SUDAN UNIVERSITY OF SCIENCE & TECHNOLOGY KHARTOUM, SUDAN

COLLEGE OF POST GRADUATE STUDIES

DIAGNOSIS OF OVARIAN FACTOR OF SUDANEESE FEMALE PRIMARY INFERTILITY USING ENDOVAGINAL ULTRASOUND

تشخيص العامل المبيضى للع قم الأولى لدى السودانيات باستخدام مسبار الموجات فوق الصوتية المهبلي

A thesis submitted fur fulfillment for PhD degree in medical ultrasound

BY:AMNA AHMED MOHMED MOKHTAR

Supervisor:

Prof. MOTASIM AHMED ALSEED

Co-Supervisor: DR. ALWIA MOHMED OSMAN HASSEN

MAY, 2015

Dedication

.....To my **FAMILY** who always supports me And to *the* **soul of my Mother and Father God bless them**

Acknowledgment

 $\ldots I$ thank God

My great thanks and appreciation to Dr.Motasim Ahmed Allseed who is the supervisor of this research and also to Dr.Alwia Mohamed Osman Hassen who is the co-supervisor.

Great thanks to Dr. Mohamed Omer the principle of the College of Radiological Sciences and Dr. Mohamed Elfadil Mohamed for their encouragement.

My great thanks extended to Dr.Mohamed Abd Algafoor who is general manager of Banoon for Assisted Reproduction Obsfevic and Gynecology and everybody help and support me.

Great thanks to my husband General Salih Mahmood Alwad, my daughter Omnia Salih and my son Mahmood Salih.

My great thanks extended to my colleagues who were of great help and support.

В

ABSTRACT

Endovaginal ultrasound is a test used to look at a woman's reproductive organs, including the uterus, ovaries, and <u>cervix</u>. The main objective of this study was to diagnose ovarian factor of Sudanese female primary infertility using Endovaginal ultrasound scan. The data of this study consisted of 300 random samples of Sudanese female suffering from primary infertility during the period from 2009 to 2015 in Banoon Center for assisted reproduction and obstetric and gynecology in Khartoum.

The result of this study showed that 40.7% of the cases had polycystic ovarian syndrome, 49.7% normal ovary with other infertility remarks e.g. Tube blocked, fibroids and male factor, 5.6% with unknown reason under induction treatment and 4% with ovarian cuyst. In conclusion the results highlights that the increases of female age (average) in relation to the increases of marriage duration (average) together portrayed the pattern of the infertility problem in ascending fashion from polycystic ovarian syndrome, ovarian cyst, unknown obvious cause and normal ovaries with other infertility causes.

The recommendations were given dealing with all infertility investigation must be carried out using Endovaginal probe, the duration of marriage and female age should be taken as indicator for infertility problems and the size of the follicles in induction treatment should be related to the age of the female, which gives a good estimate of the time needed to reach a proper size.

الخلاصة

استعمال الموجات فوق الصوتيه من خلال المهبل هو كشف يجرى للنظر في الأعضاء التناسليه للمرأه بما في ذلك الرحم ، المبيض وعنق الرحم.

الغرض من هذه الدراسة هى تشخيص حالات الع قم الإبتدائى للنساء السودانيات ذات العلا قه بالمبيض باستعمال الموجات فوق الصوتيه من خلال المهبل.

معطيات الدراسة اخذت من 300عينه عشوائيه لسيدات سودانيات يعانين من الع قم الإبتدائي في الفتره من 2009م -2015م بمركز بنون لإطفال الأنابيب وأمراض النساء والتوليد بالخرطوم.

نتيجة الدراسة خلصت الى أن 40.7% يعانين من متلازمة المبيض متعدد التكيسات ، 49.7% المبيضين طبيعيين مع وجود اسباب اخرى للع قم كانسداد قناة فالوب أو وجود لحمية أو عامل متعلق بالزوج و 5.6% نتيجة سبب غير معروف يخضعن للتنشيط و 4% مبيض متكيس.

خلصت الدراسة الى أن متوسط عمر المرأه ومتوسط طول فترة الزواج مؤشر واضح فى زيادة المشاكل التى تؤدى الى الع قم الإبتدائى بما فى ذلك متلازمة المبيض متعدد التكيسات وتكيس المبيض وحالات الع قم الغير معروفة السبب وأسباب الع قم الأخرى.

أوصت الدراسة أن كل الكشوفات التى تجرى لحالات الع قم الإبتدائى بالموجات فوق الصوتيه يجب أن تجرى عن طريق المهبل لد قة التشخيص وأن عمر المرأة ومدة الزواج يجب أن تؤخذ كمؤشرات مهمة لتشخيص اسباب الع قم . فى حالات التنشيط عند تحديد حجم الحويصلة يجب أن يوضع عمر المرأة فى الإعتبار حيث أن ذلك يعطى مؤشر للزمن الذى تصل فيه الحويصلة للحجم المناسب.

6CONTENTS

	Торіс	Page
Dedi	icationa	
Ackı	nowledgementb	
Absr	rract (in English)i	
Abst	tract (in Arabic)ii	
Chaj	pter one : Introduction1	
1.1	Problem of the study2	
1.2	Objective of the Study3	
1.3	Significance of the study3	
1.4	Overview of the study3	
Chaj	pter two : Lierature review4	2 -1
Med	lical ultrasound5	
	2-1-1 Medical ultrasound-germination and growth	
	2-1-2 Gray scale imaging7	
	2-1-3 Probes	Ð
	2-1-3-1 Types	of
	pobes9	

2-1-3-1-1 Anorectal 3D 2052	9	2-1-3-
1-2 Burr-Hole 886310		
2-1-3-1-3 Curved Array 8823	11	
2-1-3-1- 4 Craniotomy 8862	12	
2-1-3-1-5 Curved Array 8820e	13	
2-1-3-1-6 Curved Array 8830	14	
2-1-3-1-7 Curved Array 8830	15	
2-1-3-1-8 Curved Array 8802	16	
2-1-3-1-9 Endfire Curved Array 8667	17	
2-1-3-1-10 End cavity Biplane 8848	18	
2-1-3-1-11 Endovaginal 8819	19	
2-1-3-1-12 High Frequency Linear Array 8870	20	
2-1-3-1-13 Hockey Stick 8809	21	
2-1-3-1-14 Intraoperative 8815	22	
2-1-3-1-15 Intraoperative Biplane 8824	23	
2-1-3-1-16 Linear Array 8811	24	
2-1-3-1-17 Linear Array 8670	25	
2-1-3-1-18 ProART [™] Robotic Drop In 882	26	
2-1-3-1-19 Prostate Biplane 8808e	27	
2-1-3-1-20 Prostate Triplane 8818	28	
2-1-3-1-21 Rigid Laparoscopic 8836	29	

2-1-3-1-22 Small Footprint Cardiac 882730
2-1-3-1-23 Small Footprint Cardiac 883731
2-1-3-1-24 T-Shaped Intraoperative 881632
2-1-3-1-25 Vascular 882233
2-1-3-1-26 3DART™ 883834
2-1-3-1-27 10L2w Wide Linear35
2-1-3-1-28 13L4w Wide Linear
2-1-3-1-29 14L3 Linear37
2-1-3-1-30 18L5 High Frequency Linear
2-1-3-1-31 5P1 Small Footprint Cardiac
2-1-3-1-32 6C2 Curved40
2-1-3-1-33 6C2s Small Curved41
2-1-3-1-34 E10C4 End cavity42
2-1-3-1-35 E14C4 Endfire Curved43
2-1-3-1-36 E14C4t Prostate Triplane44
2-1-3-1-37 E14C4t Prostate Triplane45
2-1-3-1-38 E14CL4b Endocavity Biplane46
2-1-3-1-39 N13C5 Curved47
2-1-3-1-40 4-Way Laparoscopic 8666-RF
2-1-4 Biological effects of possible relevance to safety49
2-1-4-1 Introduction49

2-1-4-2 Types of biological effects/
2-1-4-2-1 Thermal51
2-1-4-2-2 Non-thermal 52
2-1-4-2-3 Cavitations
2-1-4-2-4 Other effects 53
2-1-4-3 Measurement of biological effects53
2-1-5 Guidelines and regulations56
2-1-5-1 Ultrasound Examination Procedures
2-1-5-2 Communication59
2-2 The ovary90
2-2-1 Anatomy91
2-2-1-1 Structure91
2-2-2 Physiology105
2-2-2-1 The major endocrine glands108
2-2-2-1-1 Pituitary gland108 2-2-2-1-2 Thyroid gland110
2-2-2-1-3 Parathyroid glands111
2-2-2-1-4 Pancreas111

2-2-2-1-5 Gonads	
2-2-2-1-6 Pineal gland	
2-2-1-7 Other hormone-producing	3 structure
2-2-2 The female cycle . 	
2-2-3 Menstruation	
2-2-3 Ultrasound ap ovary	
2-2-4 Follicle measurements and tracing	
2-2-4-1 Folliculogenesis 	
2-2-4-2 Chronology154	
2-2-4-3 The process155	
2-2-4-4 The primordial follicle	
2-2-4-5 Recruitment157	

	Mechanism 158			
	THE PREANTRAL	FOLLIC	CLE	
	Primary			
	Seco			
	Tertiary Follicle 168			
	THE GRAAFIAN 170	FOLLICL	E	
	Cla			
	Selection			
	The			
	Autocrinology 178		paracrin	ology
	Ultrasound mo			
2-2-5 Pol	lycystic ovarian syndro	mes		

2-2-5-1 ovarian cyst		
2-2-5-2		Polycystic
ovaries		
2-2-5-2 ovarian torsion		
2-2-6 ovarian masses		
2-2-6-1 Cystic and semi-cystic ovarian	masses	
2-2-6-2 Solid ovarian masses		191
2-3 Feamle infertility	•••••	198
2-3-1		Definition
199		
2-3-1-1		Prevalence
200		
2-3-2 Causes	and	factors
201		
2-3-2-1		Acquired
201		
2-3-2-2 <u>Age and female fertility</u>		202
2-3-2-3 Tobacco smoking		202

2-3-2-4 Sexually transmitted infections2	03
2-3-2-5 Body weight and eating disorders2	03
2-3-2-6 Chemotherapy	204
2-3-2-7 Other acquired factors	05
2-3-2-8 Genetic factors2	205
2-3-2-9 Hypothalamic-pituitary factors	210
2-3-2-10 Ovarian factors2	10
2-3-2-11 Tubal (ectopic)/peritoneal factors2	211
2-3-2-12 Uterine factors2	11
2-3-2-13 Cervical factors	211
2-3-2-14 Vaginal factors	211
2-3-3 Diagnosis	.211
2 -3-4 Examination and imaging	212
2-3-5 Prevention	}
Social stigma214	2-3-6
2-3-7 Marital role	215
2-3-8 Domestic abuse	217
2-3-9 Mental and psychological impact	217
Chapter three: Methodology	218
3-1 Material	219

3-2 Population of the study	219
3-3 Sample and size of the study	219
3-4 Design of the study	219
3-5 Method of data collection	219
3-5-1 Techniques	219
3-6 Protocols	222
3-7 Data analysis	224
Chapter four: Results	225 4
5 Chpater five:Discussion, conclusion and o	ommendation235
5-1 Discussion	235
5-2 Conclusion	237
5-3 Recommendatios	238
References	239
Appendix A	257
A-1 Form for recording results,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
A-2 Master data sheet	258
Appendix B	272
Ultrasound images	272

Chapter one Introduction

Chapter one Introduction

Ultrasound is no longer used simply to distinguish a cystic and solid mass within the abdomen and pelvis. With improved image resolution and software, subtle differences in tissue texture can be demarcated and pelvic organs clearly identified.

