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STUDIES AND APPOINTMENTS
Born January 31, 1922 in Kristinehamn, Sweden. Studies in Medicine at Karolinska Institute in Stockholm. License as a physician February 6, 1952, M.D. April 21, 1952 at the Karolinska Institute. Associate professor in Medical Isotope Research 1952, also at the Karolinska Institute. 1953 Rockfeller Foundation Fellow at the University of California, Berkeley and Stanford. Intern and Resident in Obstretics and Gynecology at the Sabbatsberg Hospital, Karolinska Institute 1954 – 1961. Research Fellow of the Swedish Medical Research Council at the same department 1961 – 1966. Ph.D. in Physics at the University of Uppsala, April 22, 1966. Appointed Professor of Medical Biophysics at the new University of Umeå, July 1, 1966. Retired from this position on June 30, 1988 and Emeritus Professor at the same department since then, due to recent reorganisation: Department of Medical Biosciences.
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SOCIAL Married since 1952. Wife: Nurse at the unit of Transfusion Medicine, University Hospital, Umeå. Four children, born 1954, 1955, 1959 and 1963. Three of them married. Ten grandchildren.

BOARD ACTIVITIES, AWARDS ETC
Treasurer, Swedish Soc for Medical Physics 1964 – 1972.
Secretary, same Society 1973 – 1979.
Chairman Umeå Biophysical Society since 1975.
Member WHO Task Force on Sperm Migration 1972 – 1977.
Chairman, Committee for Associate Professorships, Umeå University 1979 – 1984.
Chairman Committee VI for Environmental Health 1982 – 1988.

Awarded the Mångberg Prize for NMR in Neurosciences 1985.
Awarded the Eberling Prize in Medical Physics 1978.
Awarded the Prize of Argentine Soc. of Bioethics 1986.
Awarded the R.E. Deegan Prize in Natural Family Planning in 1988.
Government Representative at the Radioisotope Conference in Mexico City 1961.
Instituted the NFP teacher training courses as university courses at the University of Umeå since 1989 and has finished three course, mainly arranged for midwifes. Course no. 7 is presently running at our university. These courses are conducted as distance education over the whole of Sweden. This curriculum indicate invited lectures abroad and give a summary of my rsearch on cervical mucus and Natural Family Planning.
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INVITED LECTURES ON CERVICAL MUCUS (OUTSIDE SWEDEN)

Argentina
Buenos Aires 1974, 1975, 1986

Austria
Vienna 1987

Australia
Sydney 1967, 1977, 1983, 1984, 1986, 1987, 1988, 1990, 1992
Melbourne 1983, 1984, 1986, 1987, 1990, 1992, 1995, 1997
Canberra 1983, 1986
Newcastle 1983
Perth 1986

Belgium
Lovain, 1984

Brazil
Rio de Janeiro 1974

Canada
Montreal 1989
Toronto 1992
Calgary 1992
Bogota 1986

England
Oxford 1989
Birmingham 1989
Cardiff 1989
Brighton 1990

Colombia
Bogota 1986

India
Delhi 1977
Madras 1986
Bangalore 1986

Italy
Rome 1984, 1986, 1988, 1993, 1994, 1996
Milano 1988
Bologna 1988
Torino 1994

Japan
Tokyo, 1989
Sapporo, 1989

Mexico
Mexico City, 1982
Acapulco 1982

Netherlands
Nijmegen 1984

New Zealand
Auckland 1983

Spain
Madrid 1987, 1996
Barcelona 1994
LaCoruna 1990, 1994, 2001
Murcia 1995, 1998
Malaga 1992

Uruguay
Montevideo 1986

USA
Honolulu 1983, 1984
St Cloud 1988, 1996
Los Angeles 1986
Houston 1987
San Antonio 1991
Omaha 1987
Seattle, 1971 1977
Wichita 1988
Burlington 1990
Minneapolis 1986, 1988, 1998

Venezuela
Caracas 1986, 1987

OTHER LECTURES BY INVITATION, VARIOUS TOPICS

1953 Oak Ridge, USA, Autoradiography
1958 N.Y., Am. Cancer Society, Autoradiography
1959 N.Y. Academy of Sciences, Conf. on the Vagina
1959 N.Y. Trace elements. Activation Analysis
1968 Houston, Am. Soc. for Colposcopy
1982 San Francisco, Seminar on Bronchial mucus
1987 Edinburgh, Pro-life Conf.: ”The Splintered Image” Lecture on Neurosciences and Fetal life.

