appropriate controls and the results must be viewed with a trained eye. Treatment of males whose infertility may be caused by high levels of antisperm antibodies is an area in which little progress has been made. Corticosteroids have been used to decrease serum antibody levels (6). Some researchers (7,8) have had success in giving men with agglutinating antibodies doses of Prednisolone for 2 weeks prior to their wife's expected ovulation dates. A combination of inhibition of spermatogenesis plus steroids has also been suggested. Unfortunately, studies on therapy for antibodies require a great deal of time because the efficacy criterion is the occurrence of pregnancy.

REFERENCES

1. Rose, N.R., Hjort, T., Rümke, P., Harper, M.J.K., and Vyazov, O. 1976. Techniques for detection of iso- and autoantibodies to human spermatozoa. Clin. Exp. Immunol. 23:175.
2. Rümke, P. 1969. Clinical aspects of autoimmunity to spermatozoa in men. Immunology and Reproduction (R. G. Edwards, ed.). London: International Planned Parenthood Federation, p. 251.
3. Fjällbrant, B. 1968. Interrelation between high levels of sperm antibodies, reduced penetration of cervical mucus by spermatozoa, and sterility in man. Acta Obstet. Gynecol. Scand. 47:102.
4. Alexander, N.J., and Fulgham, D.L. 1978. Antibodies to spermatozoa in male monkeys: Mode of action. Fertil. Steril. 30:334.
5. Tung, K.S.K., Cooke, W.D., Jr., McCarty, T.A., and Robitaille, M. 1976. Human sperm antigens and antisperm antibodies. II. Age-related incidence of antisperm antibodies. Clin. Exp. Immunol. 25:73.
6. Rümke, P., and Hellinga, G. 1959. Auto-antibodies against spermatozoa in sterile men. Am. J. Clin. Path. 32:357.
7. Halim, A., Antoniou, D., Lane, J., and Blandy, J. 1974. The significance of antibodies to sperm in infertile men and their wives. Brit. J. Urol. 46:65.
8. Shulman, S. 1976. Treatment of immune male infertility with methylprednisolone. Lancet 2:1243.

NANCY J. ALEXANDER, Ph.D.
Oregon Regional Primate Research Center
Beaverton, Oregon 97005

The Publication Committee solicits your comments, suggestions and criticisms concerning the "Highlights in Andrology." Please address your comments to Dr. Nancy J. Alexander, Oregon Regional Primate Research Center, 505 N.W. 185th Avenue, Beaverton, Oregon 97005.

HIGHLIGHTS IN ANDROLOGY

Published by
The Publication Committee
American Society of Andrology

Volume 1, Number 2
December 1978

This publication is intended to provide members of the American Society of Andrology with a better access to the Society's current activities and with a forum for opinions and questions. In addition, the HIGHLIGHTS IN ANDROLOGY provides summaries of advances in basic and clinical sciences related to Andrology.

FROM THE PUBLICATION COMMITTEE

In this, our second and final issue for the year 1978, we wish to take this opportunity to thank each of you for your support of "Highlights in Andrology." We are looking forward to our publication improving with future editions and trust you will each stand behind us in our endeavor.

Each member of The Publication Committee would like to wish you a very happy, joyful and prosperous holiday season.

FROM THE PROGRAM CHAIRMAN

Fourth Annual ASA Meeting and Postgraduate Course
March 13-16, 1979, Houston, Texas

The arrangements for the Meeting and the Course are progressing well. Preliminary program and registration forms were mailed on November 28th. In view of numerous inquires by members and nonmembers of the society both in the USA and abroad, we anticipate good attendance.

The program will include three state-of-art lectures: "The Funcional Significance of the Blood-Testis Barrier" by B. P. Setchell; "Experimental Approach to the Etiology of Benign Prostatic Hypertrophy" by P. C. Walsh and "The Role of Nutrition and Obesity in Male Reproductive Function" by R. S. Swerdloff. A workshop on "Semen Evaluation" has been scheduled for Wednesday evening for those registered at the meeting. (No special registration fee will be required to attend the workshop.) Dr. Nancy Alexander (organizer) and several other experts in this field will lead the discussions.

Seventy abstracts of brief communications have been selected for presentation from the podium out of a much larger total number of abstracts submitted. We will have a good balance between basic and clinical topics which will be of great interest to both the research investigators and clinicians.

The Postgraduate Course (March 13th, 8:00 a.m. - 3:00 p.m.) "Recent Advances in Andrology" will cover the following topics: Basic Biology of Vas Deferens - Dr. D. Hamilton; Microsurgery of the Male Reproductive Tract - Dr. S. Silber; Surgical Therapy of Male Infertility - Dr. L. Dubin; Micro- vs. Macrosurgery - Dr. A. Belker and Medical Therapy of Male Infertility - Drs. P. Troen and S. L. Winters. The Postgraduate Course meets the criteria for 6 credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association.

We are also planning a film session on various educational subjects and commercial exhibits. We think we will have a very good meeting and hope that you will be here to enjoy it.

Happy Holidays!

ANNA STEINBERGER, Ph.D.

HYPERPROLACTINEMIA AND IMPOTENCE

Excessive release of prolactin (PRL), hyperprolactinemia, is usually caused by adenomatous tumors of the pituitary. It can also be due to a chronic exposure to tranquilizers, opiates or estrogens or may lack any obvious etiology. In women, hyperprolactinemia can be associated with amenorrhea and anovulatory sterility and, less frequently, with galactorrhea. Suppression of PRL release in these patients by administration of a synthetic dopamine receptor agonist, 2-Bromo-α-ergocriptine mesylate (bromocriptine, CB-154; PARLODEL, Sandoz), or by surgical removal or irradiation of the pituitary tumors, abolishes inappropriate lactation and restores menstrual cyclicity and fertility. Several recent reports indicate that hyperprolactinemia can also interfere with sexual function in men (1-6). Impotence is the most common complaint, but various degrees of hypogonadism have also been described. Gonadotropin levels are normal or slightly suppressed and response to an LH-RH challenge may be impaired. Treatment with bromocriptine restores libido and potency in the majority of these patients (2-6) and can also improve testicular function (2,4,5).

A causal relationship of the excessive PRL release and the sexual dysfunction is strongly suggested by these observations. However, a possibility remains that hyperprolactinemia, impotence and hypogonadism represent unrelated symptoms of hypothalamic/pituitary disease in men with adenohypophyseal adenomas. Furthermore, bromocriptine could improve potency by a direct action on central and peripheral dopaminergic neurons involved in the control of the erectile response (5). In other words, it remains to be conclusively demonstrated that restoration of libido and potency by bromocriptine is due solely to suppression of PRL release. A need for futher studies in this area is emphasized by comparable improvement of sexual function in bromocriptine- and placebo-treated men in one study (7), by lack of correlation between the decrease in libido and potency and the increase in peripheral PRL levels in a group of 65 men with pituitary tumors (8), and by impotence of some patients with pituitary tumors and normal PRL levels (9).

The mechanism by which excessive PRL release could interfere with libido and potency is not understood. The ability of PRL to affect dopaminergic neurons in several regions of the brain could account for both impotence and impairment of gonadotropin release. The presence of PRL in the cerebrospinal fluid and the recent evidence that the adenohypophysis can secrete PRL directly to the brain add some credence to this possibility. The observation that gonadotropin levels are not elevated in hyperprolactinemic hypogonadal men provides evidence of hypothalamic dysfunction in this syndrome (10). Altered secretory activity of the adrenals in hyperprolactinemic men (11) must also be considered in attempts to explain the etiology of hypogonadism and impotence in this group of patients.

A suitable animal model could aid greatly in the study of the mechanism of PRL action on the hypothalamic-pituitary-testicular axis and on sexual behavior. Results from several laboratories indicate that hyperprolactinemia and various symptoms of sexual dysfunction can be induced in male rats and mice. Transplantation of PRL-producing tumors to adult male rats produces testicular atrophy, suppression of testosterone production, adrenal enlargement and elevation of plasma gonadotropin levels (12). Transplantation of several pituitary glands under the renal capsule causes chronic hyperprolactinemia and suppression of LH-RH- or castration-induced gonadotropin release (13, 14). Basal gonadotropin levels can also be suppressed and adrenal weight is increased (15), but testicular weight and plasma testosterone levels are not affected (14, 15). Male rats and mice rendered hyperprolactinemic by multiple pituitary grafts exhibit striking deficiencies in copulatory behavior (16).

It is of interest to note that while pathological elevation of PRL release can suppress sexual function, physiological amounts of PRL may normally stimulate gonadal activity in men (17) and in experimental animals (18). Reports of delayed puberty in a hyperprolactinemic patient (19), and in a patient with a diminished PRL reserve (20) provide an example of differential effects of normal and excessive PRL levels.

REFERENCES:

1. Boyar, R.M., Kapen, S., Finkelstein, J.W., Perlow, M., Sassin, J.F., Fukushima, D.K., Weitzman, E.D. and Hellman, L. J. Clin. Inves. 53:1588, 1974.
2. Tolis, G. and Van Vliet, S. Clin. Res. 24:279, 1976.
3. Asfour, M., L'Hermit, M., Hedouin-Quincampoix, M. and Fossati, P. Acta Endocrinol. 84:738, 1977.
4. Faglia, G., Beck-Peccoz, P., Travaglini, P., Ambrosi, B., Rondena, M. Paracchi, A., Spada, A., Weger, G., Bara, R. and Bouzin, A. In: Crosignani, P.G. and Robyn, C. (Eds) Prolactin and Human Reproduction, Academic Press, London, 1977, p. 225.
5. Thorner, M.O. and Besser, G.M. Acta Endocrinol. 88, Suppl. 216:131, 1978.
6. Werder, K.V., Fahlbusch, R., Landgraf, R., Pickardt, C.R., Rjosk, H.K. and Scriba, P.C. J. Endocrinol. Invest. 1:47, 1978.

7. Ambrosi, B., Bara, R., Travaglini, P., Weber, G., Beck Peccoz, P., Rondena, M., Elli, R. and Faglia, G. Clin. Endocrinol. (Oxf.) 7:417, 1977.
8. Lundberg, P.O. and Wide, L. Fertil, Steril. 29:175, 1978.
9. Kovacs, K., Horvath, E., Van Loon, G.R., Rewcastle, N.B., Ezrin, C. and Rosenbloom, A.A. Fertil, Steril. 29:622, 1978.
10. Silverman, V., Cunningham, G.R. and Boyd, A.E., III. Progr. 60th Meeting Endocr. Soc. p. 357, 1978.
11. Vermeulen, A., Sny. E. and Rubens, R. J. Clin. Endocr. Metab. 44:1222, 1977.
12. Fang, V.S., Refetoff, S. and Rosenfield, R.L. Endocrinology 95:991, 1974
13. Grandison, L., Hodson, C., Chen, H.T., Advis, J., Simpkins, J. and Meites, J. Neuroendocrinology 23:312, 1977.
14. Winters, S.J. and Loriaux, D. L. Endocrinology 102:864, 1978.
15. Bartke, A., Smith, M.S., Michael, S.D., Peron, F.G. and Dalterio, S. Endocrinology 100:182, 1977.
16. Doherty, P.C., Jr., Michael, S.D. and Svare, B.B. Program 11th Meeting Soc. Study Reprod. p. 65A, 1978.
17. Rubin, R.T., Gouin, P.R., Lubin, A., Poland, R.E. and Pirke, K.M. J. Clin. Endocrinol. Metab. 40:1027, 1975.
18. Bartke, A., Hafiez, A.A., Bex, F.J. and Dalterio, S. Biol. Reprod. 18:44, 1978.
19. Koenig, M.P., Zuppinger, K. and Liechti, B.J. Clin. Endocrinol. Metab. 45:825, 1977.
20. Spitz, I.M., Landau, H., Almaliach, U., Rosen, E., Brautbar, N. and Russell, A. J. Clin. Endocrinol. Metab. 45:412, 1977.

