FROM THE ISOTOPE LABORATORY, DEPARTMENT OF GYNECOLOGY (DIRECTOR: PROF. P. WETTERDAL) SABBATSBERGS SJUKHUS, KAROLINSKA INSTITUTET, AND THE NOBEL INSTITUTE OF PHYSICS (DIRECTOR: PROF. M. SIEGBAHN) STOCKHOLM, SWEDEN

PROTON MAGNETIC RESONANCE OF HUMAN CERVICAL MUCUS DURING THE MENSTRUAL CYCLE

by

Erik Odeblad and *Ulla Bryhn*

Cyclic changes in the human cervical mucus were observed as early as the middle of the 19th century and have in the last two decades been the subject of extensive investigations. Among other matters studied have been the macroscopic and general appearances (SEGUY and VIMEUX 1933) and the crystallization pattern (*e. g.* by PAPANICOLAOU 1945, 1946, by RYDBERG 1948, and by ZONDEK 1954). The amount of dry substance (BERGMAN 1950), the viscosity (LAMAR, SHETTLES and DELFS 1940), 'flow-elasticity' and 'Spinnfähigkeit' (CLIFT 1945), and the amount of reducing substance (VIERGIVER and POMMERENKE 1946) have also been investigated. The studies have mainly been undertaken in order to correlate changes in the properties of the mucus with the time of ovulation, these being of considerable practical importance, especially for timing the optimal day of conception in cases of reduced fertility. In addition, changes in the cervical mucus are of considerable interest from theoretic viewpoints. In the present study we briefly report some preliminary observations on the proton magnetic resonance spectra of the human cervical secretion in various phases of the menstrual cycle.

Principles of nuclear magnetic resonance. Proton magnetic resonance spectroscopy is specific for the hydrogen nuclei in any chemical or physical state. The resonance or absorption line occurs in the radiofrequency part of the electromagnetic spectrum when a sample containing hydrogen nuclei is placed in a magnetic field of several thousand gauss; it is due to the elementary process of absorption of a low-energy electromagnetic quantum when a proton spin flips from a lower to a higher energy orien-

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tation in the bulk magnetic field. The total ensemble of proton spins may return back to their original distribution of orientations by the process of 'spin-lattice relaxation'.

The ideal shape of a resonance spectrum, or signal, will be a single, very sharp peak or line. In gaseous, liquid, and solid matter minor perturbations of different kinds of the proton resonance signal occur. These perturbations reflect the chemical and physical environments of the hydrogen nuclei and are therefore of great importance in studying the chemical and physical state of the sample. Signal size, signal width, and signal position, may be affected by these perturbations.

An introductory presentation of these problems is given in a review of nuclear magnetic resonance in biology and medicine (ODEBLAD 1956). The excellent book by ANDREW (1955) contains the physical essentials of nuclear magnetic resonance and is referred to for more detailed information.

Clinical material. About three hundred women employees were subjected to routine gynecologic examination and specimens taken from a number. The samples investigated fulfilled the following criteria: 1) The general and local condition of the patient appeared to be perfectly normal on examination. 2) Homogenous cervical mucus, which could be removed easily by suction and essentially without any mechanical trauma or irritation of the cervix was present. 3) No contamination of the specimens from blood or vaginal contents was permitted. Some women were subjected to repeated collecting of mucus. Most samples were concomitantly examined for the amount of dry substance and crystallization pattern, and vaginal smears were also collected. A satisfactory phase determination could be obtained by comparing menstrual data, the amount of dry substance in the mucus, the crystallization pattern and the vaginal smears as well as the basal body temperature. A total of 24 examined specimens form the basis of the present report.

Magnetic resonance technique. Samples of about 10 to 30 mg of human cervial mucus were introduced in small thin-wall test tubes and placed in the radiofrequency transmitter coil of the spectrometer, described in detail by LINDSTRÖM and BHAR (1956). During the recording, the sample was rotated at a speed of 15 to 60 c/s. The magnetic field was 3,825 gauss, the radiofrequency 12.3 MC/sec, and the sweep-rate of the field through the resonance condition about 4 milligauss/sec (or about 1 ppm/sec). The resolution was about 0.3 ppm (ppm = parts per million).

Results. Some typical magnetic resonance signals are shown in Fig. 1. As indicated, the postmenstrual signal consists mainly of a single line of a width of about 1 ppm. As the cyclic phase approached midcycle, this narrow peak decreased in size and a new, usually broad, component