Besides these lectures of a more formal nature there have been several informal lectures, discussions and tutorials during my travels, often arranged for smaller but very interested groups of people in NFP or research connected with NFP.
There are also available several videos related to NFP in which I take part. Due to the progress of scientific research, some of these videos are now old and not representative for our present state of knowledge.

Besides and in parallel with my research on the cervix and cervical mucus, several other findings have been made, e.g. the occurrence of a lymph node and inguinal swollenness around the time of ovulation ("Inguinal syndrome") or changes in the heart rate at ovulation ("Heart rate sign") or changes in the pupilla of the eye at ovulation ("The Belladonna sign"). I have also described the recirculation of water and solutes in the vagina and the possible role of the element Manganese (Mn - not to be confused with magnesium, Mg) in this context.

A REVIEW OF MY SCIENTIFIC CONTRIBUTIONS ON CERVICAL MUCUS

Besides cervical mucus I have published papers in general obstetrics and gynecology, heart and circulation, biophysics, radioisotopes, radiological physics and radiation biology. My most significant contributions are, however, on the structure and function of the cervical secretory system and cervical mucus. This review mainly concerns this field.

Number of publication list

(22) I received my M.D. in 1952 (Thesis on ovarian phosphate metabolism, paper no 22) at the Karolinska Institute in Stockholm and became an Associate Professor the same year.

(11) My first paper on cervical mucus was, however, published already in 1951(paper no 11) and reported on a study on Mycoplasma (at that time called PPLO = Pleuropneumonia-Like Organisms) in women with and without pelvic inflammatory disease. During that study my attention was drawn to the very pronounced cyclic changes of the

cervical mucus and I decided to continue my research on the physical characteristics of the cervical mucus and their cyclic variations.

I spent the year of 1953 at the University of California, Berkeley and Stanford, as a Rockfeller Foundation fellow, and learned about new techniques for the study of cervical mucus, mainly Nuclear Magnetic Resonance (NMR) and Activation Analysis. After returning home to Sweden I continued my clinical work in obstetrics and gynecology and removed samples of cervical mucus for research. The NMR and Activation Analysis studies were first carried out at the Nobel Institute of Physics in Stockholm.

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(136)(146) The first paper on NMR (no 136) was published in 1957, the first one on Activation analysis (146) was published in 1958.

A unit for NMR was now built at the Department of Obstetrics and Gynecology in order to facilitate NMR studies which were most informative.

(164) In 1959 I published a study (164) in which a molecular model for the sperm conductive mucus was presented.

(166) In a discussion to that paper (166) I proposed for the first time that the cervical mucus contained different types of secretions coming from different crypts, a rather temerary suggestion at that time.

A method was now developed to obtain and analyse mucus produced in single crypts without contamination from other crypts in the cervix. This word resulted in my Ph.D, thesis in physics, paper no 212, in 1966.

(212) The same year I moved to Umeå in North Sweden and became the first professor in Medical Biophysics at the new university of Umeå. I could now continue and expand my research in the cervix and its secretions.

(255)(272) In 1969 two types of mucus could be identified and characterised (paper no 255), They were called type E (estrogen-stimulated) and type G (gestagen-stimulated). About the same time the first therapeutic application was developed, the microsurgical operations on diseased cervical crypts, published 1971

(no. 272).

(316) (318) (326) Continued studies indicated that the type E mucus was in fact composed of two types, now called L and S of which only type S propagates sperm, while L mucus attracted malformed and slow-swimming sperm, published in three papers,(316) (318) (326) in the years 1977 – 78.

The most important practical application of these new results was to explain the fertile and infertile periods in women using Natural Family Planning (NFP), and also help to extend the use of NFP to groups with difficulties to use NFP such as post-pill women, and in various diseases.

(361)(373) The ”build-up” of the fertile period could now be explained on the basis of the L + S mucus model (papers 361, 1983 and 373, 1986).

(365) In the meantime, the G mucus was subdivided into two types, called G- and G+ (before and after ovulation, respectively), and a variety of the L mucus coming from the transformation zone on the portio was identified (Lt), paper 365, 1984.

The microsurgical treatment of diseased crypts was also succesiely developed, especially to help women with difficulties to conceive. This approach very often involved microsurgical intervention in the uppermost part of the cervix, and as a result of these attempts a previously unknown secretion called mucus type P was discovered and identified in 1991. The letter P allitterates to “peak”, the day of peak fertility, which is usually the last day of the mucus symptom in NFP.