Ultrasound is now established as the primary imaging investigation in all cases of suspected female infertility.

Thus, it has become a significant tool in the diagnosis of female infertility. Description The definition of infertility varies considerably, particularly in relation to the length of time of regular unprotected intercourse. It is usually defined as difficulty in conceiving after 12 months of regular unprotected intercourse.

The female causes of infertility include ovulatory causes (20%), tubal causes (14%), endometriosis (6%) and uterine causes (1%).

1-1 Problem of the study

Primary infertility is one of the major problem that encountered by copules so often and most of the time attributed to female as social trend issue. Therefore exploring the factors associated with primary infertility can speed the process of treatment and it can save a lot of money spended in uneffecient procedures including the traditional one. Ultrasound scaning using endovaginal probe might provide valuble information regarding this problem either if it concern the ovary or the related reproductive system or it might indicate that the problem does not concern the female.

1-2 Objective of the Study:-

The main objective of this study is to evaluate the application of endovaginal ultrasound in diagnosing ovarian factor of Sudanese female infertility.

Specific objectives:

To find the causes of primary infertility in female using endovadginal probe .

To find the frequencies of the factors lead to primary infertility

To relate the type of factors behind infertility with female age and duration of marriage

1-3 Significance of the study

This study will provide rich information about the primary infertility and highlights the underline causes of this problem safely with minimum cost. Also it will facilitate the approtch of mangment and follow up of the treatment process.

1-4 Overview of the study

This study falls into five chapters, with chapter one is an introduction which includes; problem of the study, objective and significant of the study. While chapter two deals with background and scolary literature in previous study format. Chapter three will include material used to collect the data and the method followed to obtain those data, similarly chapter four will present the results of this study using tables and figure and finally chapter five will discuss the result of this study as well as the conclusion and recommendation

Chapter two Literature review

Chapter two Literature review

2.1 Medical ultrasound.

2.1.1 Medical ultrasound-germination and growth.

John Eric Edgcumbe Fleming was born in 1934. He started his career with the EMI Engineering Development Ltd in 1951. Between 1951and 56, he worked on the development of specialised test equipment for radar and later on computer development with John Drage and Godfrey Houndsfield; Drage went on to lead the team which developed the first desk calculator and Houndsfield to develop Computerised Tomography. During his time at EMI Fleming obtained a HNC with distinctions in Electrical Engineering.

In 1956 he moved to Ferranti Ltd as a Development Engineer on computer logic elements and data transmission systems. Then to avoid the increasing involvement in military projects he moved to Smiths Industries Ltd in Glasgow, Scotland. There he joined <u>Tom Brown</u> who was working with <u>Professor Ian Donald</u>. Following Brown's move to another company Fleming became responsible for the development of medical ultrasonic products, principally the Diasonograph. This static B-Scan machine was the first scanner to go into commercial production. However only twelve had been delivered when Smiths decided to close the factory in Glasgow. After the sale of the medical ultrasound interest production and further development continued at Nuclear Enterprises Ltd in Edinburgh under Brian Fraser, from Smiths, and Tom Brown who had returned to the ultrasound world.

For some time before Smiths' closure Angus Hall had also been working on medical ultrasound. Following the closure in 1967 they both joined Professor Donald in the University of Glasgow at his Department of Midwifery in the newly built Queen Mother's Hospital. The personal connection with Fraser and Brown fostered active cooperation between Professor Donald's department and Nuclear Enterprises. In 1982 Hall moved to become Head of Medical Physics at St James's University Hospital, Leeds.

In 1984 partly as a result of having agreed to care for the original contact scanner (built by Tom Brown in 1954) and used by Ian Donald, Fleming was asked by the <u>British Medical Ultrasound Society (BMUS)</u> to establish an Historical Collection. In 1988 following an agreement between the University of Glasgow's Hunterian Museum and BMUS the Museum undertook to provide long term care for the Collection. Fleming was appointed Honorary Assistant Keeper of Ultrasonic Equipment to the Museum.

The Collection now contains over sixty items of hardware, scanners and associated equipment, a wide range of manufacturer's literature and a substantial and increasing archive of unique documents.

Since 1995 Fleming has been working closely with Dr Malcolm Nicolson of the Wellcome Unit for the History of Medicine, University of Glasgow. They, together with Dr Ian Spencer, are co-authoring a book on the history of ultrasound development in Glasgow. Fleming's work in establishing the BMUS Collection was recognised in 1994 with the award of Honorary Membership of the Society and the Geddes-Davis Shield, from the British Institute of Non Destructive testing in 1997.

Mr. Fleming has contributed to over 60 papers on ultrasonics and given numerus lectures and talks at important International meeings. In addition to his work in establishing the Historical Collection Fleming contributed to BMUS as Honorary Treasurer, 1972 - 78, and in the organisation of the BMUS Annual Meetings in 1972 and 1988. Additionally he was Financial Director for the World Federation meeting in Brighton, UK (WFUMB 1982). Following retirement in 1995 John Fleming retains a close link with the University as an Honorary Research Associate. He continues as Coordinator of the <u>BMUS Historical Collection</u> until 2004.



Fig.2-1 Mr. Fleming with a few of the scanners in the BMUS Historical Collection c. 1996. In the foreground are machines from KretzTechnik®, Philips®, Siemens® and ADR®.

2-1-2 Gray scale imaging.

Ultrasound or ultrasonography is a medical imaging technique that uses high frequency sound waves and their echoes. The technique is similar to the echolocation used by bats, whales and dolphins, as well as SONAR used by <u>submarines</u>. In ultrasound, the following events happen: the ultrasound machine transmits high-frequency (1 to 5 megahertz) sound pulses into your body using a probe , the sound waves travel into your body and hit a boundary between tissues (e.g. between fluid and soft tissue, soft tissue and bone) , some of the sound waves get <u>reflected</u> back to the probe, while some travel on further until they reach another boundary and get reflected , the reflected waves are picked up by the probe and relayed to the machine , the machine calculates the distance from the probe to the tissue or organ (boundaries) using the speed of sound in tissue (5,005 ft/s or1,540 m/s) and the time of the each echo's return (usually on the order of millionths of a second) , and the machine displays the distances and intensities of the echoes on the screen, forming a two dimensional image like the one shown below.

The Ultrasound Machine:- A basic ultrasound machine has the following parts: transducer probe - probe that sends and receives the sound waves , central processing unit (CPU) - computer that does all of the calculations and contains the electrical power supplies for itself and the transducer probe and transducer pulse controls - changes the amplitude, frequency and duration of the pulses emitted from the transducer probe .(Antiou,2003)



Fig.2-2 Photo courtesy Dynamic Imaging Limited Ultrasound machine with various transducer probes

2.1.3 Probes.

Transducer probes come in many shapes and sizes, as shown in the photo above. The shape of the probe determines its field of view, and the frequency of emitted sound waves determines how deep the sound waves penetrate and the resolution of the image. Transducer probes may contain one or more crystal elements; in multiple-element probes, each crystal has its own circuit. Multiple-element probes have the advantage that the ultrasounc beam can be "steered" by changing the timing in which each element gets pulsed; steering the beam is especially important for cardiac ultrasound. In addition to probes that can be moved across the surface of the body, some probes are designed to be inserted through various openings of the body (vagina, rectum, esophagus) so that they can get closer to the organ being examined (uterus, prostate gland, stomach); getting closer to the organ can allow for more detailed views.

2-1-3-1 Types of probes.

2-1-3-1-1 Anorectal 3D 2052

Specification : frequency Range 16 - 6 MHz , transducer Categories transrectal, transvaginal , focal Range Up to 50 mm , image field(expanded) 360° and weight 850 g. Detailed, High-Resolution Images : see all rectal wall layers , evaluate the Radial, Longitudinal Extension of Sphincter Tears , assess the extent of anal sphincter damage , acquire deep penetrating, clear dataset images and measure detailed pelvic floor architecture in all x, y and z planes, accurately.Easy to Use 3D : scan your patient and examine their data at any time, on any PC , 3D cube provides accurate distance, area, angle, and volume measurements , reproduce your work with ease, one-touch operator-independent acquisition and cut through the data cube to see anatomical details in the best plane.



2-1-3-1-2 Burr-Hole 8863

Specification : frequency Range 10 - 3.8 MHz , transducer Categories **Intraoperative**, **Neurosurgery**, Contact Surface 10 x 8.6 mm, .4 x .34 in , Focal Range 5-57 mm, .2-2.2 in and weight 50 g .

High resolution burr-hole transducer for neurosurgical imaging: locate the ventricular system more easily , insert ventricular drains and implant CSF shunts. Perform Precise Puncture Procedures: brain lesion biopsy, intracerebral abscess and intracranial cyst puncture. The 8863 features a sterile, <u>single use needle guide (UA1346)</u>. The needle guide snaps easily on and off the transducer, so shunts stay in place. The 8863 can also be easily attached to a LEYLA arm, to stay in place during surgery.



Fig.2-4

2-1-3-1-3 Curved Array 8823

Specification : frequency Range 6 - 1.8 MHz , transducer Categories Abdominal, Fetal, Pediatric, Urology, contact Surface 31 x 12 mm , scanning modes B, M, Doppler, BCFM, Contrast, Tissue Harmonic , dimensions 94 x 44 mm and weight 150 g .

Easy Access to Kidney Diagnostics : superior image quality and minimizes patient discomfort. Exceptional Image Quality: clearly view structures using deep penetration at higher frequencies obtaining a high image resolution with coded excitation , measure renal blood flow with superb spectral Doppler , visualize anatomic variations and residual tumor after RF and cryoablation with contrast imaging , find kidney stones easily with harmonic imaging , Ideal for Interventional Procedures and single-use and reusable needle guides for convenient interventional procedures.

8823 applications: kidney, bladder, pediatric and difficult to access areas.



Fig.2-5

2-1-3-1- 4 Craniotomy 8862

Specification : Frequency Range 10 - 3.8 MHz ,transducer categories intraoperative, neonatal, neurosurgery, nediatric, contact Surface 29 x10mm/1.1x.4 in , focal Range 5-68mm/.2-2.6 in and weight 50 g. Real clinical impact with high-resolution neurosurgical imaging : determine the adequacy of a resection , guide biopsy procedures , differentiate vascular malformation from adjacent hematoma , the 8862 has a sterile, <u>single-use</u> needle guide (UA1345) and the transducer can also be easily attached to a LEYLA arm, to stay in place during surgery.



Fig.2-6

2-1-3-1-5 Curved Array 8820e

Specification: frequency Range 6 - 2 MHz, Transducer Categories
Abdominal, Fetal, Obstetrics, Urology, contact Surface 62.5 x 13 mm, focal Range 12 - 200 mm, scanning modes B, M, Doppler, BCFM, Tissue Harmonic, and contrast, dimensions 104 x 77 mm and weight 180 g. Deep Penetration and High Resolution. Clearly visualize deep anatomical structures and coded excitation. Comfortable Ergonomic Design. A control button right on the handle and slim design and rounded handle enables lighter grip with minimum pressure.3D and harmonic imaging for easier identification of lesions : use 3D as a diagnostic tool and visualization of lesions in 3 planes appears to allow improved assessment of capsular disruption.

8820e Applications : liver , pancreas , bladder , general abdominal and obstetric scanning and interventional procedures.



Fig.2-7

2-1-3-16 Curved Array 8830

Specification:- frequency Range 6 - 2 MHz , transducer categories abdominal, fetal, fbstetrics, pediatric , contact Surface 67.5 x 13 mm , scanning modes B, M, BCFM, Doppler, Tissue Harmonic , image field(expanded) 60° and weight 155 g .The 8830 gives you sharp images and clear details at all depths. Simple and Convenient Interventional Procedures. Easy-to-use reusable and single-use needle guides. The 8830 needle guides are designed specifically for performing intervention in the abdominal region. The single-use needle guide is designed to guide ablative procedures. Continually monitor the path of the needle on the screen. Comfortable Design: - slim and rounded handle for easy positioning and start and stop scanning and freeze and unfreeze images with a simple click on the integrated control button. Superior Image Quality for All-Round Abdominal Imaging: - ideal for abdominal, urological and OB/GYN scanning.