ANDRZEJ BARTKE, Ph.D.
The University of Texas
Medical School
San Antonio, Texas

INHIBIN

It has been recognized for a long time that the testes regulate pituitary secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH) by negative feedback mechanisms. Clinical observations and experiments in animals demonstrated that castration causes an elevation of both gonadotropins in circulation and in the pituitary gland, whereas germ cell depletion often results in a selective increase of FSH. Testosterone has been generally accepted as the main factor responsible for the feedback regulation of LH secretion, however, factors which control the secretion of FSH have not been fully elucidated. Since all gonadal steroids tested to date suppress LH more efficiently and none of the steroids suppress FSH selectively, it appears that a nonsteroidal factor produced by the testes may be involved in the negative feedback regulation of FSH. Such a factor has been postulated over forty years ago and named "inhibin" by McCullagh (1).

Recently, direct experimental evidence has been provided for the existence of inhibin in several mammalian species. Various crude preparations and partly purified aqueous extracts of bull, ram and rat testis (2,3), ram and boar rete testis fluid (4), human and bull seminal plasma (5), and bull spermatozoa (6) were shown to suppress FSH secretion when injected into appropriate animal models or when tested *in vitro* using pituitary cell cultures. However, there is no good agreement between different laboratories regarding the effects of these materials on LH secretion. This could be at least partly due to the use of various inhibin preparations and assay procedures. Inhibin appears to be of large molecular size (> 10,000 Daltons) and to be sensitive to heat and proteolytic enzymes, suggesting that it may be polypeptide or protein in nature. A similar inhibin-like substance has been also found in ovarian follicular fluid.

There has been considerable controversy regarding the cell type(s) responsible for inhibin production in the testis. Several investigators considered the late spermatids to be the most likely source of inhibin, while others suggested that Sertoli cells and/or spermatogonia may be involved in the FSH feedback regulation.

Direct evidence for the ability of Sertoli cells to secrete an FSH-inhibiting substance was provided by experiments *in vitro* (7) when cultures of isolated populations of rat Sertoli cells were shown to secrete a heat-labile macromolecule (> 12,000), Sertoli Cell Factor (SCF), which selectively suppresses the basal and GnRH-stimulated FSH release by rat anterior pituitary cells *in vitro*. subsequently, SCF was also shown to selectively suppress FSH synthesis (8). These studies illustrated that inhibin can affect FSH secretion by acting directly on the pituitary.

After approximately forty years of relative quiescence, active research on inhibin is now being conducted in numerous laboratories in the U.S.A. and abroad. Investigations focus on the purification and physico-chemical characterization of the active principle, its mechanism of action and the regulation of its production. All of these studies have been hindered by the lack of standardized and sensitive assays for the quantitation of inhibin activity. Efforts are, therefore, being made to develop a suitable bio- and radioimmunoassay.

The physiological significance of inhibin in male reproduction needs to be clarified, particularly since the role of FSH in the regulation of spermatogenesis in the mature male remains unknown.

REFERENCES:

1. McCullah, D.R. *Science* 76:19, 1932.
2. Keogh, E.J., Lee, V.W.K., Rennie, G.C., Burger, H.G., Hudson, B. and DeKretser, D.M. *Endocrinology* 98:997, 1976.
3. Nandini, S.G., Lipner, H., and Moudgal, N.R. *Endocrinology* 98:1460, 1976.
4. Setchell, B.P., Davies, R.V., and Main, S.J. In: Johnson, A.D., and Gomes, W.R. (eds): *The Testis, Vol. 4.* Academic Press, New York, 1977, pp. 189-238.
5. Franchimont, P., Chari, S., Hazee-Hagelstein, M.T., Debruche, M.L., and Duraiswami, S. In: Troen, P., and Nankin, H.R. (eds): *The Testis in Normal and Infertile Men.* Raven Press, New York, 1977, pp. 253-270.
6. Lugaro, G., Casellato, M.M., Mazzola, G., Fachini, G., and Carrea, G. *Neuroendocrinology* 15:62, 1974.
7. Steinberger, A., and Steinberger, E. *Endocrinology* 99:918, 1976.
8. Chowdhury, M., and Steinberger, A. *Endocrinology* 101:644, 1978.

ANNA STEINBERGER, Ph.D.
The University of Texas
Medical School
Houston, Texas

QUESTIONS AND COMMENTS

Question: *When should one initiate immunological studies during the evaluation of an infertile couple?*

Answer: A properly timed Sims-Huhner postcoital examination, performed 24 to 36 hours prior to expected ovulation, after two days of coital abstinence, and within two hours of coitus, is a good screening test for the possibility of immunologic sperm-cervical mucus incompatability. If agglutinated or immotile spermatozoa are noted, the sperm-cervical mucus contact test of Kremer and Jager (Fertil. Steril. 27:335, 1976) is a simple *in vitro* office test which differentiates immunologic from non-immunologic agglutination. If sperm antibodies are present, either in the cervical mucus or in the semen sample, the motile spermatozoa with forward progression become stationary with a shaking type of motility pattern as soon as contact between the sperm and the cervical mucus occurs.

Proper controls are mandatory. Donor cervical mucus, either human or bovine (Blandau *et al.*, Fertil. Steril. 29:707, 1978) and donor semen are needed to cross match specimens from the couple and to identify which partner has the problem (Ansbacher, Fertil. Steril. 24:305, 1973). Additional testing of serum, semen, and cervical mucus requires the submission of such specimens to those specialized laboratories performing immunologic procedures.

RUDI ANSBACHER, M.D., M.S.
COL, MC, USA (F.A.C.O.G.)
Chief, Dept. Ob-Gyn
P.O. Box 235
Letterman Army Medical Center
Presidio of San Francisco,
California 94129

THE UNIVERSITY OF TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

MEDICAL SCHOOL

6431 Fannin
Texas Medical Center

Post Office Box 20708
Houston, Texas 77025
(713) 792-2121

November 22, 1978

Dr. Andrzej Bartke
Associate Professor
Department of Obstetrics and Gynecology
The University of Texas Medical School
Health Science Center at San Antonio
7703 Floyd Curl Drive
San Antonio, Texas 78284

Dear Andrzej,

I certainly appreciate your help in writing the review for "Highlights in Andrology." As always you are a man of your word and you delivered when promised.

Thanking you again and with best regards to you and your lovely wife from the crew down here.

Sincerely,

Emil Steinberger, M.D.
Professor and Chairman
Department of Reproductive
Medicine and Biology

ES/aw

HIGHLIGHTS IN ANDROLOGY

Published by
The Publication Committee
American Society of Andrology

Eugenia Rosemberg, Chairman
Nancy Alexander
Andrzej Bartke
William J. Bremner
Larry Ewing
Richard J. Sherins
Emil Steinberger
Philip Troen

Volume 1, Number 1
October 1978

This publication is intended to provide members of the American Society of Andrology with a better access to the Society's current activities and with a forum for opinions and questions. In addition, the HIGHLIGHTS IN ANDROLOGY provides summaries of advances in basic and clinical sciences related to Andrology.

FROM THE PRESIDENT

By means of this inaugural issue of **HIGHLIGHTS IN ANDROLOGY,** your Executive Council hopes to initiate an effective means of communicating with the membership-at-large. Furthermore, these newsletters should provide scientists and clinicians interested in the field of Andrology with a podium to air their views, initiate needed action, etc. Last summer when it became clear that ASA will be unable to negotiate an acceptable agreement with Andrologia or with the new International Journal of Andrology, Dr. Don Fawcett, the President, and the officers of ASA were directed to explore the development of a separate journal. Discussions carried out since the Annual Meeting of the Society in Nashville clearly demonstrated that this will not be an easy task. Therefore in June 1978 at the interim Council meeting of ASA, it was decided to proceed immediately with a newsletter. I am grateful to the Publication Committee for their splendid efforts. We shall continue to explore all options to have a journal for the Society and by the next annual meeting in Houston we should be able to appraise the membership with the results of Council's labors concerning this issue.

C. ALVIN PAULSEN, M.D.

FROM THE SECRETARY

In the June 1978 mailing pertaining to the 1979 Annual Meeting of ASA, I enclosed a questionnaire to the Membership requesting information (name, degree, current mailing address, etc.) in order to be able to update our computerized information on each and every member of the Society. To date, I have received 97 completed questionnaires. This represents only one-fourth of our current membership. **PLEASE RETURN THE QUESTIONNAIRE!**

RUDI ANSBACHER, M.D., M.S.
Department Ob/Gyn, P.O. Box 235
Letterman Army Medical Center
Presidio of San Francisco, California 94129
Telephone (415) 561-2433

FROM THE PROGRAM CHAIRMAN

HAVE YOU MARKED THE DATES OF MARCH 13-16, 1979 ON YOUR CALENDAR???

The 4th Annual Meeting of ASA will be held March 13-16, 1979 in Houston, Texas. We worked very hard to organize an exciting program with respect to scientific sessions and social events. There will be 3 invited key-note speakers, 6 sessions of brief communications, a workshop on semen evaluation and 1-2 film sessions on selected topics of interest to andrologists. The Postgraduate Course will meet the criteria for 6 credit hours in Category I of the Physician's Recognition Award (AMA) and 10 cognates by ACOG. The preliminary program, the registration forms, etc. will be mailed in December. I hope you will attend the Annual Meeting and submit an abstract of your original work in either basic or clinical aspects of andrology. Also, please share this information with those who are not currently ASA members, but may be interested in attending the Meeting. Your active participation is essential to make our next Annual Meeting a success! I am looking forward to seeing "y'all" in Houston next March. ABSTRACTS MUST BE POSTMARKED OCTOBER 1, (FOREIGN); OCTOBER 15 (U.S.A.). For additional information and abstract forms please write to:

Address of
Dr. Emil Steinberger

ANNA STEINBERGER, Ph.D.
Department of Reproductive Medicine and Biology
The University of Texas Medical School
P. O. Box 20708
Houston, Texas 77025

MEASUREMENT OF ANDROGENS FOR EVALUATION OF TESTICULAR FUNCTION

The testis is both an endocrine and an exocrine organ. Its endocrine (the production of androgens) and exocrine (the production of spermatozoa) functions are interrelated since androgens are essential for spermatogenesis. Thus, there is considerable interest in the measurement of androgens by the clinician attempting to evaluate testicular function. Methods for the measurement of androgens may be divided into three general categories: (1). biological assays; (2). chemical methods; and (3). saturation analyses.

BIOASSAYS rely on a specific biological response to the hormone being measured, e.g., growth of the capon's comb, enlargement of various muscles, increased weight of the sex accessory glands, etc. Bioassays are seldom employed today and only for special purposes rather than for routine clinical use.