(413) The microsurgical proceures and the P mucus are described in some detail in the teacher training manual (413) used in the university course for NFP teachers at Umeå University, but presently available only in Swedish. This teacher training manual also shows proton NMR spectra of the mucins from G, L, S and
P mucus as well as proton NMR relaxation spectra, and the crystallisation patterns.

All this information together strongly support the hypothesis that the four mucus types do not arise from various degrees of dilution or concentration of one type of mucin, but that there are four different mucins produced by different areas of secretion in the cervix. We also know that these different secretory units respond differently to

hormonal stimulation. G units (crypts) respond to progesterone and other gestagenes, L units to increasing estrogen levels, S to maximum estrogen levels and P to decreasing estrogen levels. These different responses are probably due to different receptor properties. There is also strong evidence that noradrenaline promotes the secretion of S and P mucus and may in part inhibit the L mucus secretion while the G secretion is not affected.

One fundamental question is the submicroscopic structures of the G, L, S and P mucins. Chemical and microbiological studies seem to be important to clarify this question, and, especially, studies with transmission and scanning electron microscopy are supposed to have very great value in this respect. Collaboration was therefore established with Helvia Temprano and Mikaela Menarguez, both in Spain.

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(433) A significant methodological advance was made some years ago when special cotton swabs were designed for obtaining very thin spread-out specimens of cervical mucus. The thinking behind the design was to use as little cotton as possible to minimise the absorption of water (and dissolved substances) and to restrain the cotton material in thin rings, so that the cells which happen to be localised between these rings do not receive any mechanical damage. The method, published in 1996, made it possible to identify and study in detail the secretory processes and cell morphology of cervical secretory cells.

(434) Such a study was published in 1997, together with its historical background of mucus investigation. In this report cells of the various mucus types S, L, G, P2 and P6, and also the Z cells were studied.

The P6 cells were especially as an object for investigating the biosynthesis and release of mucus and cell sequencies rest – biosynthesis – release – rest were identified. The Z cells turned out to be especially interesting.

They seem to release the small “granules” which have been described earlier in the litterature and seem to contain mucolytic enzyme activity, which slowly breaks down all mucus types and in that way may have a regulatory function of mucus activity, perhaps important in sperm

migration and selection.

(441) Cells are regularly exfoliated together with the mucus in all the secreting structures in the cervix, however as experience indicates, the cells present in the P6 type mucus are most easy to recognise and study.

The reason for this is that the mucus recently secreted from the P6 cells shows a very typical triangular pattern in the well spread-out, thin, dried and unstained specimens. The studies reported in papers 433 and 434 has been continued during the last 4 – 5 years, in part together with dra Helvia Temprano in la Coruña, Spain and dra Mikaela Menarguez in Murcia, Spain. These studies has also been put in relation to recent advances in cell and
molecular biology in order to try to understand more about the physiological processes occurring in the P6 mucus in the cervix.

In the cervical smears obtained with the spread-out technique using these specially designed cotton swabs it has been possible to identify mucus "units" emanating from single P6 crypts, count the number of exfoliated cells and
classify them according to their secretary states and states of degeneration (apoptosis, necrosis, etc).

The P6 cells producing the typical triangular patterns are called the Pt cells. As already mentioned they are seen in various states of mucus biosynthesis and release. It seems that in any of these secretory states the Pt cells can be subjected to apoptosis, and less commonly, to necrosis. The Pt mucus itself can be detached from the cells and confluence to larger mucus masses. Probably the mucus undergoes post-secretory changes so that it
looses its capacity to form these regular crystallisation and more irregular patterns are formed and finally disappear.

(442) Also, pieces of mucus, still retaining their regular triangular patterns can occur and adhere to other cells such as lymphocytes and leucocytes and even to sperm cells, and, in case vaginal epithelial cells can contaminate the samples, also to vaginal cells. All these adherence phenomena may be due to interaction between Pt mucus and the membrane glycoproteins of other cells. The adhesion to sperm cells may be of importance for sperm selection and in certain cases of infertility, but much more future studies are required to elucidate these

questions.

We have also found that there exist Pt mucus of different varieties. Besides the hormel P6 form we have with certainty identified one with four-fold symmetry, P4 and there may be at least two other forms. They are all less common than the ordinary P6. We do not yet know how these varieties develop. They may occur due to some kind of mutation or alternative transcription (isoforms), depend on single nucleotid polymorphism (SNP) or other factors
in the transcription or translation.

There may also occur factors in the vesicular traffic in the cell which may favour one or the other of different variants of the synthesised mucus. Further research may through more light on the cellular events involved in mucus production and biological properties. We also know that lymphocytes, leucocytes and macrophages are present in the crypt mucus, their role will also be studied in ongoing studies.