Fig.2-8

2-1-3-1-7 Curved Array 8830

Specification:- frequency Range 6 - 2 MHz , transducer categories abdominal, fetal, obstetrics, pediatric, contact Surface 67.5 x 13 mm , scanning modes B, M, BCFM, Doppler, Tissue Harmonic , image field(expanded) 60° and Weight 155 g . Superior Image Quality for All-Round Abdominal Imaging. Ideal for abdominal, urological and OB/GYN scanning. The 8830 gives you sharp images and clear details at all depths.Simple and Convenient Interventional Procedures :-easy-to-use reusable and single-use needle guides , the 8830 needle guides are designed specifically for performing intervention in the abdominal region , the singleuse needle guide is designed to guide ablative procedures and continually monitor the path of the needle on the screen.Comfortable Design:- slim and rounded handle for easy positioning and start and stop scanning and freeze and unfreeze images with a simple click on the integrated control button.



Fig.2-9

2-1-3-1-8 Curved Array 8802

Specification:- Frequency Range 6 - 3 MHz , transducer Categories Abdominal, Fetal, Obstetrics, Pediatric, contact Surface 52 x 8 mm , focal Range 6-114 mm and Weight 150 g . Excellent Image Quality:- broad bandwidth gives excellent image quality , deep penetration for clear images and ergonomic design. Quick and Easy Disinfection. Compatible with modern sterilization methods. 8802 Applications :- pelvic Floor , abdominal , obstetric , pediatric , Interventional procedures and tissue harmonic imaging



Fig.2-10

2-1-3-1-9 Endfire Curved Array 8667

Specification :- frequency Range 10 - 5 MHz , transducer Categories **Transrectal**, **Urology** , contact Surface 50 mm2 , focal Range 5 - 50 mm , scanning modes B, M, BCFM, Doppler, Tissue Harmonic, Power Doppler , dimensions 300 x 36 mm and weight 260 g .Endfire prostate imaging. wide endfire image plane assists in locating lesion. Convenient puncture :- the needle's path starts at the tip of the probe and monitor the needle from the start of the puncture to the actual biopsy site. 8667 Applications:- endorectal scanning , interventional procedures , spectral, CFM and Power Doppler examinations and tissue harmonic imaging.



Fig. 2-11

2-1-3-1-10 Endocavity Biplane 8848

Specification :- frequency Range 12 - 4 MHz , transducer Categories **Transrectal, Transvaginal, Urology**, focal Range 3 - 60 mm , scanning modes B,M, Doppler, BCFM, Tissue Harmonic Imaging , rame Rate >150 , image field(expanded) 180°(transverse) and weight 250 g .Image guided prostate therapy:- sagittal scanning of any size prostate from base to apex , clear and detailed image, for accurate volume studies and source dose planning , customizable sagittal grids and preferences for brachytherapy , clear visualization of seminal vesicles and clear view of needle placement. Pelvic Floor scanning :- best broad view of anterior and posterior compartments for functional and anatomical studies , reproducible 3D studies with external mover and detailed high-resolution biplane with 6.5 cm. linear and convex views



Fig. 2-12

2-1-3-1-11 Endovaginal 8819

Specification: - frequency Range 9 - 5 MHz, transducer categories **fetal**, **transrectal**, **transvaginal**, contact Surface 26 x 5 mm and weight 140 g. Versatile Endovaginal Transducer:- ideal all-round ultrasound tool for routine gynecological investigations, offers good penetration and gives you detailed images at all depths, simple and convenient needle guide clicks easily and securely into place and helps simplify interventional procedures, easy follicle measurement and visual guidance of aspiration, ergonomic design makes it comfortable to use and slim design minimizes the discomfort of a transvaginal examination. 8819 Applications:- endovaginal scanning, transrectal scanning and spectral and CFM Doppler examinations



Fig. 2-13

2-1-3-1-12 High Frequency Linear Array 8870

Specification :- frequency Range 18 - 6 MHz , transducer Categories **Musculoskeletal, Peripheral Vascular, Small Parts** , contact Surface 38.4 x 3.5 mm , focal Range 3 - 60 mm , scanning modes B, M,BCFM , doppler,tissue , harmonic imaging , frame Rate >150 Hz and weight 100 g . High Frequency Imaging with the 8870. Linear array, fine pitch 18 MHz transducer offers:- high Resolution, Detailed Images of Superficial Structures , greater confidence during scanning of fingers, toes, wrists, forefoot, ankles and elbows. High Doppler frequencies allow superb flow visualization of superficial areas. Easy System Control. Operate system at the touch of a transducer button – leaves both hands free for scanning.Easy and Thorough Cleaning and Disinfection. Compatible with modern disinfection and sterilization techniques.



Fig. 2-14

2-1-3-1-13 Hockey Stick 8809

Specification:- frequency Range 15 - 6 MHz , transducer Categories **Intraoperative, Musculoskeletal, Peripheral Vascular, Small Parts** , contact Surface 24 x 3.5 mm , focal Range 3 - 55 mm , scanning modes B, M, Doppler, CFM and weight 80 g . Reach difficult to access areas easily:small, flexible tip fits into tight spots and tip can be set at various angles. Excellent resolution in the extreme near field:- very high frequency (15 MHz) for high resolution and visualize flow with outstanding Doppler sensitivity.Puncture in tight places :- unique puncture guide that follows transducers flexible tip and perfect for guiding intraoperative and percutaneous interventional procedures. 8809 Applications :-intraoperative vascular , general intraoperative , musculoskeletal , small part and Interventional,



2-1-3-1-14 Intraoperative 8815

Specification :- frequency Range 10 - 4 MHz , transducer Categories **Intraoperative**, **Pediatric** , contact Surface 14 x 60 mm , focal Range 5 – 95 mm , scanning modes B, M, Doppler , BCFM , contrast Imaging , tissue Harmonic Imaging , frame Rate (max.) 230 Hz and weight 250 g .

Designed Especially for Interventional Ultrasound During Surgery. I-shaped intraoperative transducer. Guided intraoperative biopsy with a variety of angles and positions .Safer intervention with needle guide lock. High image quality with large footprint and wide near field image .Easily capture 3D images, review and send to a colleague. Contrast-enhanced* ultrasound for detection and assisting in characterization of suspicious masses.



Fig. 2-16

2-1-3-1-15 Intraoperative Biplane 8824

Specification :- frequency Range 10 - 3.75 MHz , transducer Categories **Intraoperative, Musculoskeletal, Peripheral Vascular, Small Parts** , Scanning modes B, M, Doppler, BCFM, Tissue Harmonic, Contrast , dimensions 1.4 x 3.3 x 5.1 cm and weight 45 g .8824 - Simultaneous Biplane Imaging:- choose between the I, T or simultaneous imaging , combined I and T array for improved orientation , flexibility to take free hand biopsies from the front, back, left, or right , excellent Images , near field and good penetration and high frequency coded excitation.Compact Size. Easy access in tight spaces. Easy to hold in intraOperative condition.



Fig. 2-17

2-1-3-1-16 Linear Array 8811

Specification:- frequency Range 12 - 5 MHz , transducer Categories Intraoperative, Musculoskeletal, Peripheral Vascular, Small Parts, Urology , contact Surface 50 x 4 mm , focal Range 2 - 55 mm , dimensions 105 x 64 x 22 mm and weight 98 g . A Clear Choice for Cost-Effective Imaging. High frequency. Large footprint. Doppler sensitivity. True Echo Harmonics. Puncture Guides for Convenient Biopsy. Puncture guides available have:- 30, 45 and 60 angles of insertion and variable diameter, allowing you to choose the desired needle size. Disposable needle guides and sterile transducer covers are also available. Fast Lesion Assessment. Provides image clarity and contrast resolution. Determine necessity for biopsy on the spot. Perform aspiration or biopsy immediately .



Fig. 2-18

2-1-3-1-17 Linear Array 8670

Specification:-frequency Range 12 - 4 MHz , transducer Categories **Musculoskeletal, Pediatric, Peripheral Vascular, Small Parts, Urology** , contact Surface 45 x 14 mm , focal Range 0 - 70 mm , scanning modes B, M, BCFM, Doppler, Tissue Harmonic , dimensions 91 x 52 x 21 mm and weight 130 g . Quality, Versatility and Convenience in One Transducer. Small part, musculoskeletal and vascular scanning. The 8670 supports a number of ultrasound applications, such as small part, breast and orthopedics, rheumatology and sports medicine.Easy switching between near and far views. Very high image detail . Excellent choice for penile Doppler and testis . Optimized for small part, musculoskeletal and vascular scanning:-easy-to-use puncture and biopsy guide , small part , breast , testis , penile Doppler. Musculoskeletal. Peripheral vascular. Interventional procedures. Contrast Imaging.



Fig. 2-19

2-1-3-1-18 ProART[™] Robotic Drop In 8826

Specification: - frequency Range 12 - 5 MHz, transducer Categories **Intraoperative**, **Urology**, image field (expanded) Sector 36° and weight 25 g. Unique specialized ultrasound transducer for robotic-assisted surgery. Premium Performance and Excellent Image Quality. Curved linear array with the largest field of view on the market today. High resolution 12–5 MHz transducer. Premium image quality with excellent contrast and detail resolution. Unique 3D rendering visualization. Designed for Ease of Use:-"Fingertip" control - fin located directly over transducer array , designed to fit Prograsp^{TM1} for maximum control , fits through a standard trocar



Fig. 2-20

2-1-3-1-19 Prostate Biplane 8808e

Specification: - frequency Range 10 - 5 MHz , transducer Categories **Transrectal**, **Urology** , scanning modes B, M,BCFM, Doppler, Tissue Harmonic Imaging , image field(expanded) 126° and weight 250 g.Simultaneous biplane. Efficient and confident prostate examinations. Precise Biopsies with Simultaneous Biplane. The 8808e gives you real-time images of both the sagittal and transverse planes which is invaluable for orientation. Simultaneous images of the sagittal and transverse planes provide a clear indication of needle placement for quicker and more confident biopsies.Streamlined Workflow. Save time and effort with the transducer's one touch operation. Switch between views, freeze, print and save without touching the scanner. Slender Design. The 8808e's sterile, single-use and reusable needle guides are an integral part of the transducer minimizing patient discomfort.



Fig. 2-21

2-1-3-1-20 Prostate Triplane 8818

Specification :- frequency Range 12 - 4 MHz , transducer Categories transrectal, transvaginal, urology , contact Surface 34.4 x 5.5 mm , focal Range 3 - 60 mm , scanning modes B, M,BCFM, Doppler, Contrast , tissue Harmonic , frame Rate 60 Hz , image field(expanded) Triplane / 140° , dimensions 36 x 39 x 323 mm and weight 230 g .Triplane – all prostate zones with one transducer , images in three visionary planes , switch between prostate zones at the touch of a button and increase diagnostic value with 3D, Contrast and Doppler. Easy and comfortable to use take confident apical biopsies with endfire array, biopsy the peripheral, transition and central zones with simultaneous biplane , one-time insertion and minimal manipulation using disposable dual guide. 8818 Applications:-transrectal prostate scanning , transrectal puncture and biopsy , transperineal puncture and biopsy , transvaginal scanning , spectral and CFM Doppler examinations , Tissue harmonic imaging and contrast imaging.