CHEMICAL METHODS. For many years urinary 17-keto steroids were utilized as the primary measurement of testicular androgen production. These determinations are nonspecific and do not reflect testicular androgen production since 70% of urinary keto steroids are metabolites of adrenal steroids. There are a number of chemical methods with great specificity for testosterone. Some rely on recently developed techniques for chromatographic separation of steroids combined with radiochemical techniques, e.g. the double isotope derivative procedure, the use of gas-liquid chromatography or gas-liquid chromatography followed by mass spectrometry. These procedures are specific, precise and sensitive but also laborious and expensive. Thus, they cannot be applied for routine clinical use. Other chemical methods such as *in vitro* incubation of testicular fragments to study androgen formation from labeled precursors and the measurement of testosterone production rates *in vivo* are primarily research tools, impractical for routine clinical use.

SATURATION ANALYSES. In the saturation analyses techniques, a known amount of labeled androgen is allowed to compete for binding sites on a protein with unlabeled unknown amounts of androgen present in a biological sample. After an equilibrium is reached, the bound and free forms are separated and radioactivity is determined. Under appropriate conditions, the radioactivity is a function of the amount of unlabeled androgen in the system. There are numerous variations of this basic technique which generally relate to the type of binding protein employed and/or the method used to separate free and bound forms. Saturation analyses are sensitive and precise but are sometimes less specific than certain chemical methods. However, because of their simplicity and availability, they become the method of choice for both the clinician and the researcher. The development of saturation analyses is an interesting saga in modern endocrinology. It can best be described in historical terms related to the development of appropriate binding proteins. An early approach (competitive protein binding method) employed binding proteins normally present in the human serum. These proteins, however, bound a variety of different androgens and other steroids. To measure a particular androgen, one had to extract the sample and separate the steroid chromatographically. To overcome this problem an androgen was covalently linked to a protein and this complex was used to generate specific antisera which in turn were utilized as ligands. Competitive protein binding assays thus became radioimmunoassays as the serum-binding proteins were replaced by specific antisera. The early antisera to testosterone were generated by linking the steroid at carbon 17 (C17) position with a protein. They were generally nonspecific, reacting with many steroids. The second generation of antisera was prepared by linkage through C3. These were more specific but frequently cross reacted with dihydrotestosterone. The third generation was prepared by linkage through C6, C7, C11 or C15. Linkage through C6, C7 or C11 resulted in antisera with cross reactivities similar to those developed against C3 conjugates. The C15 antisera was somewhat unique in that it exhibited very low cross reaction with dihydrotestosterone but unfortunately it reacted with several Δ 4-3 keto steroids, some of which were not even androgens. Recently a fourth generation of testosterone antisera utilizing C19 conjugates has been developed (1). This antisera exhibits minimal cross-reactivity with dihydrotestosterone and other steroids. Thus, it may be used to measure testosterone in biological fluids after a simple extraction, yielding an assay which is specific yet relatively simple.

A variety of androgen radioimmunoassay methods are currently available to the researcher and the clinician in the form of standardized reagents and "kits." Unfortunately, the application of radioimmunoassay methodology has grown so rapidly that in many cases insufficient attention has been directed toward the quality, particularly toward specificity and accuracy of the assays. The clinician frequently is not made aware of the magnitude of assay error or the specificity of the antibody used.

In addition to the limitation of the radioimmunoassay techniques themselves, there are limitations in the interpretation of the data on circulating levels of testosterone or other androgens. In adult males the normal range for plasma testosterone is 2 to 12 ng/ml. Some of this variability may arise from variations between assays. However, the plasma testosterone levels change dramatically within a short period of time (2). In addition to these oscillations, there is a diurnal pattern for plasma testosterone levels with an early morning peak. Consequently, a single determination should be interpreted with

caution. A more accurate measure may be gained by multiple or integrated blood sampling techniques (3,4). Furthermore, testosterone circulates largely bound to serum-binding proteins. Variations in levels of the carrier proteins may affect the circulating concentrations. Circulating levels also reflect the net result of production, degradation and excretion. Anything that affects these will also alter the circulating androgen concentrations. Finally, serum androgen concentrations in the low part of the normal range may reflect subtle deficiencies in androgen production which may affect fertility (5,6).

REFERENCES:

1. Rao, P.N., Moore, P. H., Jr., Peterson, D.M., and Tcholakian, R. K. J Steroid Biochem. 9:539, 1978.
2. Smith, K. D., Tcholakian, R. K., Chowdhury, M., and Steinberger, E. Fert. Steril. 25:965, 1975.
3. Goldzieher, J. W., Dozier, T. S., Smith, K. D., and Steinberger, E. J. Clin. Endoc. Metab. 43:824, 1976.
4. Santen, R. J., and Bardin, C. W. J. Clin. Invest. 52:2617, 1973.
   Rodriguez-Rigau, L. J., Weiss, D. B., Smith, K. D., and Steinberger, E. Acta Endoc. 87:400, 1978.
6. Nankin, H. R., Castaneda, E., and Troen, P. In: Troen, P., and Nankin, H. R. (eds), The Testis in Normal and Infertile Men. New York, Raven Press, 1977, p. 529.

H. E. GROTJAN, Ph.D.
The University of Texas
Medical School
Houston, Texas

RECENT PROGRESS IN UNDERSTANDING THE BIOCHEMICAL ASPECTS OF SPERM MOTILITY

The biochemical mechanisms which trigger and sustain sperm motility are not as yet completely understood. A complex interrelationship between metabolic and mechanical events is no doubt involved. An attempt will be made here to briefly summarize some of the data which suggest that cyclic AMP (cAMP) and at least one protein factor are involved in the regulation of motility (1).

The evidence for an influence of cyclic nucleotides, and in particular cAMP, upon sperm respiration and motility has been summarized by Hoskins and Casillas (2). Briefly, phosphodiesterase inhibitors are known to increase sperm cAMP levels and to increase respiratory rates in epididymal and ejaculated sperm in the presence of exogenous substrates. More recently, Kopf and Garbers (3) have demonstrated a statistically significant correlation between sperm cAMP levels and respiratory rates in two species of sea urchin sperm diluted with sea water. Cyclic AMP derivatives and phosphodiesterase inhibitors have also been shown to maintain motility in epididymal sperm from a number of species (2). As an outgrowth of these studies, Barkay *et al* (4) and others have reported the use of caffeine to enhance motility properties of frozen human semen. Although some data indicate that the effect of cAMP on respiration is secondary to its effect on motility, this question has not been completely resolved.

The findings that cAMP influences sperm motility and respiration have given impetus to a number of attempts to demonstrate components of typical cAMP-responsive systems in sperm and to link these components functionally to physiological events. Such components generally include hormone-responsive adenylate cyclase, cAMP-phosphodiesterase, cAMP-dependent protein kinase, substrates whose functions are changed by phosphorylation, and protein phosphatase. Epididymal sperm contain a particulate adenylate cyclase which is not stimulated by fluoride, polypeptide hormones or catecholamines and is activated only by relatively high concentrations of triiodothyronine (2). Cation effects appear to be species-specific. Suggestions for possible physiological activators include spermine (5) and specific factors released from eggs (6).

Tash (7) described two phosphodiesterases in ram spermatozoa and estimated that their concentration was high enough relative to adenylate cyclase activity to constitute a significant factor in the control of sperm cAMP levels. Stephens *et al* (8) have recently shown that bovine epididymal sperm possess five forms of phosphodiesterase which become more particulate as the sperm traverse the epididymis.

As described by Hoskins and Casillas (2), cAMP-dependent protein kinase is present in sperm in high concentration relative to total cellular protein. The soluble activity has been resolved into several molecular species. However, the definition of specific substrates of the protein kinases, especially of particulate proteins which could conceivably mediate motility, has proved difficult. Hoskins and Casillas (2) were unable to detect significant phosphorylation of the particulate fraction from bovine spermatozoa but noted some cAMP-dependent phosphorylation of cytosol proteins. However, Huacuja *et al* (9) have recently investigated the question of cAMP-stimulated protein phosphorylation in human spermatozoa with some success. In the presence of the synthetic phosphodiesterase inhibitor SQ 20009, these workers demonstrated a stimulation by cAMP of ^{33}P-inorganic phosphate incorporation into both whole sperm and membrane fractions. The phosphorylated material was resolved into three peaks upon electrophoresis, one of which appeared only after exposure of the sperm to cAMP. The roles of these proteins and the effect of phosphorylation on their function are not known. Finally, Tang and Hoskins (10) have partially purified a phosphoprotein phosphatase from bovine epididymal sper-

matozoa which is found primarily in the cytosol and tail fragments.

The search for links between transport through the epididymis, responsiveness of the cAMP-dependent systems, and acquisition of motility have led to some very interesting findings. Cascieri *et al* (11) observed that although fresh bovine testicular, caput, caudal and ejaculated sperm all possessed adenylate cyclase, protein kinase and phosphodiesterase, treatment of testicular sperm with caffeine raised cAMP and increased glucose utilization but did not increase motility or 0_2 consumption. In contrast, dilution of caudal sperm caused an increase in cAMP level and a decrease in ATP which preceded the development of motility. Caput epididymal fluid, sex accessory gland fluid or buffer were equally suitable for dilution, suggesting to these authors that the composition of the fluid was not a factor in triggering these events.

Similarly, Hoskins and his coworkers observed that the level of cAMP increased in sperm during their transit through the epididymis and that caudal sperm became motile upon dilution or, after washing, upon addition of phosphodiesterase inhibitors (2). These workers attempted to produce motility in caput sperm by addition of phosphodiesterase inhibitors and noted that after a lag phase, 10mM theophylline raised cellular cAMP levels and initiated a twitching motion but not forward motion in the sperm (12). Seminal plasma itself had no effect on either motility or cAMP levels but, in conjunction with theophylline, promoted forward motility. Hoskins and his coworkers have since determined that a glycoprotein which they term Forward Motility Factor is presented in high concentrations specifically in the cauda epididymis (13). In a recent review, Hoskins *et al* (13) discuss the evidence which leads them to postulate that sperm bind Forward Motility Factor during their transit through the epididymis. The combination of the gradual elevation of intracellular cAMP levels and the binding of this protein factor presumably are responsible for the progressive forward motility observed by caudal sperm upon dilution.

The biochemical mechanisms relating to the control of sperm mobility remain to be elucidated. Nonetheless, the studies described here have opened up new avenues of exploration and hold promise of yielding some very important information on this subject.

REFERENCES:

1. Due to the nature of this article, references are limited. An attempt is made to cite reviews wherever possible in order to direct the reader to a more exhaustive bibliography. The author is grateful to Dr. D. Hoskins for permission to quote information in press.
2. Hoskins, D., and Casillas, E.R. In: Greep, R. O., and Astwood, E. B. (eds), Handbook of Physiology - Vol. 5. Washington, D.C., Am. Physiol. Soc., 1975, p. 453.
3. Kopf, G. S., and Garbers, D. L. Biol. Reprod. 18:229, 1978.
4. Barkay, J., Zuckerman, H., Sklan, D., and Gordon, S. Fert. Steril. 28:175, 1977.
5. Shah, G. V., Sheth, A. R., Mugatwala, P. P., and Roa, S. S. Experientia 31:631, 1975.
6. Garbers, D. L., and Kopf, G. S. J. Reprod. Fert. 52:135, 1978.
7. Tash, J. S. J. Reprod. Fert. 47:63, 1976
8. Stephens, D. J., Wang, J-L, and Hoskins, D. D. Biol. Reprod., in press, Nov., 1978.
9. Huacuja, L., Delgado, M., Merchant, H., Pancardo, R. M., and Rosado, A. Biol. Reprod. 17:89, 1977.
10. Tang, F. Y., and Hoskins, D. D. Biochem. Biophy. Res. Commun. 62:328, 1975.
11. Cascieri, M., Amann, R. P., and Hammerstedt, R. H. J. Biol. Chem. 251:787, 1976.
12. Hoskins, D. D., Hall, M. L., and Munsterman, D. Biol. Reprod. 13:168, 1975.
13. Hoskins, D. D., Brandt, H., and Acott, T. S. Federation Proceedings, in press, 1978.