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References cited in the Review:

11 Scand. J. Clin & Lab. Inv. 3: 47 – 51, 1951. Pleuropneumonia-like organisms in the female genito-urinary tract. Co-author: B. Melén.

22 Acta Radiol. Suppl. 93, 1952. Contributions to the Theory and Technique of Quantitative Autoradiography with P32 with special reference to the Granulosa Tissue of the Graafian Follicles in the Rabbit. Thesis for M.D.

136 Acta Radiol. 47: 315 – 320, 1957. Proton Magnetic Resonance of Human Cervical Mucus during the Menstrual Cycle. Coauthor: U. Bryhn.

146 Acta Radil. 49: 137 – 140, 1958. Determination of Sodium and Phosphorus in Human Cervical Mucus with Activation Analysis. Coauthors: B. Westin and K.G. Malmfors.

164 Acta Obst. and Gyn. Scand. 38, Suppl. 1, 1959, 44 – 58. The Physics of the Cervical Mucus.

166 Acta Obst. and Gyn. Scand. 38, Suppl. 1, 1959, 126 – 127. Discussion to the preceeding paper.

212 Acta Obst. and Gyn. Scand. 45, Suppl. 2, 1966. Micro-NMR in High

Permanent-magnetic Fields. Thesis for Ph.D.

255 Acta Obst. and Gyn. Scand. 47, Suppl. 8, 1968 – 69, Biophysical Composition of Cervical Mucus and Spermigration during Treatment with Conluten and Conlunett.

272 Proc. 7th World Congr. Fert. and Ster., Tokyo and Kyoto, 1971. Internat. Congr. Ser. No 278, p. 124 – 125. Microsurgery of cervical glands. Co-author: C. Rudolfsson-Åsberg.

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316 Mucus in Health and Disease. Adv. Exp. Biol. and Med. 89: 217 – 225, 1977. Physical Properties of Cervical Mucus.

318 The Uterine Cervix in Reproduction. Work Conf. in Rottach-Egern. P. 129 – 134, 1977. Sperm Penetration in Cervical Mucus, a Biophysical and Group-theoretical Approach. Co-author: A. Höglund.

326 Contributions to Gynecology and Obstetrics, Basel, 4: 132 – 142, 1978. Cervical Factors.

361 Int. Rev. Nat Fam. Planning 7: 1 – 56, 1983. The Biophysica Properties of the Cervical-Vaginal Secretions. Co-authors: A Ingelman-Sundberg, L. Hallström, A. Höglund, U. Leppänen, K. Lisspers, E. Perenyi, C. Rudolfsson-Åsberg, K. Sahlin, C. Lindström-Sjögren, C. Sjöström, L. Strandberg-Bergström, L. Wikström and M. Wikström.

373 Int. Rev. Nat. Fam. Planning 10: 303 – 313. The Mucus Symtom´s Length and Subphases during the Fertile Age. Co-author: L. Bergström, K. Smyth, A. Smith and D. Dunn.

365 365 Acta Obst. and Gyn. Scand. 63: 667 – 668, 1984. Proton Magnetic Relaxation Times T1 and T2 for Normal Types of Cervical Secretions. Co-auhors: A. Ingelman-Sundberg, C. Rudolfsson-Åsberg, A. Höglund and L. Strandberg-Bergström.

413 Lectures in Natural Family Planning, in Swedish: Föreläsningar i Naturlig Familjeplanering. Text-book for the NFP Teacher Training Course at the Univeristy of Umeå, 1992

433 Bull. Ovulation Method Res. and Ref. Center of Australia 23 (2) 3 – 20. How to study the cervical secretory system and its role in Natural Family Planning. Co-authors: M. Menarguez,J. Slettvoll and H. Temprano, 1966

434 J. Irish Coll. Physicians and Surgeons, 26 (1), 27 – 32, 1997. Cervical mucus and their functions.

441 Caracterizacion morfologica de diversos tipos de moco cervical humano mediante microscopia de luz (ML) y microscopia electronica de barrido (MEB). XIX Reunion Soc. Esp. Microscopia electronica 28 – 30 April 1999, 169 – 170.

442 Letzte Forschungsergebnisse zur menschlichen Unfruchtbarkeit. Schweitz. Stifung fur deie Familie, XIX Internat. Kongress fur die Familie, Luzern, Mai 1999, P. 224 – 240

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Umeå, Sweden, December 2001 Erik Odeblad, Professor emeritus