2-1-3-1-21 Rigid Laparoscopic 8836

Specification: - frequency Range 12 - 5 MHz, transducer Categories **Intraoperative**, scanning modes B, M, Doppler, BCFM, Tissue Harmonic Imaging and Contrast Imaging. Premium performance, more control, easier access. Superb detail and contrast resolution of difficult-to-access anatomy. Curved array giving wide field of view. Durable, easy-grip handle. Fits through standard 10 mm trocar. Compatible with modern sterilization methods. Applications:-minimally invasive intraoperative procedures, liver, gall bladder, kidney and uterus.



Fig. 2-23

2-1-3-1-22 Small Footprint Cardiac 8827

Specification:- frequency Range 4 - 2 MHz , transducer categories **cardiac**, **transcranial** , contact Surface 16 x 13 mm , focal Range 10 - 134 mm , frame Rate >200 Hz , image field(expanded) Phased 90°, weight 74 g .



Fig. 2-24

2-1-3-1-23 Small Footprint Cardiac 8837

Specification: - frequency Range 5 – 1 MHz, transducer categories **abdominal**, **cardiac**, **transcranial**, contact Surface 19.2 x 13.5 mm, focal Range 10 – 34 mm, scanning modes B, M, Doppler, BCFM, CW Doppler, Tissue Harmonic Imaging and weight 74 g. Ergonomic Design, Suitable for All Patients: - easy to hold, ergonomically designed handle, ideal for intercostal imaging with small footprint, orientation mark on the handle for imaging plane orientation and dynamic cardiac examinations. Sensitive to movement with phased array technology and a high frame rate.Single-crystal transducer technology for optimal imaging conditions with high resolution and uniform images in all depths. Wide imaging angle (90°) to see entire myocardium. Super image quality and cardiac calculations .Tissue Harmonic imaging provides outstanding visualization of cardiac structures.High Doppler sensitivity for fast flow measurements.



Fig. 2-25

2-1-3-1-24 T-Shaped Intraoperative 8816

Specification:- frequency Range 10 - 4.3 MHz , transducer categories abdominal, intraoperative , contact Surface 5 x 51 mm , focal Range 5 - 95 mm , scanning modes B, M, Doppler, BCFM, contrast, tissue harmonic imaging and weight 55 g . Small Intraoperative Transducer with Wide Near Field View. Small, T-shaped transducer designed primarily for hepatic surgery. Excellent image quality. Wide near field view. Coded excitation technology for high resolution with deeper penetration. Contrast Imaging for improved sensitivity and accuracy of lesion detection and classification. Compatible with modern sterilization techniques. 8816 Applications: intraoperative scanning, abdominal scanning, spectral and CFM Doppler examinations, coded excitation for deeper penetration and contrast and harmonic imaging.



Fig. 2-26

2-1-3-1-25 Vascular 8822

Specification: - frequency Range 9 - 3.5 MHz, transducer Categories **Peripheral Vascular**, scanning modes B, M, CFM, Doppler, tissue harmonic imaging and weight 98 g .Peripheral Vascular Imaging. Excellent image quality in depth. Wide field of view. Broad bandwidth. Tissue Harmonic Imaging. Easy interventional Procedures and Biopsy. Sterilizable needle guide with puncture line on image.3 puncture lines: 30°, 45°, 60°.3 needle diameters.Designed for Easy Use:-customizable finger-tip control button, easy to hold and completely immersible for cleaning and disinfection.



Fig. 2-27

2-1-3-1-26 3DART^{тм} 8838

Specification :- frequency Range 12 - 4 MHz (Depending on system) , transducer categories transrectal, transvaginal, urology, focal Range 3 - 60 mm , image field(expanded) 65mm wide acoustic surface able to rotate 360° and weight 450 g . Unique High Resolution Color and 3D Imaging. The World's first electronic transducer for endovaginal, endoanal and transrectal imaging, with built-in high resolution 3D. Unique Built-In 3D Acquisition. Built-in linear array rotates 360° inside the transducer. No need for additional accessories or mover. No moving parts come in contact with the patient, for excellent patient comfort. Excellent Image Quality:-for both dynamic 2D and 3D scanning. Designed for Easy Operation. Slim 16mm (0.6) diameter for more comfortable patient imaging. Easy to hold and manipulate. 2D scanning plane controlled remotely from the system keyboard. Silent operation. Unparalleled capabilities for both prostate 3D and pelvic floor imaging.



Fig. 2-28

2-1-3-1-27 10L2w Wide Linear

Specification: - transducer Categories **Peripheral Vascular** , contact Surface $57 \ge 10 \text{ mm}$.



Fig. 2-29

2-1-3-1-28 13L4w Wide Linear

Specification:-transducer Categories **Musculoskeletal**, **Pediatric**, **Peripheral Vascular**, **Small Parts**, contact Surface 57 x 10 mm.



Fig. 2-30

2-1-3-1-29 14L3 Linear

Specification: - transducer categories **musculoskeletal**, **pediatric**, **peripheral vascular** and **small Parts** and Contact Surface 45 x 14 mm.



Fig. 2-31

2-1-3-1-30 18L5 High Frequency Linear

Specification:- transducer categories **m**usculoskeletal, **p**ediatric, **p**eripheral vascular and **s**mall Parts.

Contact Surface 48 x 13mm.



Fig. 2-32

2-1-3-1-31 5P1 Small Footprint Cardiac

Specification: - transducer categories **abdominal**, **cardiac**, **transcranial**.

Contact Surface 26 x 20 mm.



Fig. 2-33

2-1-3-1-32 6C2 Curved

Specification:- transducer categories **a<u>bdominal</u>**, **f<u>etal</u>**, **m<u>usculoskeletal</u>**, **o<u>bstetrics</u>**.

Contact Surface 69 x 19 mm.



Fig. 2-34

2-1-3-1-33 6C2s Small Curved

Specification:-transducer categories **a<u>bdominal</u>**, **f<u>etal</u>**, **o<u>bstetrics</u>**, **p<u>ediatric</u>**.

Contact Surface 33 x 12 mm.



Fig. 2-35

2-1-3-1-34 E10C4 Endocavity

Specification: - transducer categories **f<u>etal</u>**, **o<u>bstetrics</u>**, **t<u>ransrectal</u>**, **t<u>ransvaginal</u>**.

Contact Surface 22 x 18 mm



Fig. 2-36

2-1-3-1-35 E14C4 Endfire Curved

Specification

- Transducer Categories Transrectal, Transvaginal,
- Contact Surface 20 mm



Fig. 2-37

2-1-3-1-36 E14C4t Prostate Triplane

- Transducer Categories Transrectal, Transvaginal,
- Contact Surface 20 mm



Fig. 2-38

2-1-3-1-37 E14C4t Prostate Triplane

- Transducer Categories Transrectal, Transvaginal,
- Contact Surface 20 mm



Fig. 2-39

2-1-3-1-38 E14CL4b Endocavity Biplane

- Transducer Categories Transrectal, Transvaginal,
- Contact Surface 20 mm



Fig. 2-40

2-1-3-1-39 N13C5 Curved

- Transducer Categories Neonatal,
- Contact Surface 29 x 10 mm



Fig. 2-41

2-1-3-1-40 4-Way Laparoscopic 8666-RF

Specification:- frequency Range 10 - 4.3 MHz , transducer categories intraoperative, urology, contact Surface 30 x 5 mm , focal Range 5 - 95 mm , scanning modes B, M, Doppler, BCFM, tissue Harmonic Imaging and Contrast Imaging , dimensions 302 x 178 mm and weight 475 g. The Most Advanced Laparoscopic Ultrasound Transducer on the Market. Built-in facilities for LUS-guided biopsies. Ethanol or contrast agent injections cryoablation. Microwave ablation. Flexible for difficult to reach areas or rigid for manipulating structures. 8666-RF Applications: - laparoscopic, intraoperative, radiofrequency tumor ablation (RFA) and biopsy.(Doody C,1999)



Fig. 2-42

2-1-4 Biological effects of possible relevance to safety.

2-1-4-1 Introduction.

In the 1920s, the availability of piezoelectric materials and electronic devices made it possible to produce ultrasound (US) in water at high amplitudes, so that it could be detected after propagation through large distances. Laboratory experiments with this new mechanical form of radiation showed that it was capable of producing an astonishing variety of physical, chemical and biologic effects. In this review, the early findings on bioeffects are discussed, especially those from experiments done in the first few decades, as well as the concepts employed in explaining them. Some recent findings are discussed also, noting how the old and the new are related. In the first few decades, bioeffects research was motivated partly by curiosity, and partly by the wish to increase the effectiveness and ensure the safety of therapeutic US. Beginning in the 1970s, the motivation has come also from the need for safety guidelines relevant to diagnostic US. Instrumentation was developed for measuring acoustic pressure in the fields of pulsed and focused US employed, and standards were established for specifying the fields of commercial equipment. Critical levels of US quantities were determined from laboratory experiments, together with biophysical analysis, for bioeffects produced by thermal and nonthermal mechanisms. These are the basis for safety advice and guidelines recommended or being considered by national, international, professional and governmental organizations.

After the end of World War II, advances in ultrasound (US) technology brought improved possibilities for medical applications. The first major efforts in this direction were in the use of US to treat diseases. Medical studies were accompanied by experiments with laboratory animals and other model systems to investigate basic biological questions and to obtain better understanding of mechanisms. Also, improvements were made in methods for measuring and controlling acoustical quantities such as power, intensity and pressure. When diagnostic US became widely used, the scope of biological and physical studies was expanded to include conditions for addressing relevant safety matters. In this historical review, a major part of the story is told by 21 investigators who took part in it. Each was invited to prepare a brief personal account of his/her area(s) of research, emphasizing the "early days," but including later work, showing how late and early work are related, if possible, and including anecdotal material about mentors, colleagues, etc.

We briefly review my early contacts with bioacoustics and the bioacoustic work at the University of Pennsylvania that took place from the early 1950s to 1975. It was carried out with E. L. Carstensen, K. Li, A. Smith, H. Pauly, J. Reid, P. Edmonds and many students. The emphasis was first on basic biophysical studies. The work with E. Carstensen and H. Pauly was primarily concerned with the mechanism causing the high absorption typical for tissues and cell suspensions. Macromolecular content was shown to be largely responsible for the absorption. Practical applications concerned the relative merits of electromagnetic and ultrasonic diathermy techniques. P. Edmonds extended the range of macromolecular studies to 100 MHz and initiated work on the attenuation in lung tissues. After J. Reid came to Pennsylvania, the development of echocardiography took place.

Biological effects of ultrasound are the potential biological consequences due to the interaction between the ultrasound wave and the scanned tissues.

The use of ultrasound for cardiac imaging has not known significant adverse biological effects. Concern about the safety of ultrasound prompted several agencies to devise regulatory limits on the machine output intensities. The visual display of thermal and mechanical indices during ultrasound imaging provides an aid to limit the output of the machine. Sonographic evaluation of the human body, including potentially sensitive tissues, such as developing fetus and the eye, have been performed on millions of patients without documentation of serious adverse events. However, ultrasound waves have the potential to cause significant biological effects, depending on ultrasound wave characteristics and scanned tissues sensitivity. Physicians and sonographers must be aware of these potential biological effects in assessing the overall safety of the procedure. (Dalecki,2007)

2-1-4-2 Types of biological effects.

The biological effects of ultrasound depend on the total energy applied to a given region. Thus, varying duration of exposure to wave emission, intensity and frequency of the ultrasound beam, pulsed or continuous emission modality and acoustic power, may lead to significant biological effects, that are commonly divided in thermal and non-thermal effects.

2-1-4-2-1 Thermal.