B. M. SANBORN, Ph.D.
The University of Texas
Medical School
Houston, Texas

SPECIAL ANNOUNCEMENT

The 6th NICHD Workshop on the Testis will be held March 10-13, 1979 at the Shamrock Hilton Hotel in Houston, Texas. It will precede the 4th Annual Meeting of the American Society of Andrology scheduled for March 13-16, 1979 at the same hotel.

The 2½ day Workshop will focus on "Comparative Aspects of Testicular Development, Structure and Function." It will include sessions on testicular development and sex determination; spermatogenesis, steroidogenesis and their hormonal regulation; sperm motility and energetics; cyclic changes in testicular function; and transport mechanisms. If you are interested in attending, please submit a brief description of the material you would like to present to:

ANNA STEINBERGER, Ph.D.
Department of Reproductive Medicine and Biology
The University of Texas Health Science Center at Houston
Medical School
P. O. Box 20708
Houston, Texas 77025

HYPERPROLACTINEMIA AND IMPOTENCE

Excessive release of prolactin (PRL), hyperprolactinemia is usually caused by adenomatous tumors of the pituitary but can also be due to a chronic exposure to tranquilizers, opiates or estrogens or lack any obvious etiology. In women, hyperprolactinemia can be associated with amenorrhea and anovulatory sterility and, less frequently, with galactorrea. Suppression of PRL release in these patients by administration of a synthetic dopamine receptor agonist, 2-Bromo-α-ergocriptine mesylate (CB-154; PARLODEL, Sandoz), or by surgical removal or irradiation of the pituitary tumors abolishes inappropriate lactation and restores menstrual cyclicity and fertility. Several recent reports indicate that hyperprolactinemia can interfere with sexual function also in men (1 - 6). Impotence is the most common complaint, but various degrees of hypogonadism have also been described. Gonadotropin levels are normal or slightly suppressed and response to LH-RH challenge may be impaired. Treatment with bromoergocriptine restores libido and potency in the majority of these patients (2 - 6) and can also improve testicular function (2, 4, 5).

A causal relationship of the excessive PRL release and the sexual dysfunction is strongly suggested by these observations. However, a possibility remains that hyperprolactinemia, impotence and hypogonadism represent unrelated symptoms of hypothalamic/pituitary disease in men with adenohypophyseal adenomas. Furthermore, bromocriptine could improve potency by a direct action on central and peripheral dopaminergic neurons involved in the control of the erectile response (5). In other words, it remains to be conclusively demonstrated that restoration of libido and potency by ergocriptine is solely due to suppression of PRL release. A need for further studies in this area is emphasized by comparable improvement of sexual function in bromocriptine- and placebo-treated men in one study (7), by lack of correlation between the decrease in libido and potency and the increase in peripheral PRL levels in a group of 65 men with pituitary tumors (8), and by an impotence of some patients with pituitary tumors and normal PRL levels (9).

The mechanism by which excessive PRL release could interefere with libido and potency is not understood. The ability of PRL to affect dopaminergic neurons in several regions of the brain could account for both impotence and impairment of gonadotropin release. The presence of PRL in the cerebrospinal fluid and the recent evidence that the adenohypophysis can secrete PRL directly to the brain add some credence to this possibility. The observation that gonadotropin levels are not elevated

in hyperprolactinemic hypogonadal men provides evidence of hypothalamic dysfunction in this syndrome (10). Altered secretory activity of the adrenals in hyperprolactinemic men (11) must also be considered in attempts to explain the ethiology of hypogonadism and impotence in this group of patients.

A suitable animal model could aid greatly in the study of the mechanism of PRL action on the hypothalamic/pituitary/testicular axis and on sexual behavior. Transplantation of PRL-producing tumors to adult male rats produces testicular atrophy, suppression of testosterone production, adrenal enlargement and elevation of plasma gonadotropin levels (12). Transplantation of several pituitary glands under the renal capsule causes chronic hyperprolactinemia and suppression of LH-RH - or castration-induced gonadotropin release (13,14). Basal gonadotropin levels can also be suppressed (15), but testicular weight and plasma testosterone levels are not affected (14, 15). Male rats and mice rendered hyperprolactinemic by multiple pituitary grafts exhibit striking deficiencies in copulatory behavior (16).

It is of interest to note that while pathological elevation of PRL release can suppress sexula functions, physiological amounts of PRL may normally stimulate gonadal activity in men (17) and in experimental animals (18). Reports of delayed puberty in a hyperprolactinemic patient (19), and in a patient with diminished PRL reserve (20) provide an example of differential effects of normal and excessive PRL levels.

A. BARTKE, Ph.D.
University of TExas Health Science Center
San Antonio, Texas

REFERENCES:

1. Boyar, R.M., Kapen, S., Finkelstein, J.W., Perlow,M., Sassin, J.F., Fukushima, D.K., Weitzman, E.D. and Hellman, L. J. Clin. INvest. 53:1588,1974.
2. Thorner, M.O. and Besser, G.M. Acta Endocrinol.88, Suppl.216:131,1978.
3. Tolis, G. and Van Vliet, S. Clin. REs. 24:279,1976.
3. Asfour, M., L'Hermite, M., Hedouin-Quincampoix,M. and Fossati, P. Acta Endocrinol.84:738,1977.
4. Faglia, G., Beck-Peccoz,P., Travaglini, P., Ambrosi, B., Rondena, M., Paracchi,A., Spada, A., Weger, G., Bara, R. and Bouzin, A. In: Crosignani,P.G. and Robyn, C (Eds) Prolactin and Human Reproduction, Academic Press, LOndon, 1977, pp 225.
6. Werder, K.V., Fahlbusch, R., Landgraf, R., Pickardt, C.R., Rjosk, H.K. and Scriba, P.C. J. Endocrinol. Invest. 1:47,1978.
7. Ambrosi, B., Bara, R,, Travaglini, P., Weber, G., Beck Peccoz, P., Rondena, M., Elli, R. and Faglia, G. Clin. Endocrinol. (Oxf.)7:417,1977.
8. Lundberg, P.O. and Wide, L. Fertil. Steril.29:175, 1978.
9. Kovacs, K., Horvath, E., Van Loon, G.R., Rewcastle, N.B., Ezrin, C. and Rosenbloom, A.A. Fertil, Steril. 29:622,1978.
10. Silverman, V., Cunningham, G.R. and Boyd, A.E.,III. Progr. 60th Meeting Endocr. Soc. p.357, 1978.
11. Vermeulen, A., Exx Sny xand xRxx Rubens Sny, E. and Rubens, R. J. Clin. Endocr. Metab. 44:1222,1977.
12. Fang, V.S., Refetoff, S. and Rosenfield, R.L. Endocrinology 95:991,1974.
13. Grandison, L., Hodson, C., Chen, H.T., Advis, J., Simpkins, J. and Meites, J. Neuroendocrinology 23: 312,1977.
14. Winters, S.J. and Loriaux, D.L. Endocrinology 102:864,1978.
15. Bartke, A., Smith, M.S., Michael, S.D., Peron, F.G. and Dalterio, S. Endocrinology 100:182,1977.
16. Doherty, P.C.,Jr., Michael, S.D. and Svare, B.B. Program 11th Meeting Soc. Study. Reprod. p.65A,1978.
17. Rubin, R.T., Gouin, P.R., Lubin, A., Poland, R.E. and Pirke, K.M. J.Clin.Endocrinol. Metab. 40:1027,1975.
18. Bartke, A., Hafiez, A.A., Bex, F.J. and Dalterio, S. Biol. Reprod.18:44,1978.
19. Koenig, M.P., Zuppinger, K. and Liechti, B. J. Clin. Endocrinol. Metab.45:825,1977.
20. Spitz,I.M., Landau, H., Almaliach, U., Rosen, E., Brautbar,N. and Russell,A. J. Clin. Endocrinol. Metab. 45:412,1977.

14 lines - 130 words

54 lines

~550 words

67 lines

part:

24 lines

~150 words

150
5
750 words

130 lines

1+3 according to the enclosed format, Thank you, A B

HYPERPROLACTINEMIA AND IMPOTENCE

Excessive release of prolactin (PRL), hyperprolactinemia, is usually caused by adenomatous tumors of the pituitary. It may but can also be due to a chronic exposure to tranquilizers, opiates or estrogens or lack any obvious etiology. In women, hyperprolactinemia can be associated with amenorrhea and anovulatory sterility and, less frequently, with galactorrhea. Suppression of PRL release in these patients by administration of a synthetic dopamine receptor agonist, 2-Bromo-α-ergocriptine mesylate (CB-154; PARLODEL, Sandoz), or by surgical removal or irradiation of the pituitary tumors, abolishes inappropriate lactation and restores menstrual cyclicity and fertility. Several recent reports indicate that hyperprolactinemia can also interfere with sexual function ~~also~~ in men (1 - 6). Impotence is the most common complaint, but various degrees of hypogonadism have also been described. Gonadotropin levels are normal or slightly suppressed and response to an LH-RH challenge may be impaired. Treatment with bromoergocriptine restores libido and potency in the majority of these patients (2 - 6) and can also improve testicular function (2, 4, 5).

A causal relationship of the excessive PRL release and the sexual dysfunction is strongly suggested by these observations. However, a possibility remains that hyperprolactinemia, impotence and hypogonadism represent unrelated symptoms of hypothalamic/pituitary ~~dysfunction~~ disease in men with adenohypophyseal adenomas. Furthermore, bromocriptine could ~~be~~ improve potency by a direct action on central and peripheral dopaminergic neurons involved in the control of the erectile response (5). In other words, it remains to be conclusively demonstrated that restoration of libido and potency ~~in~~ by ergocriptine is ~~indeed~~ solely due to suppression of PRL release. A need for further studies in this area is emphasized by comparable improvement of sexual function in bromocriptine- and placebo-treated men in one study (7), by lack of correlation between the decrease in libido and potency and the increase in peripheral PRL levels in a group of 65 men with pituitary tumors (8), and by a ~~reduction~~ in impotence of some patients with pituitary tumors and normal PRL levels (9).

The mechanism by which excessive PRL release could interefere with libido and potency is not understood. The ability of PRL to affect dopaminergic neurons in several regions of the brain could account for both impotence and impairment of gonadotropin release. The presence of PRL in the cerebrospinal fluid and the recent evidence that the adenohypophysis can secrete PRL directly to the brain add some credence to this possibility. The observation that gonadotropin levels are not elevated

in hyperprolactinemic hypogonadal men provides evidence of hypothalamic dysfunction in this syndrome (10). Altered secretory activity of the adrenals in hyperprolactinemic men (11) must also be considered in attempts to explain the etiology of hypogonadism and impotence in this group of patients.