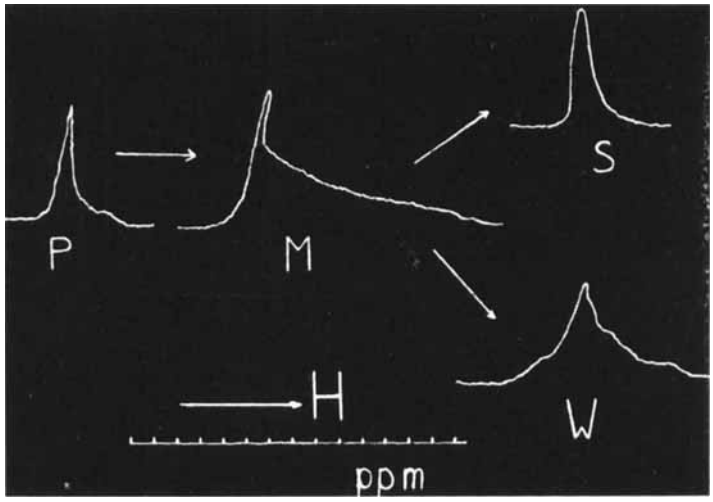

Fig. 1. Typical proton magnetic resonance signals of human cervical secretion. P = postmenstrual signal, M = midcycle signal, S = signal in secretory phase and W = signal in late phase of menstrual cycle without signs of corpus luteum-function. Abscissa: Scale in ppm. Ordinates (not comparable): Signal amplitude. H = direction of bulk magnetic field.

slightly displaced towards a higher field occurred. At midcycle, nearly the whole spectrum consisted of this broad peak, which then appeared to be displaced about 5 ppm from the narrow component and to have half-width of about 3 ppm. The narrow peak was now detected only with difficulty. The total area of the resonance signal was probably considerably larger at midcycle than in the beginning of the cycle though this observation was somewhat uncertain owing to the indefinite reproducability of the signal amplification and variations in the amount or in the coil-filling factor of the cervical sample under study. After midcycle was passed the proton magnetic resonance signal seemed to depend upon whether any luteal activity had occurred or not. If signs of an active corpus luteum were present (diphasic temperature curve, disappearance of arborization, increased dry substance in the cervical mucus, or cytologic evidence) the signal appeared to return more or less to the early post-menstrual pattern. In cases in which it was suspected that no formation of corpus luteum had taken place the signal contained a broad, non-displaced component, or was similar to a signal shortly before midcycle was reached. The fraction of total magnetic resonance signal area occupied by the broad component during the secretory cycle is shown schematically in Diagram 1.

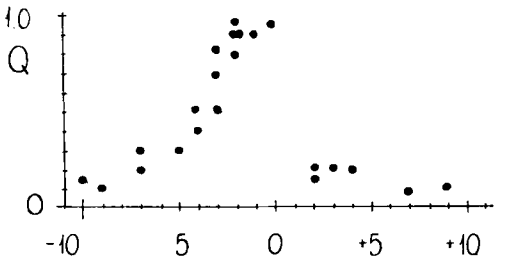

Diagram 1. Variation of Q (= ratio of broad component to total signal area) in the menstrual cycle. Cycles normalized to midcycle (presumed day of ovulation = 0).

Discussion

The present experiments indicate that extensive changes in the proton magnetic resonance signals occur in the human cervical mucus during the normal menstrual cycle. It seems reasonable to believe that increased stimulation of the cervical glands with oestrogens gives rise to the change in the resonance signal at midcycle as well as with other physio-chemical alterations occurring at that time (see references given in the introduction). The return to the postmenstrual pattern in the normal secretory phase is suspected to be due to the additional effect of progesterone on the cervical glands, since it has been shown by PALMER (1941, 1944), ABARBANEL (1946), and ZONDEK (1954), that progesterone in an appropriate concentration inhibits most of the other typical changes in the cervical secretion brought about by oestrogens. The shape of the resonance signal in cases of probable deficient corpus luteum function support this view.

It is also of great importance to try to interpret the observed signals as far as possible physically. An attempt at interpretation on the basis of the present report and some additional observations will be presented in a forthcoming paper.

Finally it may be stated that the present investigation using proton magnetic resonance spectroscopy for cervical mucus has revealed some previously unknown findings connected with the physico-chemical structure of the mucus and disclosed a property subjected to normal cyclic variations. These findings have necessitated extended investigations which are currently being performed. Due to the simplicity of the method, provided that nuclear magnetic resonance equipment is available, the findings may also be of practical value in the future for estimating the phase of the genital cycle as reflected in the cervical function.

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SUMMARY

Changes in the properties of the cervical mucus in relation to the time of ovulation are of practical and theoretic interest and prompted the present investigation. Preliminary observations on the proton magnetic resonance spectra of the cervical secretion in various phases of the menstrual cycle are presented.

ZUSAMMENFASSUNG

Veränderungen der Eigenschaften des Vaginalschleimes in Beziehung zur Ovulationszeit sind von praktischem und theoretischem Interesse und haben zu der vorliegenden Studie stimuliert. Präliminäre Beobachtungen an protonmagnetischen Resonanzspektren des Cervixsekretes in verschiedenen Phasen des Menstruationszyklus werden vorgelegt.

RÉSUMÉ

Les modifications des propriétés du mucus cervical en fonction de la date de l'ovulation ont un intérêt pratique et théorique et ont incité à faire les présentes recherches. Les auteurs présentent des remarques préliminaires sur les spectres de résonance magnétique des protons de la sécrétion cervicale aux diverses phases du cycle menstruel.

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