The biological effects of ultrasound energy are related primarily to the production of heat. Heat is generated whenever ultrasound energy is absorbed, and the amount of heat produced depends on the intensity of the ultrasound, the time of exposure, and the specific absorption characteristics of the tissue. As much as 70% of the total temperature increase associated with ultrasound occurs within the first minute of exposure ¹, but temperature continues to rise as exposure time is prolonged. Minimizing the exposure time is probably the single most important factor for ensuring patient safety from thermal injury. Other important parameters to be considered are: - The relative protein content of each tissue, since absorption coefficients vary

between 1 (skin, tendon, spinal cord) and 10 (bone) dB/cm MHz. The perfusion of the tissue, which has a dampening effect on heat generation and physically allows heat to be carried away from the point of energy transfer.

Emission modality, since pulsed-wave ultrasound is extremely unlikely to significantly heated tissues.

Beam width, since a wider beam width reduces the rate and extent of temperature rise by permitting the energy to be distributed over a larger perfusion territory.

2-1-4-2-2 Non-thermal

Ultrasound energy creates also mechanical forces independent of thermal effects, thereby causing biologic effects that are not related to temperature rise alone, such as cavitations, torque forces, oscillatory shear, radiation, pressure and micro streaming.

2-1-4-2-3 Cavitations

The interaction of ultrasound with gas bubbles or contrast agents causes rapid and potentially large changes in bubble size. This process, termed cavitations, may increase temperature and pressure within the bubble and thereby cause mechanical stress on surrounding tissues, precipitate fluid micro jet formation, and generate free radicals . Gas-containing structures (e.g., lungs, intestines) are most susceptible to the effects of acoustic cavitations. Ultrasound wavelength has an important role in bubble formation and growth: short wavelength ultrasound (observed at higher frequencies) does not provide sufficient time for significant bubble growth; therefore, cavitations are less likely under these circumstances compared with long wavelengths. The short half-life of cavitations nuclei prevents most cavitations-related biological effects, unless ultrasound contrast agents are also present. Contrast agents markedly reduce the threshold intensity for cavitations. However, because of the relatively high viscosity of blood and soft tissue, significant cavitations is unlikely and cavitations has not been shown to occur with the ultrasound exposure commonly used during a diagnostic examination.

2-1-4-2-4 Other effects

A variety of other physical forces may also be produced by ultrasound energy. Although each of these effects can be demonstrated in vitro, there is no evidence that any of these physical phenomena has a significant biological effect on patients. (Daleki,2007)

2-1-4-3 Measurement of biological effects

The biological effects of ultrasound are generally discussed in terms of power (the amount of acoustic energy per unit of time), and the units of power are in the mill watt range. Intensity (acoustic power per unit of area) is usually expressed as watts per meter squared (W/m2) or in mill watts per centimeter squared (mW/cm2). To calculate the energy from a pulsed ultrasonic beam, it is necessary to know the duty factor, which is a measure of the fraction of time during which the transducer emits ultrasound. The maximum overall intensity is then described as the highest exposure within the beam (spatial peak) averaged over the period of exposure (temporal average) and is known as the spatial peak temporal average (SPTA) intensity. Another common measure is the spatial peak pulse average (SPPA), defined as the average pulse intensity at the spatial location where the pulse intensity is maximum. Commercial ultrasound instruments operating in pulsed-wave modality for two-dimensional imaging have spatial

peak, temporal averaged intensities ranging from 0.001 to more than 200 mW/cm2. Pulsed Doppler imaging, however, may have a spatial peak, temporal average as high as 1900 mW/cm2, considerably greater than 100 mW/cm2 level that has been most extensively studied and has never been shown to produce a biologic effect. The relatively short periods of pulsing, coupled with the fact that the transducer is constantly moving so that no single area is imaged for a long period, contribute to the low likelihood of delivering significant heat to the tissue.

A major limitation of measuring the intensity of ultrasound exposure is that estimating the actual tissue exposure is difficult, due to attenuation and other interactions with the tissue. Furthermore, tissue exposure is limited only to transmission periods and to the time the ultrasound beam dwells at a specific point, both of which are considerably shorter than the total examination time. Other indices that incorporate these factors have been developed to better define the exposure levels with diagnostic ultrasound. These measures include the mechanical index (MI) and tissue thermal index (TTI). The thermal index (TI) and mechanical index (MI) were introduced to provide the operator with an indication of the potential for ultrasoundinduced bioeffects. The TI provides an on-screen indication of the relative potential for a tissue temperature rise. MI provides an on-screen indication of the relative potential for ultrasound to induce an adverse bio-effect by a non-thermal mechanism such as cavitations. Thermal indices are conservatively determined to ensure patient safety. Under most clinical conditions, the thermal index closely approximates or overestimates the maximum temperature increase for ultrasound exposure. Three different thermal indices (depending on the structures encountered in the path of the ultrasound beam, soft tissue or TIs, bone or Tip and cranium or Tic) are used to estimate temperature increases associated with an ultrasound beam. In fact, thermal indices in soft tissue or bone provide fairly accurate in vivo

estimates of ultrasound-related temperature rise in the tissue types . Contemporary ultrasound equipment has the theoretic capability to cause a tissue temperature increase greater than 4°C at the focal point.The MI describes the relationship between cavitations formation and acoustic pressure and is defined as the ratio of the peak rare factional negative pressure adjusted for tissue attenuation and square root of the frequency. The MI was originally formulated based on the threshold for acoustic cavitations in water and blood, and hence may not specifically consider the type of tissue in which this process occurs.

The American Institute of Ultrasound in Medicine (AIUM) has proposed guidelines for limits below which ultrasound clearly has been demonstrated to be safe¹. These guidelines include:

A diagnostic exposure that produces a 1°C or less temperature elevation above normal.

An exposure intensity less than 1 W/cm2 for focused ultrasound beams.

Current diagnostic ultrasound systems have outputs ranging from 10 mW/cm2 (SPTA) for imaging to as high as 430 mW/cm2 (SPTA) for pulsed Doppler ultrasound. There has been no evidence to date to suggest adverse effects of echocardiography at these ultrasonic outputs.

During transoesophageal imaging, especially during intraoperative imaging, the probe may remain nearly stationary for extended periods. The heat generated by the transducer itself must also be considered. Although there are no reports of significant injury resulting from even prolonged intraoperative transoesophageal echocardiography, attention to these issues is recommended. Limited imaging time, occasional repositioning of the probe and constant monitoring of the probe temperature will all help to ensure an impeccable safety record.

All evidence to date suggests that diagnostic ultrasound, particularly which used in echocardiography, is an extremely safe tool with no demonstrated adverse effects even with the use of newer technology and more powerful instrumentation. Although this is reassuring and justifiably inspires continued confidence in ultrasound imaging, the desire for more and better diagnostic information should never occur at the expense of patient safety. Therefore, limiting the scan time to a minimum, knowing the power output and exposure intensity of different modalities of each instrument, and keeping up to date on any new scientific findings or data relating to possible adverse effects, should always be a consideration.(Fowlekes GB,2008)

2-1-5 Guidelines and regulations

The sonographer should:- Recognise his/her scope of practice and work within its boundaries ensure that a locally agreed written scheme of work is in place accept properly delegated responsibility, in accordance with local practice and guidelines An ultrasound examination should not be carried out unless a valid request has been received. The request should include such clinical details as are relevant to the examination, clear identification of the person requesting the examination and to whom the report should be directed.

The sonographer should be responsive to:- potential bio-effects of ultrasound and the need to minimise dose at all times , potential hazards arising from the particular ultrasound equipment , relative risks for each application , conditions where current recommendations contra-indicate the use of certain types of ultrasound equipment and current guidelines regarding replacement of ultrasound equipment.

The sonographer is expected to: - have detailed knowledge of ultrasound equipment in order to ensure that it is appropriate for purpose , manipulate the equipment correctly so that patient diagnosis and management are not compromised , ensure that an agreed quality assurance programme is in place that incorporates the regular and inspection of ultrasound machines and auxiliary equipment.

The stated aim of quality assurance procedures applied to ultrasound equipment is to ensure consistent and acceptable levels of performance of the imaging system and image recording facilities. Most quality assurance protocols focus on the consistency. The acceptability of image quality may not be apparent from measurable changes in the parameters tested. The issue of what constitutes unacceptable equipment performance is still very difficult to assess objectively. In the absence of nationally accepted performance standards for ultrasound equipment, local and subjective evaluation is required.

This programme should include a policy on:- electrical safety tests carried out at least once a year by qualified personnel , baseline/acceptance testing of all new or upgraded equipment, and following major repair and user tests including weekly inspection of cables, transducers, monitor and image recording facilities.

A quality assurance programme should be developed in discussion with medical physics or service engineers, for each individual machine. This should be based on its clinical uses, the modes and functions utilized, the transducer types and frequencies and the auxiliary equipment attached. The programme should indicate clearly the limits of acceptability for each test, what and by whom action should be taken when these are exceeded.

The sonographer's responsibilities in relation to the ultrasound equipment should include:- appropriate selection for the examination and awareness of its limitations within that clinical context, manipulation of the controls to maximize the clinical information observed, awareness of system artifacts and how to interpret their appearances, ensuring that the equipment is suitably maintained to provide optimal images, ensuring that all transducers are appropriately prepared and cleaned according to the manufacturers' guidelines, with especial reference to intra-cavity probes, awareness of and adherence to local infection control procedures, ensuring that the recorded image is an accurate record of the displayed real-time information, following the proper shut-down procedure for the equipment, so that stored data and settings are not corrupted or lost, inspection for electrical and mechanical safety, ensuring that apparently unsafe equipment is not used until it has been checked and repaired, agreement of equipment performance criteria for each type of examination undertaken. (This should be updated regularly, in line with new developments in equipment carry performance), reporting any concerns in relation to the performance of specific equipment, and awareness of current guidelines regarding the replacement of ultrasound equipment.(Fowlekes GB,2008)

2-1-5-1 Ultrasound Examination Procedures.

Relating to all ultrasound examinations, the sonographer should be aware of locally agreed standards of practice and current guidelines of other professional bodies and organizations.

The following points should be considered for all ultrasound examinations:the clinical details provided are sufficient to carry out the examination requested and the correct examination has been requested , relevant information is available from the case notes, previous investigations and other sources , the role of the ultrasound examination is understood in the clinical context for the patient , informed consent is obtained before proceeding with the examination , the necessity for the presence of a chaperone and/or an interpreter , a systematic scanning approach that can be modified according to the individual patient , the implications should the examination be incomplete , the need to extend the ultrasound examination, and/or proceed to additional imaging techniques .where necessary in accordance with locally agreed protocol , the after care of the patient , the potential risks involved in the procedure to the patient and appropriate national and local Health and Safety regulations including infection control.

2-1-5-2 Communication.

The sonographer should:-obtain sufficient verbal and/or written information from the referring clinician to undertake correctly the examination requested , be mindful of the need to use interpreters as and when necessary to communicate adequately with the patient , greet the patient using his or her full name and status , be able to discuss the relative risks and benefits of the examination with the patient , explain the scanning procedure appropriately to the patient , obtain informed consent* from the patient or their representative being mindful of his/her capacity to understand , be aware of the individual patient's special needs including chaperoning and privacy during the examination , be professional and understanding throughout the examination; manage the interaction between the patient and any accompanying adults and children in a way that enables the examination to be carried out to a competent standard , explain and discuss the findings with the patient , Interpret and communicate the appropriately and in a timely fashion to the referring clinician , ensure appropriate arrangements have been made for further care before the conclusion of the examination , display - displays the image from the ultrasound data processed by the CPU , keyboard/cursor - inputs data and takes measurements from the display , disk storage device (hard, floppy, CD) - stores the acquired images and printer prints the image from the displayed data

The transducer probe is the main part of the ultrasound machine. The transducer probe makes the sound waves and receives the echoes. It is, so to speak, the mouth and ears of the ultrasound machine. The transducer probe generates and receives sound waves using a principle called the piezoelectric (pressure electricity) effect, which was discovered by Pierre and Jacques Curie in 1880. In the probe, there are one or more <u>quartz</u> crystals called piezoelectric crystals. When an electric current is applied to these crystals, they change shape rapidly. The rapid shape changes, or vibrations, of the crystals produce sound waves that travel outward. Conversely, when sound or pressure waves hit the crystals, they emit electrical currents. Therefore, the same crystals can be used to send and receive sound waves. The probe also has a sound absorbing substance to eliminate back reflections from the probe itself, and an acoustic lens to help focus the emitted sound waves.