A suitable animal model could aid greatly in the study of the mechanism of PRL action on the hypothalamic/pituitary/testicular axis and on sexual behavior. Transplantation of PRL-producing tumors to adult male rats produces testicular atrophy, suppression of testosterone production, adrenal enlargement and elevation of plasma gonadotropin levels (12). Transplantation of several pituitary glands under the renal capsule causes chronic hyperprolactinemia and suppression of LH-RH - or castration-induced gonadotropin release (13,14). Basal gonadotropin levels can also be suppressed and adrenal weight is increased (15), but testicular weight and plasma testosterone levels are not affected (14, 15). Male rats and mice rendered hyperprolactinemic by multiple pituitary grafts exhibit striking deficiencies in copulatory behavior (16).

It is of interest to note that while pathological elevation of PRL release can suppress sexual functions, physiological amounts of PRL may normally stimulate gonadal activity in men (17) and in experimental animals (18). Reports of delayed puberty in a hyperprolactinemic patient (19), and in a patient with a diminished PRL reserve (20) provide an example of differential effects of normal and excessive PRL levels.

A. BARTKE, Ph.D.
University of TExas Health Science Center
San Antonio, Texas

REFERENCES:

1. Boyar, R.M., Kapen, S., Finkelstein, J.W., Perlow,M., Sassin, J.F., Fukushima, D.K., Weitzman, E.D. and Hellman, L. J. Clin. INvest. 53:1588,1974.
5. Thorner, M.O. and Besser, G.M. Acta Endocrinol.88, Suppl.216:131,1978.
2. Tolis, G. and Van Vliet, S. Clin. REs. 24:279,1976.
3. Asfour, M., L'Hermite, M., Hedouin-Quincampoix,M. and Fossati, P. Acta Endocrinol.84:738,1977.
4. Faglia, G., Beck-Peccoz,P., Travaglini, P., Ambrosi, B., Rondena, M., Paracchi,A., Spada, A., Weger, G., Bara, R. and Bouzin, A. In: Crosignani,P.G. and Robyn, C (Eds) Prolactin and Human Reproduction, Academic Press, LOndon, 1977, p. 225.
6. Werder, K.V., Fahlbusch, R., Landgraf, R., Pickardt, C.R., Rjosk, H.K. and Scriba, P.C. J. Endocrinol. Invest. 1:47,1978.
7. Ambrosi, B., Bara, R,, Travaglini, P., Weber, G., Beck Peccoz, P., Rondena, M., Elli, R. and Faglia, G. Clin. Endocrinol. (Oxf.)7:417,1977.
8. Lundberg, P.O. and Wide, L. Fertil. Steril.29:175, 1978.
9. Kovacs, K., Horvath, E., Van Loon, G.R., Rewcastle, N.B., Ezrin, C. and Rosenbloom, A.A. Fertil, Steril. 29:622,1978.
10. Silverman, V., Cunningham, G.R. and Boyd, A.E.,III. Progr. 60th Meeting Endocr. Soc. p.357, 1978.
11. Vermeulen, A., Sny, E. and Rubens, R. J. Clin. Endocr. Metab. 44:1222,1977.
12. Fang, V.S., Refetoff, S. and Rosenfield, R.L. Endocrinology 95:991,1974.
13. Grandison, L., Hodson, C., Chen, H.T., Advis, J., Simpkins, J. and Meites, J. Neuroendocrinology 23: 312,1977.
14. Winters, S.J. and Loriaux, D.L. Endocrinology 102:864,1978.
15. Bartke, A., Smith, M.S., Michael, S.D., Peron, F.G. and Dalterio, S. Endocrinology 100:182,1977.
16. Doherty, P.C.,Jr., Michael, S.D. and Svare, B.B. Program 11th Meeting Soc. Study Reprod. p.65A,1978.
17. Rubin, R.T., Gouin, P.R., Lubin, A., Poland, R.E. and Pirke, K.M. J.Clin.Endocrinol. Metab. 40:1027,1975.
18. Bartke, A., Hafiez, A.A., Bex, F.J. and Dalterio, S. Biol. Reprod.18:44,1978.
19. Koenig, M.P., Zuppinger, K. and Liechti, B. J. Clin. Endocrinol. Metab.45:825,1977.
20. Spitz,I.M., Landau, H., Almaliach, U., Rosen, E., Brautbar,N. and Russell,A. J. Clin. Endocrinol. Metab. 45:412,1977.

REFERENCES:

1. Boyar, R.M., Kapen, S., Finkelstein, J.W., Perlow, M., Sassin, J.F., Fukushima, D.K., Weitzman, E.D. and Hellman, L. J. Clin. Invest. 53: 1588, 1974.
2. Tolis, G. and Van Vliet, S. Clin. Res. 24:279, 1976.
3. Asfour, M., L'Hermite, M., Hedouin-Quincampoix, M. and Fossati, P. Acta Endocrinol. 84:738, 1977.
4. Faglia, G., Beck-Peccoz, P., Travaglini, P., Ambrosi, B., Rondena, M., Paracchi, A., Spada, A., Weger, G., Bara, R. and Bouzin, A. In: Crosignani, P.G. and Robyn, C. (Eds) Prolactin and Human Reproduction, Academic Press, London, 1977, p. 225.
5. Thorner, M.O. and Besser, G.M. Acta Endocrinol. 88, Suppl. 216:131, 1978.
6. Werder, K.V., Fahlbusch, R., Landgraf, R., Pickardt, C.R., Rjosk, H.K. and Scriba, P.C. J. Endocrinol. Invest. 1:47, 1978.
7. Ambrosi, B., Bara, R., Travaglini, P., Weber, G., Beck Peccoz, P., Rondena, M., Elli, R. and Faglia, G. Clin. Endocrinol. (Oxf.) 7:417, 1977.
8. Lundberg, P.O. and Wide, L. Fertil. Steril. 29:175, 1978.
9. Kovacs, K., Horvath, E., Van Loon, G.R., Rewcastle, N.B., Ezrin, C. and Rosenbloom, A.A. Fertil. Steril. 29:622, 1978.
10. Silverman, V., Cunningham, G.R. and Boyd, A.E., III. Progr. 60th Meeting Endocr. Soc. p. 357, 1978.
11. Vermeulen, A., Sny, E. and Rubens, R. J. Clin. Endocr. Metab. 44:1222, 1977.
12. Fang, V.S., Refetoff, S. and Rosenfield, R.L. Endocrinology 95:991, 1974.
13. Grandison, L., Hodson, C., Chen, H.T., Advis, J., Simpkins, J. and Meites, J. Neuroendocrinology 23:312, 1977.
14. Winters, S.J. and Loriaux, D.L. Endocrinology 102:864, 1978.
15. Bartke, A., Smith, M.S., Michael, S.D., Peron, F.G. and Dalterio, S. Endocrinology 100:182, 1977.
16. Doherty, P.C., Jr., Michael, S.D. and Svare, B.B. Program 11th Meeting Soc. Study Reprod. p. 65A, 1978.
17. Rubin, R.T., Gouin, P.R., Lubin, A., Poland, R.E. and Pirke, K.M. J. Clin. Endocrinol. Metab. 40:1027, 1975.
18. Bartke, A., Hafiez, A.A., Bex, F.J. and Dalterio, S. Biol. Reprod. 18: 44, 1978.
19. Koenig, M.P., Zuppinger, K. and Liechti, B.J. Clin. Endocrinol. Metab. 45:825, 1977.
20. Spitz, I.M., Landau, H., Almaliach, U., Rosen, E., Brautbar, N. and Russell, A. J. Clin. Endocrinol. Metab. 45:412, 1977.

pressed and adrenal weight is increased (15), but testicular weight and plasma testosterone levels are not affected (14,15). Male rats and mice rendered hyperprolactinemic by multiple pituitary grafts exhibit striking deficiencies in copulatory behavior (16).

It is of interest to note that while pathological elevation of PRL release can suppress sexual function, physiological amounts of PRL may normally stimulate gonadal activity in men (17) and in experimental animals (18). Reports of delayed puberty in a hyperprolactinemic patient (19), and in a patient with a diminished PRL reserve (20) provide an example of differential effects of normal and excessive PRL levels.

Results from several laboratories indicate that hyperprolactinemia and various symptoms of sexual dysfunction can be induced in male rats and mice.

double-space, please

bromocriptine,

HYPERPROLACTINEMIA AND IMPOTENCE

Excessive release of prolactin (PRL), hyperprolactinemia, is usually caused by adenomatous tumors of the pituitary. It can also be due to a chronic exposure to tranquilizers, opiates or estrogens or may lack any obvious etiology. In women, hyperprolactinemia can be associated with amenorrhea and anovulatory sterility and, less frequently, with galactorrhea. Suppression of PRL release in these patients by administration of a synthetic dopamine receptor agonist, 2-Bromo- α-ergocriptine mesylate (CB-154; PARLODEL, Sandoz), or by surgical removal or irradiation of the pituitary tumors, abolishes inappropriate lactation and restores menstrual cyclicity and fertility. Several recent reports indicate that hyperprolactinemia can also interfere with sexual function in men (1-6). Impotence is the most common complaint, but various degrees of hypogonadism have also been described. Gonadotropin levels are normal or slightly suppressed and response to an LH-RH challenge may be impaired. Treatment with bromo~~ergo~~-criptine restores libido and potency in the majority of these patients (2-6) and can also improve testicular function (2,4,5).

A causal relationship of the excessive PRL release and the sexual dysfunction is strongly suggested by these observations. However, a possibility remains that hyperprolactinemia, impotence and hypogonadism represent unrelated symptoms of hypothalamic/pituitary disease in men with adenohypophyseal adenomas. Furthermore, bromocriptine could improve potency by a direct action on central and peripheral dopaminergic neurons involved in the control of the erectile response (5). In other words, it remains to be conclusively demonstrated that restoration of libido and potency by ~~ergo~~-criptine is due solely to suppression of PRL release. A need for further studies in this area is emphasized by comparable improvement of sexual function in bromocriptine- and placebo-treated men in one study (7), by lack of correlation between the decrease in libido and potency and the increase in peripheral PRL levels in a group of 65 men with pituitary tumors (8), and by impotence of some patients with pituitary tumors and normal PRL levels (9).

bromo

The mechanism by which excessive PRL release could interfere with libido and potency is not understood. The ability of PRL to affect dopaminergic neurons in several regions of the brain could account for both impotence and impairment of gonadotropin release. The presence of PRL in the cerebrospinal fluid and the recent evidence that the adenohypophysis can secrete PRL directly to the brain add some credence to this possibility. The observation that gonadotropin levels are not elevated in hyperprolactinemic hypogonadal men provides evidence of hypothalamic dysfunction in this syndrome (10). Altered secretory activity of the adrenals in hyperprolactinemic men (11) must also be considered in attempts to explain the etiology of hypogonadism and impotence in this group of patients.

A suitable animal model could aid greatly in the study of the mechanism of PRL action on the hypothalamic-pituitary-testicular axis and on sexual behavior. Transplantation of PRL-producing tumors to adult male rats produces testicular atrophy, suppression of testosterone production, adrenal enlargement and elevation of plasma gonadotropin levels (12). Transplantation of several pituitary glands under the renal capsule causes chronic hyperprolactinemia and suppression of LH-RH- or castration-induced gonadotropin release (13,14). Basal gonadotropin levels can also be sup-

AB802.KBD
31-Oct-78
Small

October 31, 1978

Dr. Emil Steinberger
Department of Reproductive Medicine and Biology
The University of Texas Medical School
P.O. Box 20708
Houston, Texas 77025

Dear Dr. Steinberger,

Enclosed please find a brief review "Hyperprolactinemia and impotence" for the Highlights in Andrology. I tried to keep the number of references to a minimum but still ended up with twenty. I believe that the length of this review (text plus references) is comparable to those published in the first issue.