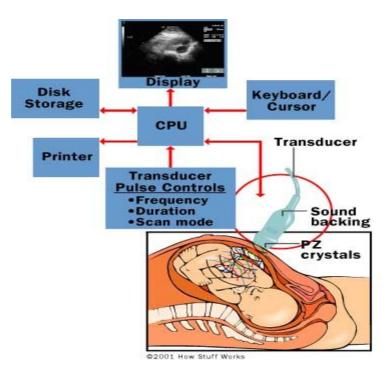


Fig. 2-43 The parts of an ultrasound machine

The CPU is the brain of the ultrasound machine. The CPU is basically a computer that contains the <u>microprocessor</u>, <u>memory</u>, amplifiers and power supplies for the microprocessor and transducer probe. The CPU sends electrical currents to the transducer probe to emit sound waves, and also receives the electrical pulses from the probes that were created from the returning echoes. The CPU does all of the calculations involved in processing the data. Once the raw data are processed, the CPU forms the image on the monitor. The CPU can also store the processed data and/or image on disk.

The transducer pulse controls allow the operator, called the ultrasonographer, to set and change the frequency and duration of the ultrasound pulses, as well as the scan mode of the machine. The commands from the operator are translated into changing electric currents that are applied to the piezoelectric crystals in the transducer probe. The display is a <u>computer monitor</u> that shows the processed data from the CPU. Displays can be black-and-white or color, depending upon the model of the ultrasound machine.

Ultrasound machines have a <u>keyboard</u> and a cursor, such as a trackball, built in. These devices allow the operator to add notes to and take measurements from the data.

The processed data and/ or images can be stored on disk. The disks can be <u>hard disks</u>, <u>floppy disks</u>, <u>compact discs</u> (CDs) or <u>digital video discs</u> (DVDs). Typically, a patient's ultrasound scans are stored on a floppy disk and archived with the patient's medical records.

Many ultrasound machines have thermal printers that can be used to capture a hard copy of the image from the display.

The ultrasound that we have described so far presents a two dimensional image, or "slice," of a three dimensional object (fetus, organ). Two other types of ultrasound are currently in use, 3D ultrasound imaging and Doppler ultrasound.

In the past two years, ultrasound machines capable of three-dimensional imaging have been developed. In these machines, several two-dimensional images are acquired by moving the probes across the body surface or rotating inserted probes. The two-dimensional scans are then combined by specialized computer software to form 3D images.



Fig. 2-44 3D ultrasound images

3D imaging allows you to get a better look at the organ being examined and is best used for: early detection of cancerous and benign tumors , examining the prostate gland for early detection of tumors , looking for masses in the colon and rectum , detecting breast lesions for possible biopsies , Visualizing a fetus to assess its development, especially for observing abnormal development of the face and limbs and visualizing blood flow in various organs or a fetus .

Doppler ultrasound is based upon the <u>Doppler Effect</u>. When the object reflecting the ultrasound waves is moving, it changes the frequency of the echoes, creating a higher frequency if it is moving toward the probe and a lower frequency if it is moving away from the probe. How much the frequency is changed depends upon how fast the object is moving. Doppler ultrasound measures the change in frequency of the echoes to calculate how fast an object is moving. Doppler ultrasound has been used mostly to measure the rate of blood flow through the heart and major arteries. Ultrasound has been used in a variety of clinical settings, including obstetrics and gynecology, cardiology and cancer detection. The main advantage of ultrasound is that certain structures can be observed without using <u>radiation</u>. Ultrasound can also be done much faster than X-rays or

other radiographic techniques. Here is a short list of some uses for ultrasound:

Obstetrics and Gynecology : measuring the size of the fetus to determine the due date, determining the position of the fetus to see if it is in the normal head down position or breech, checking the position of the placenta to see if it is improperly developing over the opening to the uterus (cervix), seeing the number of fetuses in the uterus, checking the sex of the baby (if the genital area can be clearly seen), checking the fetus's growth rate by making many measurements over time, detecting ectopic pregnancy, the lifethreatening situation in which the baby is implanted in the mother's Fallopian tubes instead of in the uterus, determining whether there is an appropriate amount of amniotic fluid cushioning the baby .Monitoring the baby during specialized procedures - ultrasound has been helpful in seeing and avoiding the baby during amniocentesis (sampling of the amniotic fluid with a needle for genetic testing). Years ago, doctors use to perform this procedure blindly; however, with accompanying use of ultrasound, the risks of this procedure have dropped dramatically. Seeing tumors of the ovary and breast.

Cardiology seeing the inside of the heart to identify abnormal structures or functions and measuring blood flow through the heart and major blood vessels.

Urology measuring blood flow through the kidney, seeing kidney stones and detecting prostate cancer early

In addition to these areas, there is a growing use for ultrasound as a rapid imaging tool for diagnosis in emergency rooms. There have been many concerns about the safety of ultrasound. Because ultrasound is energy, the question becomes "What is this energy doing to my tissues or my baby?" There have been some reports of low birthweight babies being born to mothers who had frequent ultrasound examinations during pregnancy. The two major possibilities with ultrasound are as follows: - development of heat - tissues or water absorb the ultrasound energy which increases their temperature locally and formation of bubbles (cavitation) - when dissolved gases come out of solution due to local heat caused by ultrasound

However, there have been no substantiated ill-effects of ultrasound documented in studies in either humans or animals. This being said, ultrasound should still be used only when necessary (i.e. better to be cautious).

For an ultrasound exam, you go into a room with a technician and the ultrasound machine. The following happens:- you remove your clothes (all of your clothes or only those over the area of interest , the ultrasonographer drapes a cloth over any exposed areas that are not needed for the exam , the ultrasonographer applies a mineral oil-based jelly to your skin , this jelly eliminates air between the probe and your skin to help pass the sound waves into your body , the ultrasonographer covers the probe with a plastic cover , he/she passes the probe over your skin to obtain the required images , depending upon the type of exam, the probe may be inserted into you , you may be asked to change positions to get better looks at the area of interest , after the images have been acquired and measurements taken, the data is stored on disk. You may get a hard copy of the images, you are given a towelette to clean up and you get dressed.

As with other computer technology, ultrasound machines will most likely get faster and have more memory for storing data. Transducer probes may get smaller, and more insertable probes will be developed to get better images of internal organs. Most likely, 3D ultrasound will be more highly developed and become more popular. The entire ultrasound machine will probably get smaller, perhaps even hand-held for use in the field (e.g. paramedics, battlefield triage). One exciting new area of research is the development of <u>ultrasound imaging combined with heads-up/virtual reality-</u> type displays that will allow a doctor to "see" inside you as he/she is performing a minimally invasive or non-invasive procedure such as amniocentesis or biopsy.

Ultrasound (also termed sonography, ultrasonography, and Doppler study) is a non-invasive diagnostic medical technique that uses high frequency sound waves to produce images of the internal structures of the body. These sound waves are not detectable by human hearing.

Using ultrasonography, a technician or doctor moves a device called a transducer (probe) over part of your body. The transducer emits sound waves which bounce off the internal tissues, and creates images from the waves that bounce back. Different densities of tissues, fluid, and air inside the body produce different images that can be interpreted by a physician, typically a radiologist (a physician who specializes in imaging technologies). Many studies are done by a trained technologist (sonographer) and then interpreted by a radiologist.

Ultrasound can be used as a diagnostic or screening tool to confirm medical disorders or to assist in performing medical procedures. It is also used as a therapeutic tool in treating musculoskeletal problems, renal stones (kidney stones) and gallstones .

Obstetrics and gynecology: Pregnancy ultrasound (or fetal ultrasound) is used to assess the progression of the fetus. Vaginal ultrasound, pelvic ultrasound, or transvaginal ultrasound is used to diagnose growths or tumors of the ovary, uterus, and Fallopian tubes. It can be used to assess nonpregnancy related issues as well: - lower abdominal pain , ovarian cysts . uterine fibroids , uterine growths and endometriosis .

Cardiology: Echocardiography (heart ultrasound) is a common way to evaluate the overall function of the heart. It is used to evaluate the flow of blood through the chambers and valves of the heart. It also assesses the strength of the heart beat and the volume of blood pumped through. Echocardiography is often used for the following:- heart valve problems, such as mitral valve <u>prolapsed</u> or aortic stenosis , congestive heart failure , blood clots due to irregular heart beats such as in atrial fibrillation , abnormal fluid collections around the heart, such as pericardial effusions and pulmonary artery hypertension.

Blood vessels: Ultrasound is useful in detecting problems with most of the larger blood vessels in the body. Using Doppler ultrasound technology, the flow of blood through the vessels can be observed and measured. Narrowing of vessels (stenosis) or widening of vessels (dilatation, also referred to as aneurysms) can be detected. Ultrasound testing of blood vessels includes:-carotid ultrasound , abdominal aorta ultrasound for abdominal aortic aneurysm, and blood clots in veins (superficial or deep venous thrombosis, or DVT).

Abdominal structures: Abdominal ultrasound is used to evaluate the solid organs within the abdominal cavity, including the liver, gallbladder, pancreas, kidneys, and bladder. Renal ultrasound is used to evaluate the function and structure of the kidneys. Swelling around the kidney with blockage in the urinary tract can be seen with ultrasound, making abdominal ultrasound useful in detecting kidney stones.

Liver ultrasound is used to find abnormalities in the liver tissue and ducts.

Gallbladder ultrasound can screen for gallstones or an infected gallbladder.

Appendix ultrasound is used in children or pregnant women, where it is necessary to avoid radiation from aCT scan (computerized tomography).

Testicular ultrasound: Used to diagnose testicular torsion, epididymitis (testicle infection), and testicular masses.

Neck ultrasound: The thyroid and parathyroid glands can be imaged to detect nodules, growths, and tumors.

Breast ultrasound: Used to image the breasts and to guide biopsy of breast masses to evaluate for breast cancer.

Knee ultrasound: Ultrasound can be used to evaluate the structures in the back of the knee to determine if a Baker's Cyst is present.

Eye ultrasound: An eye ultrasound is used to look at the back of the eye (retina). It is often used when a patient has cataracts that make looking into the eye difficult. The test may help diagnose retinal detachment. It can also assist in cataract surgery.

Skin ultrasound: Ultrasound can be used to help find certain types of foreign bodies that may become lodged in the skin.

Ultrasound-guided needle biopsy: Ultrasound helps medical professionals guide needles into specific areas of the body to extract cells for laboratory testing.

Ultrasound-guided needle aspiration: Ultrasound may be used to guide a needle into pockets of fluid accumulated in the body that need to be drained (for example, an abscess, pleural effusions, or ascites).

Ultrasound-assisted intravenous access: When an intravenous (IV) line is required and veins are difficult to access, ultrasound may be used to assist in finding larger veins in the neck, chest wall, or groin.

Extracorporeal shock wave lithotripsy (ESWL) is a form of ultrasound used to break up kidney stones and gallbladder stones. In many cases, the patient is given some sedation or pain medication as the high intensity waves needed to fracture the stones can cause discomfort. This technique is used often to treat stone formation.

A few physicians use HIFU (high intensity focused ultrasound) to treat cancer, while others use ultrasound for targeted drug delivery, homeostasis or thrombolytic. However, these techniques are not widely available and are still being evaluated for efficacy.

Ultrasound is often used to treat musculoskeletal injuries, and is frequently used to treat sports injuries. For example, plantar fasciitis and tendinitis are commonly treated using therapeutic ultrasound. It is believed to help reduce inflammation and increase blood flow to affected areas. However, there is little evidence that tissue therapeutic ultrasound is effective. More study is needed For the most part, ultrasound is considered a painless, non-invasive diagnostic tool. Most ultrasound scans can be performed with the transducer placed atop the skin, with the sound waves aimed at the organ or body part being tested. The patient is usually placed in a comfortable position that provides the ultrasound technician access to the part of the body being tested.

The area being studied is covered with a small amount of gel to eliminate air pockets between the transducer and the skin. The sonographer moves the transducer across the body part being studied to obtain images.

You may feel pressure as the transducer is moved over an area, and if the area is sensitive, you may feel pain, but the waves from the transducer do not cause this pain.

If Doppler ultrasound is used, you may hear pulse-like "whooshing" sounds that change in pitch as the blood flow is monitored.

Some exams are considered 'invasive ultrasounds,' where the transducer is attached to a probe and inserted into a natural opening in the body. These exams may cause some discomfort or pain due to the sensitivity of the tissue being touched by the probe, not by the ultrasound waves.

Transesophageal echocardiogram: The transducer is inserted into the esophagus to obtain images of the heart.

Transrectal ultrasound: The transducer is inserted into a man's rectum to view the prostate.

Transvaginal ultrasound: The transducer is inserted into a woman's vagina to view the uterus and ovaries.

Once the ultrasound procedure is complete, gel will be wiped off your skin and you should be able to resume your normal activities immediately in most cases or within a few hours if a more invasive study is done.

According to the Food and Drug Administration, ultrasound has an excellent safety record since it was put into regular use more than 30 years ago.

It avoids the use of radiation that is common in other diagnostic procedures by using harmless sound waves to produce images.

By using ultrasound technology to assist in other procedures, you may also reduce the risk and increase the effectiveness of those other procedures.

Specialized high intensity ultrasound waves like those used for ESWL and HIFU have the ability to cause discomfort and potentially serious damage to tissue nearby the area of treatment. These risks are minimized by good control of wave intensity exposure timing and focus techniques.

Ultrasound is not the recommended procedure for: - Bowel or organs obscured by the bowel: Air and gas can disrupt the ultrasound waves, obese patients and Internal structure of bones or certain joints: Ultrasound has difficulty penetrating bone.

An abdominal ultrasound uses reflected sound waves to produce a picture of the organs and other structures in the upper abdomen. Sometimes a specialized ultrasound is ordered for a detailed evaluation of a specific organ, such as a kidney ultrasound.

Ultrasound is a test that uses reflected sound waves to produce an image of organs and other structures in the body. It does not use X-rays or other types of possibly harmful radiation. For ultrasound testing, gel or oil is applied to the skin to help transmit the sound waves. A small, handheld instrument called a transducer is passed back and forth over the area of the body that is being examined. The transducer sends out high-pitched sound waves (above the range of human hearing) that are reflected back to the transducer. A computer analyzes the reflected sound waves and converts them into a picture that is displayed on a TV screen. The picture produced by ultrasound is called a sonogram, echogram, or ultrasound scan. Pictures or videos of the ultrasound images may be made for a permanent record.

Ultrasound is most useful for looking at organs and structures that are either uniform and solid (such as the liver) or fluid-filled (such as the gallbladder). Mineralized structures (such as bones) or air-filled organs (such as the lungs) do not show up well on a sonogram

An abdominal ultrasound can evaluate the:- abdominal aorta, which is the large blood vessel (artery) that passes down the back of the chest and abdomen. The aorta supplies blood to the lower part of the body and the legs, liver , which is a large dome-shaped organ that lies under the rib cage on the right side of the abdomen. The liver produces bile (a substance that helps digest fat), stores sugars, and breaks down many of the body's waste products, gallbladder, which is a small sac-shaped organ beneath the liver that stores bile. When food is eaten, the gallbladder contracts, sending bile into the intestines to help in digesting food and absorbing fat-soluble vitamins , spleen, which is the soft, round organ that helps fight infection and filters old red blood cells. The spleen is located to the left of the stomach, just behind the lower left ribs , pancreas , which is the gland located in the upper abdomen that produces enzymes that help digest food. The digestive enzymes are then released into the intestines. The pancreas also releases insulin into the bloodstream. Insulin helps the body use sugars

for energy and k<u>idneys</u>, which are the pair of bean-shaped organs located behind the upper abdominal cavity. The kidneys remove wastes from the blood and produce urine.

A pelvic ultrasound evaluates the structures and organs in the lower abdominal area (pelvis).

Abdominal ultrasound is done to: find the cause of abdominal pain, find, measure, or monitor an aneurysm in the aorta(An aneurysm may cause a large pulsing lump in the abdomen), check the size, shape, and position of the liver(An ultrasound may be done to evaluate jaundice and other problems of the liver, including liver masses, cirrhosis, fat deposits in the liver (called fatty liver), or abnormal liver function tests, detect gallstones, inflammation of the gallbladder (cholecystitis), or blocked bile ducts , learn the size of an enlarged spleen and look for damage or disease, find problems with the pancreas, such as a pancreatic tumor, look for blocked urine flow in a kidney. A kidney ultrasound may also be done to find out the size of the kidneys, detect kidney masses, detect fluid surrounding the kidneys, investigate causes for recurring urinary tract infections, or check the condition of transplanted kidneys, find out whether a mass in any of the abdominal organs (such as the liver) is a solid tumor or a simple fluid-filled cyst, guide the placement of a needle or other instrument during a biopsy and Look for fluid buildup in the abdominal cavity (ascites). An ultrasound also may be done to guide the needle during a procedure to remove fluid from the abdominal cavity (paracentesis).

Tell your doctor if you have had a barium enema or a series of upper GI (gastrointestinal) tests within the past 2 days. Barium that remains in the intestines can interfere with the ultrasound test.

Other preparations depend on the reason for the abdominal ultrasound test you are having.

For ultrasound of the liver, gallbladder, spleen, and pancreas, you may be asked to eat a fat-free meal on the evening before the test and then to avoid eating for 8 to 12 hours before the test.

For ultrasound of the kidneys, you may not need any special preparation. You may be asked to drink 4 to 6 glasses of liquid (usually juice or water) about an hour before the test to fill your bladder. You may be asked to avoid eating for 8 to 12 hours before the test to avoid gas buildup in the intestines. Gas could interfere with the evaluation of the kidneys, which lay behind the stomach and intestines.

For ultrasound of the aorta, you may need to avoid eating for 8 to 12 hours before the test.

This test is done by a doctor who specializes in performing and interpreting imaging tests (radiologist) or by an ultrasound technologist (sonographer) who is supervised by a radiologist. It is done in an ultrasound room in a hospital or doctor's office.

You will need to take off any jewelry that might interfere with the ultrasound scan. You will need to take off all or most of your clothes, depending on which area is examined (you may be allowed to keep on your underwear if it does not interfere with the test). You will be given a cloth or paper covering to use during the test.

You will lie on your back (or on your side) on a padded exam table. Warmed gel will be spread on your abdomen (or back) to improve the quality of the

sound waves. A small handheld unit called a transducer is pressed against your abdomen.

You may be asked to change positions so more scans can be done. For a kidney ultrasound, you may be asked to lie on your stomach.

You need to lie very still while the ultrasound scan is being done. You may be asked to take a breath and hold it for several seconds during the scanning. This lets the sonographer see organs and structures, such as the bile ducts, more clearly because they are not moving. Holding your breath also temporarily pushes the liver and spleen lower into the belly so they are not hidden by the lower ribs, which makes it harder for the sonographer to see them clearly.

The gel may feel cold when it is put on your skin unless it is first warmed to body temperature. You will feel light pressure from the transducer as it passes over your abdomen. The ultrasound usually is not uncomfortable. But if the test is being done to check damage from a recent injury, the slight pressure of the transducer may be somewhat painful. You will not hear or feel the sound waves.

There are no known risks from having an abdominal ultrasound test.

An abdominal ultrasound uses reflected sound waves to produce a picture of the organs and other structures in the abdomen.

Using abdominal ultrasound, a doctor can usually distinguish among a simple fluid-filled cyst, a solid tumor, or another type of mass that needs further evaluation. If a solid tumor is found, abdominal ultrasound cannot determine whether it is cancerous (malignant) or noncancerous (benign). A

biopsy may be needed if a tumor is found. Ultrasound may be used during the biopsy to help guide the placement of the needle.

Ultrasound is less expensive than other tests, such as a CT scan or magnetic resonance imaging (MRI) scan, that also can provide a picture of the abdominal organs. But for some problems, such as abdominal masses or an injury, a CT scan or MRI may be a more appropriate test. Also, these tests may be done if the abdominal ultrasound is normal but abdominal pain persists.

A pelvic ultrasound will be used to produce a picture of the lower abdominal (pelvic) organs and other structures inside the pelvis.

A pelvic ultrasound looks at the bladder and The ovaries The ovaries are two small glands, located on either side of a woman's uterus, that are part of the female reproductive system. The ovaries produce female sex hormones and store and release eggs (ova), which can develop into embryos if fertilized by a male's sperm.

The female sex hormones (estrogen and progesterone) help control the menstrual cycle, breast development, and other functions. Approximately once a month, about 2 weeks before a woman's next period is due, one of her ovaries releases an egg (ovulation).

The uterus is a hollow, pear-shaped organ in a woman's lower abdomen in which a fetus grows during pregnancy. When a woman is not pregnant, her monthly menstrual period flows from the uterus.

The lower part of the uterus (cervix) opens into the vagina. The opening to the cervix is narrow except during labor and birth, when it stretches and widens to allow the baby's passage out of the uterus. The cervix is the lower part of the uterus that opens into the vagina. It is part of a woman's reproductive system.

During a woman's menstrual period, blood flows from her uterus through her cervix, down her vagina, and out of her body.

During sex, the cervix makes mucus that helps sperm move up into the uterus.

During pregnancy, the cervix is tightly closed to protect the baby. But later the cervix opens up so the baby can pass through the vagina during childbirth.

A woman's two fallopian tubes lead upward from each upper side of the uterus and end near the ovaries. When an egg is released by an ovary (ovulation), it travels down a fallopian tube toward the uterus. After ovulation, egg fertilization usually happens in a fallopian tube. The fertilized egg then travels to the uterus, where it implants and grows. If a woman's fallopian tubes are blocked by scar tissue, such as from pelvic inflammatory disease, she may be unable to become pregnant or may have a tubal (ectopic) pregnancy.

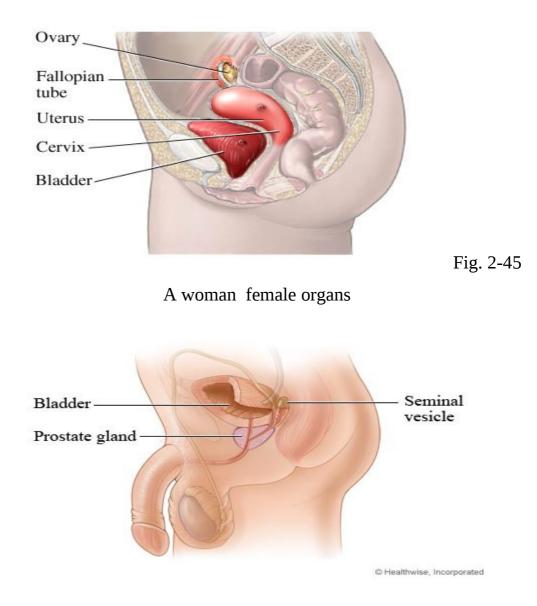


Fig. 2-46 Male organs

Pelvic ultrasound can be done three ways: transabdominal, transrectal, and transvaginal.