Warmest regards,

Andrzej Bartke, Ph.D.
Associate Professor

AB:mf

Enclosures

HYPERPROLACTINEMIA AND IMPOTENCE

Excessive release of prolactin (PRL), hyperprolactinemia, is usually caused by adenomatous tumors of the pituitary. It can also be due to a chronic exposure to tranquilizers, opiates or estrogens or may lack any obvious etiology. In women, hyperprolactinemia can be associated with amenorrhea and anovulatory sterility and, less frequently, with galactorrhea. Suppression of PRL release in these patients by administration of a synthetic dopamine receptor agonist, 2-Bromo-α-ergocriptine mesylate (bromocriptine, CB-154; PARLODEL, Sandoz), or by surgical removal or irradiation of the pituitary tumors, abolishes inappropriate lactation and restores menstrual cyclicity and fertility. Several recent reports indicate that hyperprolactinemia can also interfere with sexual function in men (1-6). Impotence is the most common complaint, but various degrees of hypogonadism have also been described. Gonadotropin levels are normal or slightly suppressed and response to an LH-RH challenge may be impaired. Treatment with bromocriptine restores libido and potency in the majority of these patients (2-6) and can also improve testicular function (2,4,5).

A causal relationship of the excessive PRL release and the sexual dysfunction is strongly suggested by these observations. However, a possibility remains that hyperprolactinemia, impotence and hypogonadism represent unrelated symptoms of hypothalamic/pituitary disease in men with adenohypophyseal adenomas. Furthermore, bromocriptine could improve potency by a direct action on central and peripheral dopaminergic neurons involved in the control of the erectile response (5). In other words, it remains to be conclusively demonstrated that restoration of libido and potency by bromocriptine is due solely to suppression of PRL release. A need for further

studies in this area is emphasized by comparable improvement of sexual function in bromocriptine- and placebo-treated men in one study (7), by lack of correlation between the decrease in libido and potency and the increase in peripheral PRL levels in a group of 65 men with pituitary tumors (8), and by impotence of some patients with pituitary tumors and normal PRL levels (9).

The mechanism by which excessive PRL release could interfere with libido and potency is not understood. The ability of PRL to affect dopaminergic neurons in several regions of the brain could account for both impotence and impairment of gonadotropin release. The presence of PRL in the cerebrospinal fluid and the recent evidence that the adenohypophysis can secrete PRL directly to the brain add some credence to this possibility. The observation that gonadotropin levels are not elevated in hyperprolactinemic hypogonadal men provides evidence of hypothalamic dysfunction in this syndrome (10). Altered secretory activity of the adrenals in hyperprolactinemic men (11) must also be considered in attempts to explain the etiology of hypogonadism and impotence in this group of patients.

A suitable animal model could aid greatly in the study of the mechanism of PRL action on the hypothalamic-pituitary-testicular axis and on sexual behavior. Results from several laboratories indicate that hyperprolactinemia and various symptoms of sexual dysfunction can be induced in male rats and mice. Transplantation of PRL-producing tumors to adult male rats produces testicular atrophy, suppression of testosterone production, adrenal enlargement and elevation of plasma gonadotropin levels (12). Transplantation of several pituitary glands under the renal capsule causes chronic hyperprolactinemia and suppression of LH-RH- or castration-

induced gonadotropin release (13,14). Basal gonadotropin levels can also be suppressed and adrenal weight is increased (15), but testicular weight and plasma testosterone levels are not affected (14,15). Male rats and mice rendered hyperprolactinemic by multiple pituitary grafts exhibit striking deficiencies in copulatory behavior (16).

It is of interest to note that while pathological elevation of PRL release can suppress sexual function, physiological amounts of PRL may normally stimulate gonadal activity in men (17) and in experimental animals (18). Reports of delayed puberty in a hyperprolactinemic patient (19), and in a patient with a diminished PRL reserve (20) provide an example of differential effects of normal and excessive PRL levels.

REFERENCES:

1. Boyar, R.M., Kapen, S., Finkelstein, J.W., Perlow, M., Sassin, J.F., Fukushima, D.K., Weitzman, E.D. and Hellman, L. J. Clin. Invest. 53: 1588, 1974.
2. Tolis, G. and Van Vliet, S. Clin. Res. 24:279, 1976.
3. Asfour, M., L'Hermite, M., Hedouin-Quincampoix, M. and Fossati, P. Acta Endocrinol. 84:738, 1977.
4. Faglia, G., Beck-Peccoz, P., Travaglini, P., Ambrosi, B., Rondena, M., Paracchi, A., Spada, A., Weger, G., Bara, R. and Bouzin, A. In: Crosignani, P.G. and Robyn, C. (Eds) Prolactin and Human Reproduction, Academic Press, London, 1977, p. 225.
5. Thorner, M.O. and Besser, G.M. Acta Endocrinol. 88, Suppl. 216:131, 1978.
6. Werder, K.V., Fahlbusch, R., Landgraf, R., Pickardt, C.R., Rjosk, H.K. and Scriba, P.C. J. Endocrinol. Invest. 1:47, 1978.
7. Ambrosi, B., Bara, R., Travaglini, P., Weber, G., Beck Peccoz, P., Rondena, M., Elli, R. and Faglia, G. Clin. Endocrinol. (Oxf.) 7:417, 1977.
8. Lundberg, P.O. and Wide, L. Fertil. Steril. 29:175, 1978.
9. Kovacs, K., Horvath, E., Van Loon, G.R., Rewcastle, N.B., Ezrin, C. and Rosenbloom, A.A. Fertil. Steril. 29:622, 1978.
10. Silverman, V., Cunningham, G.R. and Boyd, A.E., III. Progr. 60th Meeting Endocr. Soc. p. 357, 1978.
11. Vermeulen, A., Sny, E. and Rubens, R. J. Clin. Endocr. Metab. 44:1222, 1977.
12. Fang, V.S., Refetoff, S. and Rosenfield, R.L. Endocrinology 95:991, 1974.
13. Grandison, L., Hodson, C., Chen, H.T., Advis, J., Simpkins, J. and Meites, J. Neuroendocrinology 23:312, 1977.
14. Winters, S.J. and Loriaux, D.L. Endocrinology 102:864, 1978.
15. Bartke, A., Smith, M.S., Michael, S.D., Peron, F.G. and Dalterio, S. Endocrinology 100:182, 1977.
16. Doherty, P.C., Jr., Michael, S.D. and Svare, B.B. Program 11th Meeting Soc. Study Reprod. p. 65A, 1978.
17. Rubin, R.T., Gouin, P.R., Lubin, A., Poland, R.E. and Pirke, K.M. J. Clin. Endocrinol. Metab. 40:1027, 1975.
18. Bartke, A., Hafiez, A.A., Bex, F.J. and Dalterio, S. Biol. Reprod. 18: 44, 1978.
19. Koenig, M.P., Zuppinger, K. and Liechti, B.J. Clin. Endocrinol. Metab. 45:825, 1977.
20. Spitz, I.M., Landau, H., Almaliach, U., Rosen, E., Brautbar, N. and Russell, A. J. Clin. Endocrinol. Metab. 45:412, 1977.

HYPERPROLACTINEMIA AND IMPOTENCE

Excessive release of prolactin (PRL), hyperprolactinemia, is usually caused by adenomatous tumors of the pituitary. It can also be due to a chronic exposure to tranquilizers, opiates or estrogens or may lack any obvious etiology. In women, hyperprolactinemia can be associated with amenorrhea and anovulatory sterility and, less frequently, with galactorrhea. Suppression of PRL release in these patients by administration of a synthetic dopamine receptor agonist, 2-Bromo-α-ergocriptine mesylate (bromocriptine, CB-154; PARLODEL, Sandoz), or by surgical removal or irradiation of the pituitary tumors, abolishes inappropriate lactation and restores menstrual cyclicity and fertility. Several recent reports indicate that hyperprolactinemia can also interfere with sexual function in men (1-6). Impotence is the most common complaint, but various degrees of hypogonadism have also been described. Gonadotropin levels are normal or slightly suppressed and response to an LH-RH challenge may be impaired. Treatment with bromocriptine restores libido and potency in the majority of these patients (2-6) and can also improve testicular function (2,4,5).

A causal relationship of the excessive PRL release and the sexual dysfunction is strongly suggested by these observations. However, a possibility remains that hyperprolactinemia, impotence and hypogonadism represent unrelated symptoms of hypothalamic/pituitary disease in men with adenohypophyseal adenomas. Furthermore, bromocriptine could improve potency by a direct action on central and peripheral dopaminergic neurons involved in the control of the erectile response (5). In other words, it remains to be conclusively demonstrated that restoration of libido and potency by bromocriptine is due solely to suppression of PRL release. A need for further

studies in this area is emphasized by comparable improvement of sexual function in bromocriptine- and placebo-treated men in one study (7), by lack of correlation between the decrease in libido and potency and the increase in peripheral PRL levels in a group of 65 men with pituitary tumors (8), and by impotence of some patients with pituitary tumors and normal PRL levels (9).

The mechanism by which excessive PRL release could interfere with libido and potency is not understood. The ability of PRL to affect dopaminergic neurons in several regions of the brain could account for both impotence and impairment of gonadotropin release. The presence of PRL in the cerebrospinal fluid and the recent evidence that the adenohypophysis can secrete PRL directly to the brain add some credence to this possibility. The observation that gonadotropin levels are not elevated in hyperprolactinemic hypogonadal men provides evidence of hypothalamic dysfunction in this syndrome (10). Altered secretory activity of the adrenals in hyperprolactinemic men (11) must also be considered in attempts to explain the etiology of hypogonadism and impotence in this group of patients.

A suitable animal model could aid greatly in the study of the mechanism of PRL action on the hypothalamic-pituitary-testicular axis and on sexual behavior. Results from several laboratories indicate that hyperprolactinemia and various symptoms of sexual dysfunction can be induced in male rats and mice. Transplantation of PRL-producing tumors to adult male rats produces testicular atrophy, suppression of testosterone production, adrenal enlargement and elevation of plasma gonadotropin levels (12). Transplantation of several pituitary glands under the renal capsule causes chronic hyperprolactinemia and suppression of LH-RH- or castration-

induced gonadotropin release (13,14). Basal gonadotropin levels can also be suppressed and adrenal weight is increased (15), but testicular weight and plasma testosterone levels are not affected (14,15). Male rats and mice rendered hyperprolactinemic by multiple pituitary grafts exhibit striking deficiencies in copulatory behavior (16).

It is of interest to note that while pathological elevation of PRL release can suppress sexual function, physiological amounts of PRL may normally stimulate gonadal activity in men (17) and in experimental animals (18). Reports of delayed puberty in a hyperprolactinemic patient (19), and in a patient with a diminished PRL reserve (20) provide an example of differential effects of normal and excessive PRL levels.

REFERENCES:

1. Boyar, R.M., Kapen, S., Finkelstein, J.W., Perlow, M., Sassin, J.F., Fukushima, D.K., Weitzman, E.D. and Hellman, L. J. Clin. Invest. 53: 1588, 1974.
2. Tolis, G. and Van Vliet, S. Clin. Res. 24:279, 1976.
3. Asfour, M., L'Hermite, M., Hedouin-Quincampoix, M. and Fossati, P. Acta Endocrinol. 84:738, 1977.
4. Faglia, G., Beck-Peccoz, P., Travaglini, P., Ambrosi, B., Rondena, M., Paracchi, A., Spada, A., Weger, G., Bara, R. and Bouzin, A. In: Crosignani, P.G. and Robyn, C. (Eds) Prolactin and Human Reproduction, Academic Press, London, 1977, p. 225.
5. Thorner, M.O. and Besser, G.M. Acta Endocrinol. 88, Suppl. 216:131, 1978.
6. Werder, K.V., Fahlbusch, R., Landgraf, R., Pickardt, C.R., Rjosk, H.K. and Scriba, P.C. J. Endocrinol. Invest. 1:47, 1978.
7. Ambrosi, B., Bara, R., Travaglini, P., Weber, G., Beck Peccoz, P., Rondena, M., Elli, R. and Faglia, G. Clin. Endocrinol. (Oxf.) 7:417, 1977.
8. Lundberg, P.O. and Wide, L. Fertil. Steril. 29:175, 1978.
9. Kovacs, K., Horvath, E., Van Loon, G.R., Rewcastle, N.B., Ezrin, C. and Rosenbloom, A.A. Fertil. Steril. 29:622, 1978.
10. Silverman, V., Cunningham, G.R. and Boyd, A.E., III. Progr. 60th Meeting Endocr. Soc. p. 357, 1978.
11. Vermeulen, A., Sny, E. and Rubens, R. J. Clin. Endocr. Metab. 44:1222, 1977.
12. Fang, V.S., Refetoff, S. and Rosenfield, R.L. Endocrinology 95:991, 1974.
13. Grandison, L., Hodson, C., Chen, H.T., Advis, J., Simpkins, J. and Meites, J. Neuroendocrinology 23:312, 1977.
14. Winters, S.J. and Loriaux, D.L. Endocrinology 102:864, 1978.
15. Bartke, A., Smith, M.S., Michael, S.D., Peron, F.G. and Dalterio, S. Endocrinology 100:182, 1977.
16. Doherty, P.C., Jr., Michael, S.D. and Svare, B.B. Program 11th Meeting Soc. Study Reprod. p. 65A, 1978.
17. Rubin, R.T., Gouin, P.R., Lubin, A., Poland, R.E. and Pirke, K.M. J. Clin. Endocrinol. Metab. 40:1027, 1975.
18. Bartke, A., Hafiez, A.A., Bex, F.J. and Dalterio, S. Biol. Reprod. 18: 44, 1978.
19. Koenig, M.P., Zuppinger, K. and Liechti, B.J. Clin. Endocrinol. Metab. 45:825, 1977.
20. Spitz, I.M., Landau, H., Almaliach, U., Rosen, E., Brautbar, N. and Russell, A. J. Clin. Endocrinol. Metab. 45:412, 1977.

THE UNIVERSITY OF TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

MEDICAL SCHOOL

6431 Fannin
Texas Medical Center

Post Office Box 20708
Houston, Texas 77025
(713) 792-2121

August 24, 1978

MEMORANDUM

To: Members of the Publication Committee of American Society of Andrology

From: Emil Steinberger, M.D. ES

Re: "Highlights in Andrology"

Dear Chairman and Committee Members:

As you know I was asked by the President to facilitate the first issue of "Highlights in Andrology." I prepared the first page layout and decided on the color. This was done without your consultations in order to get the first issue out as rapidly and as inexpensively as possible. I see no reason why the first issue of Volume 1 should not be out by October 1, 1978, particularly, if you will lend a helping hand.

Tentatively I plan for the following content:

1. "From The President" - this will be an informational statement from Dr. Paulsen concerning the decision regarding a journal and any other information he may wish to share with the membership.

2. "Announcements" - here again we can announce out meeting dates, call for abstracts, and any announcements that the Officers or Chairmen of the various committees wish to make.

3. One or two, preferably two, relatively brief summaries of current scientific or clinical findings which may be of particular interest to the membership.

4. "Questions and Comments from the Membership."

Obviously the above as well as the format of the first page we may desire to change starting with Volume 2 which will commence with the first Number in 1979. The first issue, which I hope will come out in October, 1978, will be Volume 1, Number 1, thus we should have Volume 1, Number 2 coming out in December and Volume 2, Number 1 in February, 1979.

I got Dr. Anna Steinberger to "volunteer" to write a review on "Inhibin" which will address itself to the current status of knowledge in this area based primarily on work presented at a workshop on Inhibin which she attended in Cambridge, England in July of this year.

I will need from the Committee one more review, approximately one printed page long, on a current and interesting topic. Please volunteer! I would like to get several reviews now in order to plan the subsequent issues.

Obviously, the section on "Questions and Comments" theoretically would not be viable for the first issue since the membership obviously would not be aware of this opportunity until after the first issue comes out. However, to get the ball rolling I would like for you to solicit questions and comments from your colleagues who are not members of the Publication Committee so that we could have a viable "Question and Comments" section in the first issue.

Please forgive me for taking the bull by the horns and getting this on the road without much input from you but with the time constraint presented to me by the President, the vacation season and need for getting this on the road as soon as possible, I felt justified in taking this step.

I will be looking forward to hearing from each one of you by return mail if at all possible.

S.O.S.

Please.

copies were mailed to:

R. Ansbacher
Nancy Alexander
C. Alvin Paulsen
Richard J. Sherins
Larry Ewing
William J. Bremner
Philip Troen
A. Bartke
Eugenia Rosemberg

September 1, 1978

Dr. Emil Steinberger
Dept. Reproductive Medicine & Biology
The University of Texas Health Science
Center at Houston
Post Office Box 20708
Houston, Texas 77025

Dear Dr. Steinberger,

This is in response to your memorandum on "Highlights in Andrology".

I am very glad to hear that publiaation of the "Highlights" will commence within weeks and would be glad to contribute a review on effects of hyperprolactinemia on male reproductive and sexual functions. However, I would very much prefer to plan it for December, or for one of the subsequent issues rather than for October. With two new people joining our lab and a 10 day trip to Europe in September, the next few weeks promise to be very busy. Also, a review on hyperprolactinemia may be too similar in character to the one on inhibin (endocrine and "basic" rather than practical for a clinician) to be suitable for the same issue.

Warmest regards,

Andrzej Bartke, Ph.D.
Assistant Professor

AB:mf

DR. EMIL STEINBERGER
DEPT. REPRODUCTIVE MEDICINE & BIOLOGY

THE UNIVERSITY OF TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

MEDICAL SCHOOL

6431 Fannin
Texas Medical Center

Post Office Box 20708
Houston, Texas 77025
(713) 792-2121

August 24, 1978

MEMORANDUM

To: Members of the Publication Committee of American Society of Andrology

From: Emil Steinberger, M.D. ES.

Re: "Highlights in Andrology"

Dear Chairman and Committee Members:

As you know I was asked by the President to facilitate the first issue of "Highlights in Andrology." I prepared the first page layout and decided on the color. This was done without your consultations in order to get the first issue out as rapidly and as inexpensively as possible. I see no reason why the first issue of Volume 1 should not be out by October 1, 1978, particularly, if you will lend a helping hand.

Tentatively I plan for the following content:

1. "From The President" - this will be an informational statement from Dr. Paulsen concerning the decision regarding a journal and any other information he may wish to share with the membership.

2. "Announcements" - here again we can announce out meeting dates, call for abstracts, and any announcements that the Officers or Chairmen of the various committees wish to make.

3. One or two, preferably two, relatively brief summaries of current scientific or clinical findings which may be of particular interest to the membership.

4. "Questions and Comments from the Membership."

Obviously the above as well as the format of the first page we may desire to change starting with Volume 2 which will commence with the first Number in 1979. The first issue, which I hope will come out in October, 1978, will be Volume 1, Number 1, thus we should have Volume 1, Number 2 coming out in December and Volume 2, Number 1 in February, 1979.

I got Dr. Anna Steinberger to "volunteer" to write a review on "Inhibin" which will address itself to the current status of knowledge in this area based primarily on work presented at a workshop on Inhibin which she attended in Cambridge, England in July of this year.

I will need from the Committee one more review, approximately one printed page long, on a current and interesting topic. Please volunteer! I would like to get several reviews now in order to plan the subsequent issues.

Obviously, the section on "Questions and Comments" theoretically would not be viable for the first issue since the membership obviously would not be aware of this opportunity until after the first issue comes out. However, to get the ball rolling I would like for you to solicit questions and comments from your colleagues who are not members of the Publication Committee so that we could have a viable "Question and Comments" section in the first issue.

Please forgive me for taking the bull by the horns and getting this on the road without much input from you but with the time constraint presented to me by the President, the vacation season and need for getting this on the road as soon as possible, I felt justified in taking this step.

I will be looking forward to hearing from each one of you by return mail if at all possible.

American Society of Andrology

November 23, 1977

Professor Dr. C. Schirrens
Universität Hamburg
Department of Andrology
Universitäts Krankenhaus Eppendorf
Martinstrasse 52
2000 Hamburg 20
West Germany

Dear Professor Schirrens:

The returns from our referendum to the membership of the American Society of Andrology are now in hand, and regretfully I must report that there was very little support for continued use of Andrologia as our official journal. It is my unpleasant duty, therefore, to notify you by this letter of the termination of the affiliation of the American Society of Andrology as of December, 1977. In doing so, I take comfort in the fact that this is not an arbitrary action of a small group of the Officers or Council members but is a decision arrived at by the democratic process of referendum to the entire membership of the Society.

Some 70 members are paid up through next June and will, of course, continue to receive Andrologia until then. I have no doubt that a small number of our members will wish to continue to subscribe to your journal as individuals. Like Dr. Paulsen, I will be glad to continue to review occasional papers for the journal in the areas of my competence.

As you know the ASA has declined to adopt the International Journal of Andrology. Our annual meeting is in March, however, and our continued affiliation with CIDA will be considered at that time. Dr. Eliasson insists that in the meantime the American Society of Andrology will appear on the cover of their first issue of the International Journal of Andrology as an affiliate of CIDA because no official action of the society will have been taken before its publication.

Some of us look forward to the time when all of this maneuvering is past and we can again devote our time and energies to research and scholarship.

With kind regards,

Sincerely,

Don W. Fawcett

Don W. Fawcett, M.D.
President

cc: Dr. Edward Grosse

andrologia

First Journal for Andrology

Grosse Verlag
Kurfürstendamm 152, 1000 Berlin 31

Telefon (030) 892 40 64/65

Publisher: Dr. Eduard Grosse, M. A.

Bank für Handel und Industrie AG,
(BLZ 100 800 00), Kto. 3 098 643
Berliner Bank AG.,
(BLZ 100 200 00), Kto. 2708853700
Postscheckamt Berlin West,
(BLZ 100 100 10), Kto. 4891-109

Ph. D. Andrzej Bartke
Worc. Found. Exp. Biol.
222 Maple Ave.

Shrewsb, Mass. 01545/USA

Berlin, Oct. 11th, 1977

Dear Dr. Bartke!

ANDROLOGIA was the very first and today is the leading forum for Andrology in the world. 1978 this journal will enter the second decade of its existence.

We would like to thank you personnally like all other colleagues and readers for your trust and active cooperation. Starting January 1978, they have enabled us to increase the frequency of issues per annum from 4 to 6 and editorial content from 360 to 540 pages. At the same time, the editorial strength of ANDROLOGIA will be increased and the content broadened in both research and treatment.

Our referee system for editorial selection, developed throughout many years, will be continued in the future.

For the last 4 years, ANDROLOGIA collaborated with "Comité Internacional de Andrologia" in Barcelona, Spain. It will cease.

Beginning in 1978 it will be replaced by renewed direct partnership with national associations for Andrology. Their members will be able to order ANDROLOGIA at special reduced rates.

Details will be announced soon in issue 4/1977.

With kind regards,

Prof. Dr. C. Schirren
Editor-in-Chief

Dr. Eduard Grosse, M.A.
Publisher

MEDICAL RESEARCH INSTITUTE OF WORCESTER, INC.

CLINICAL AFFILIATE OF THE WORCESTER CITY HOSPITAL

26 QUEEN STREET

WORCESTER, MASSACHUSETTS 01610

DIRECTOR OF RESEARCH:

EUGENIA ROSEMBERG, M. D.

756-1551 (AREA CODE 617)

May 2, 1977

E.S.E. Hafez, Ph.D.
Reproductive Physiology
C.S. Mott Center for Human
Growth & Development
275 East Hancock Ave.
Detroit, MI 48201

Dear Saad,

I thought I saw you in L'Aquila. However, you did not stop to talk to me. What is the matter?

This is a joke, of course, I know you came late and you only had probably 24 hours there. Am I correct?

The reason for my letter is the following. I just received from Dr. Fawcett a copy of the minutes of the Council Meeting of ASA and I think that before you distribute these to Council Members it will be necessary for you to correct on Page 5 under VIII. Report of the Publications Committee, on line 4, instead of 3 Editors should read 2 Associate Editors, Drs. Emil Steinberger and Dr. C. Alvin Paulsen, and 1 Council Member, Dr. Anna Steinberger coordinated the review of the manuscripts.

Separately from the above, would it be possible for you to send me a copy of the design approved as the emblem for the ASA, and also a copy of the Program Book which I assume was distributed at the Meeting.

With best personal regards.

Sincerely,

Eugenia Rosemberg, M.D.
Research Director

Research Professor
University of Massachusetts
Medical School

ER/ma

Dear Eugenia
Sorry, your letter arrived after duplicating Minutes
Copies of your letter are sent
to Council Members Saad

JAN VAN GALENSTRAAT 335
AMSTERDAM - THE NETHERLANDS
P.O. BOX 1527 - TELEX 16479
TELEPHONE 020 - 515 92 22

ELSEVIER/NORTH-HOLLAND
BIOMEDICAL PRESS B.V.

Dr A Bartke
Senior Scientist
The Worcester Foundation for Experimental
Biology
SHREWSBURY Mass. 01545
U S A

DIRECT LINE: 020-515-3153

Amsterdam, 6 December 1976
dt

Dear Dr Bartke

Thank you for your recent letter concerning the possible new journal "Archives of Andrology". I certainly appreciate your comments regarding this project and, naturally, we are also awaiting the comments of a number of other active workers in the field.

Should we decide to go further with the project, I will, of course, keep you closely informed of its progress.

Thank you very much for your interest.

Kind regards,

Yours sincerely

Dr P S Jackson
Acquisition Editor

November 1, 1976

Dr. P.S. Jackson
Acquisition Editor
Elsevier/North-Holland
Jan van Galenstraat 335
Amsterdam
The Netherlands

Dear Dr. Jackson,

This is in response to your recent letter and questionnaire concerning the advisability of starting a new journal in the field of Andrology.

It would seem to me, that this issue can be decided only after careful evaluation of the existing journal in this area, ANDROLOGIA. ANDROLOGIA is published for some two years now and serves as the official journal of the International Committee of Andrology (CIDA) and the American Society of Andrology (ASA). The increasing interest in the field of andrology makes it very probable that ANDROLOGIA will increase the number of issues per year and the number of pages per issue and become a major journal in the biomedical field. Should ANDROLOGIA fail in developing into an effective and recognized vehicle for publication of work in the field of andrology, another journal will certainly be in order. I feel that starting another andrological journal at this time would create competitive situation which may weaken the growth of both ANDROLOGIA and ARCHIVES OF ANDROLOGY.

Sincerely yours,

Andrzej Bartke, Ph.D.,
Senior Scientist

JAN VAN GALENSTRAAT 335
AMSTERDAM - THE NETHERLANDS
P.O. BOX 1527 - TELEX 16479
TELEPHONE 020 - 515 92 22

ELSEVIER/NORTH-HOLLAND BIOMEDICAL PRESS B.V.

Dr. A. Bartke,
Worcester Foundation for Experimental Biology
222 Maple Ave,
Shrewsbury,
Massachusetts 01545

U.S.A.

DIRECT LINE: 020-515

Dear Dr. Bartke,

During the course of recent visits to the U.S.A. and to European countries, a number of established research workers have drawn my attention to the present difficulties of publishing material rapidly in the field of andrology and related disciplines. Many of the workers felt that there is now a large increase in the number of research papers produced in this field, and that this explosion of interest was likely to continue during the coming years. They also commented that sometimes it was difficult to have these papers satisfactorily placed in existing journals.

The suggestion was to start a new primary journal provisionally entitled "Archives of Andrology", which would specialize in publishing primary papers and short communications in all areas concerned with andrology. In view of your interest and authority in this field, I would very much appreciate it if you could let me have your reactions to such a suggestion. It would be most helpful if you could indicate whether you agree that the area of andrology would benefit from such a specialized publication, and whether you and your colleagues would be likely to support such a venture by means of publishing your papers and in recommending your library to subscribe. For your convenience, I have enclosed a quick answer questionnaire which you may prefer to utilize. As you can imagine, in the present financial climate we are approaching any such suggestion rather cautiously, and your comments would certainly be of great value.

Looking forward to hearing from you.

Best wishes,
yours sincerely,

Dr. P.S. Jackson
Acquisition Editor

Cables Elspubco Amsterdam

Sartre

ELSEVIER/NORTH-HOLLAND BIOMEDICAL PRESS B.V.

QUESTIONNAIRE

regarding the need for a proposed new research level journal entitled "ARCHIVES OF ANDROLOGY", publishing short reports and full length papers with a minimum publication delay, for studies concerned with andrology and related fields.

Please underline the category with which you agree:

1. NEED

I feel there is a strong need for this journal.

moderate need

no need

do not know

2. FREQUENCY

I feel this journal should be published monthly/bi-monthly/quarterly.

3. SUPPORT

In principle, I and my colleagues would/would not be interested in supporting this journal by publishing papers in it.

4. SUBSCRIPTION

In principle, I would/would not recommend that such a journal should be purchased by my library.

5. SCOPE

What comments would you make regarding the scope and coverage of such a journal? _____

_____

_____

_____

6. What, if any, would you consider the main "competitors" of such a journal?

_____

_____

OVERALL RECOMMENDATION

I would recommend starting such a journal.

would not

do not know

Please return this questionnaire to: Dr P S Jackson
Elsevier/North-Holland Biomedical Press B.V.
P O Box 1527
AMSTERDAM, The Netherlands

August 12, 1976

Dr. Emil Steinberger
Department of Reproductive Biology
and Endocrinology
University of Texas, Medical School
Houston, Texas 77025

Dear Emil:

Enclosed is a hastily composed letter concerning Andrologia. If it is satisfactory - fine. If not please make suggestions for its revision, and I will be glad to make appropriate modificationss

Sincerely,

Don W. Fawcett, M. D.

DWF:so

Enclosure

August 12, 1976

Dr. Emil Steinberger
Department of Reproductive Biology
and Endocrinology
University of Texas, Medical School
Houston, Texas 77025

Dear Emil:

I am writing to you on behalf of the Council of the American Society of Andrology to express our deep concern over the proposed changes in policy and format of Andrologia.

It is our considered opinion that the requirement of letter-perfect manuscripts produced on typewriters with widely varying type and without justification of the right margin will not be favorably received by our readership. These changes will seriously downgrade the appearance of the journal and its desirability as a vehicle for publication by our membership. It is feared that the quality of reproduction of halftone illustrations will also decline and that authors of papers containing photomicrographs and electron micrographs will avoid this journal. Most publications which sacrifice quality for the requirement of camera-ready copy offer the authors the compensating advantage of unusually rapid publication. It is clear that this is not envisioned by Andrologia.

We have valued our brief association with Andrologia and have looked forward to its promotion as the official publication of our new society. To date it has not been easy to induce our members to publish in a journal that appears only four times a year and one which has a very limited circulation in this country. When the proposed changes become common knowledge it will no longer be possible to convince our members to submit papers and some will surely question the wisdom of continuing their subscription.

We understand the fiscal problems of the journal which motivate the proposed changes. Elimination of free reprints and the modest increases in subscription rates and in charges for extra half-tone plates seem entirely justified, but after extensive discussion we remain convinced that the deterioration in the image of the journal; the loss in patronage of authors of high quality papers; and the probably loss of subscriptions will more than offset the small economic gains that may result from the proposed changes. We therefore urge the Publications Committee of CIDA to reconsider their decision to change from letterpress to offset, and their requirement for camera-ready manuscripts with heterogeneous type styles and page charges for retyping.

Sincerely,

Don W. Fawcett, M. D.
Vice-President

DWF:so

American Society of Andrology

SECRETARY
E.S.E. Hafez
Reproductive Physiology
C.S. Mott Center for Human
Growth & Development
275 E. Hancock Ave.
Detroit, Michigan 48201 U.S.A.
(Tel: 313 / 577-1011)

15 August 1975

Andrzej Bartke, Ph.D.
Worcester Foundation for Experimental Biology
222 Maple Ave.
Shrewsbury, Massachusetts 01545

Dear Dr. Bartke:

Thank you for your check in the amount of $40.00. As soon as it has been processed, your annual subscription for Andrologia, the official publication for the American Society of Andrology, will commence.

The first annual meeting will be March 31 - April 2, 1976, in Worcester, Massachusetts. Further information will be sent at a later date. We hope you will be able to attend.

Sincerely,

Nancy

Nancy J. Alexander, Ph.D.
Treasurer

NJA/ka

THE UNIVERSITY OF TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

MEDICAL SCHOOL

John H. Freeman Building
Texas Medical Center

Post Office Box 20708
Houston, Texas 77025
713/792-2121

August 7, 1975

TO: Officers/American Society of Andrology
Vice President - S. J. Behrman
Secretary - Saad Hafez
Treasurer - Nancy Alexander
Program Chairman - Eugenia Rosemberg

Executive Council/American Society of Andrology
Andrzej Bartke
Joseph Corriere
Fletcher C. Derrick
Tommy Evans
Donald Fawcett
C. Alvin Paulsen
Richard Sherins
Anna Steinberger
Lourens Zaneveld

FROM: Dr. Emil Steinberger
President

Re: Affiliation With Comité Internacional de Andrologia

I just received a letter dated July 25, 1975 from Dr. Rune Eliasson, President of CIDA, in which he informed me that our application for (1) affiliation with CIDA and (2) to have Andrologia serve as the publication arm of ASA have both been approved.

ES:rh