Transabdominal ultrasound. A small handheld device called a transducer is passed back and forth over the lower belly. Transrectal ultrasound. The transducer is shaped to fit into the rectum. A transrectal ultrasound is the most common test to look at the male pelvic organs, such as the prostate and seminal vesicles. Sometimes, a small sample of tissue (biopsy) may be taken with small tools inserted through the rectum during a transrectal ultrasound.Transvaginal ultrasound. The transducer is shaped to fit into a woman's vagina.

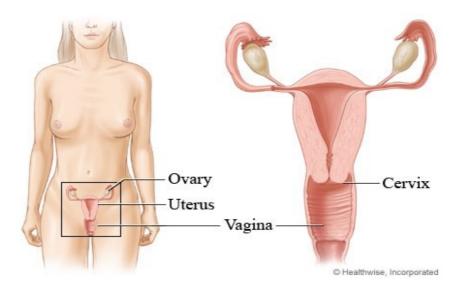


Fig. 2-47 A woman's vagina, also called the birth canal, is part of the reproductive tract and extends from the uterus to outside the body.The opening to the vagina is located between the bowel opening (anus) and the opening for the bladder (urethra).

A woman may have both transabdominal and transvaginal ultrasounds to look at the whole pelvic area. A transvaginal ultrasound is done to look for problems with fertility. In rare cases, a hysterosonogram is done to look at the inside of the uterus by filling the uterus with fluid during a transvaginal ultrasound. Sometimes, a small sample of tissue (biopsy) may be taken with small tools inserted through the vagina during a transvaginal ultrasound.

In all three types of pelvic ultrasound, the transducer sends the reflected sound waves to a computer, which makes them into a picture that is shown on a video screen. Ultrasound pictures or videos may be saved as a permanent record. For women, pelvic ultrasound may be done to: find out what is causing pelvic pain , look for the cause of vaginal bleeding , look for pelvic inflammatory disease (PID) , find an intrauterine device , look at the size and shape of the uterus and the thickness of the uterine lining (endometrium) , look at the size and shape of the ovaries , check the condition and size of the ovaries during treatment for infertility , confirm a pregnancy and whether it is in the uterus , check the cervical length in a pregnant woman at risk for preterm labor , check a lump found during a pelvic examination , check uterine fibroids found during a pelvic examination and guide a procedure to remove an ovarian follicle for in vitro fertilization.

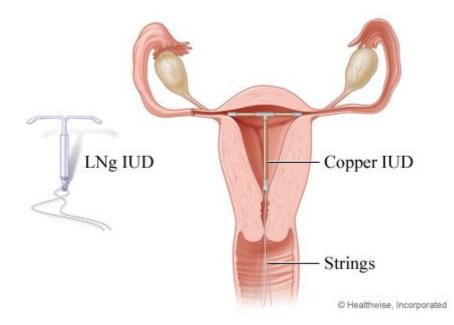


Fig. 48 An intrauterine device (IUD) is a small, plastic, T-shaped device that is inserted into the uterus to prevent pregnancy.

If you are having a transabdominal ultrasound, your doctor will ask you to drink 4 to 6 glasses of juice or water about an hour before the test to fill your bladder. A full bladder pushes the intestines (which contain air) out of the way of the pelvic organs. This makes the ultrasound picture clearer. If the ultrasound is being done in an emergency situation, your bladder may be filled with water through a thin flexible tube (catheter) inserted into your bladder. If you are having a transvaginal ultrasound, tell the doctor if you are allergic to latex so that a latex-free cover can be put on the transducer before it is used. If you are having only a transvaginal ultrasound, do not drink any fluids for 4 hours before the test. You will not need to drink fluids to fill your bladder for the test as you do in a transabdominal ultrasound.

If both a transabdominal and transvaginal ultrasound will be done, the transabdominal ultrasound will usually be done first. You will need to take off most of your clothes below the waist. You will be given a gown to use during the test. You will lie on your back (or on your side) on a padded table. Gel will be put on your belly to improve the quality of the sound waves. A small, handheld instrument called a transducer is gently moved over your belly. A picture of the organs and blood vessels can be seen on a video screen. You need to lie very still while the ultrasound is being done. You may be asked to take a breath and hold it for several seconds during the test. When the test is done, the gel is cleaned off your skin. You can urinate as soon as the test is done.

For transvaginal ultrasound, you will empty your bladder. You will be asked to lie on your back with your hips slightly raised. A thin, lubricated transducer probe will be gently inserted into your vagina. Only the tip of the transducer is put in the vagina. You need to lie very still while the ultrasound scan is being done.

If you have transabdominal ultrasound, you will likely feel pressure in your bladder and a strong urge to urinate because your bladder is full. The gel may feel cold when it is put on your belly. You will feel light pressure from the transducer as it passes over your belly. If you have an injury or pelvic pain, the light pressure of the transducer may be painful. You will not hear or feel the sound waves.You most likely will have a little pain during a transvaginal or transrectal ultrasound. You will feel pressure from the transducer probe as it is put into your vagina or rectum.If a biopsy is done during the ultrasound, you may have some pain when the sample is taken.

There is a slight risk of infection from a transvaginal or transrectal ultrasound. If a biopsy is done, the chance of infection is higher. Call your doctor if you have an abnormal discharge or fever after the test. A pelvic ultrasound uses sound waves to make a picture of the organs and structures in the lower belly (pelvis).

Pelvic ultrasound in women

Normal:	
	Your ovaries, cervix, and uterus have a normal shape and size
	and are in the normal place. No growths, tumors, fluid, or other
	problems, such as cysts, are present. Small cysts (follicles) in
	the ovaries of women who are able to have children are normal.
	If you are using an intrauterine device (IUD), it is in the uterus.
	If you are in the first trimester of pregnancy, your baby (fetus) is developing inside the uterus.
	Your bladder is normal in size and shape. No stones or abnormal growths are present. If the bladder is checked before and after
	urination, it empties completely. Urine flows normally from the
	ureters into the bladder.
Abnormal:	Your uterus is big or abnormally shaped because of uterine

_		
		ibroids. Cysts or tumors are present, such as cancerous or oncancerous tumors of the ovaries, uterus, or cervix.
	th	The thickness of the lining of the uterus (endometrium), called the endometrial stripe, is greater than normal. In some age
		roups, a thicker endometrial stripe (also called endometrial syperplasia) may mean a higher chance of endometrial cancer.
		Pelvic inflammatory disease (PID), abscesses, kidney stones, or ther problems are present.
	А	An ectopic pregnancy is present.
	А	An abnormal amount of fluid is present in the pelvis.
	st	The bladder has an abnormal shape or a thick wall. A growth or tone is seen in the bladder. If the bladder is checked before and
I.	l at	fter urination, it may not empty completely during urination.

A full bladder is needed for a transabdominal ultrasound, so that the pelvic organs can be seen clearly.

Ultrasound costs less than other tests that make pictures of organs and structures in the body, such as a computed tomography (CT) scan or magnetic resonance imaging (MRI). But in some cases, a CT scan or an MRI may also be needed to confirm a problem, such as cancer.

With pelvic ultrasound, your doctor can usually tell the difference between a fluid-filled cyst, a solid tumor, or another type of lump. This is one of the main advantages of an ultrasound. An abnormal lump needs more testing. A follow-up ultrasound is often done in 6 to 8 weeks because many problems

go away on their own within that time. Pelvic ultrasound cannot determine whether a lump is cancerous (malignant) or noncancerous (benign). A biopsy may have to be done for this.Transvaginal ultrasound is used during fertility checks to help guide the removal of ovarian follicles for in vitro fertilization.

The words diagnostic medical ultrasound, ultrasound, and ultrasonography have all been used to describe the instrumentation utilized in ultrasound. Sonography is the term used to describe a pecialized imaging technique used to visualize soft tissue structures of the body. Extensive research has verified the safety of ultrasound as a diagnostic procedure.

Diagnostic ultrasound has come to be such a valuable diagnostic imaging technique for so many different body structures for many reasons, but two are especially significant. First is the lack of ionizing radiation for ultrasound as compared with the other imaging modalities of magnetic resonance imaging (MRI), computed tomography (CT), or nuclear medicine. The second reason is the portability of the ultrasound equipment. An ultrasound may be done to evaluate jaundice and other problems of the liver, including liver masses, cirrhosis, fat deposits in the liver (called fatty liver), or abnormal liver function tests, Detect gallstones, inflammation of the gallbladder, or blocked bile ducts, Learn the size of an enlarged spleen and look for damage or disease, Find problems with the pancreas, such as a pancreatic tumor, Look for blocked urine flow in a kidney. A kidney ultrasound may also be done to find out the size of the kidneys, detect kidney masses, detect fluid surrounding the kidneys, investigate causes for recurring urinary tract infections, or check the condition of transplanted kidneys, Find out whether a mass in any of the abdominal organs is a solid tumor or a simple fluid-filled cyst , Guide the placement of a needle or other instrument during a biopsy and Look for fluid buildup in the abdominal

cavity (ascites). An ultrasound also may be done to guide the needle during a procedure to remove fluid from the abdominal cavity (paracentesis). Tell the doctor if you have had a barium enema or a series of upper GI (gastrointestinal) tests within the past 2 days. Barium that remains in the intestines can interfere with the ultrasound test. Other preparations depend on the reason for the abdominal ultrasound test you are having.

For ultrasound of the liver, gallbladder, spleen, and pancreas, you may be asked to eat a fat-free meal on the evening before the test and then to avoid eating for 8 to 12 hours before the test.For ultrasound of the kidneys, you may not need any special preparation. You may be asked to drink 4 to 6 glasses of liquid (usually juice or water) about an hour before the test to fill your bladder. You may be asked to avoid eating for 8 to 12 hours before the test to avoid gas buildup in the intestines. Gas could interfere with the evaluation of the kidneys, which lay behind the stomach and intestines.For ultrasound of the aorta, you may need to avoid eating for 8 to 12 hours before the test.

This test is done by a doctor who specializes in performing and interpreting imaging tests (radiologist) or by an ultrasound technologist (sonographer) who is supervised by a radiologist. It is done in an ultrasound room in a hospital or doctor's office.You will need to take off any jewelry that might interfere with the ultrasound scan. You will need to take off all or most of your clothes; depending on which area is examined (you may be allowed to keep on your underwear if it does not interfere with the test). You will be given a cloth or paper covering to use during the test.You will lie on your back (or on your side) on a padded exam table. Warmed gel will be spread on your abdomen (or back) to improve the quality of the sound waves. A small handheld unit called a transducer is pressed against your abdomen.You may be asked to change positions so more scans can be done. For a kidney ultrasound, you may be asked to lie on your stomach.

You need to lie very still while the ultrasound scan is being done. You may be asked to take a breath and hold it for several seconds during the scanning. This lets the sonographer see organs and structures, such as the bile ducts, more clearly because they are not moving. Holding your breath also temporarily pushes the liver and spleen lower into the belly so they are not hidden by the lower ribs, which makes it harder for the sonographer to see them clearly.You may be asked to wait until the radiologist has reviewed the information. The radiologist may want to do more ultrasound views of some areas of your abdomen.

The gel may feel cold when it is put on your skin unless it is first warmed to body temperature. You will feel light pressure from the transducer as it passes over your abdomen.

The ultrasound usually is not uncomfortable. But if the test is being done to check damage from a recent injury, the slight pressure of the transducer may be somewhat painful. You will not hear or feel the sound waves. There are no known risks from having an abdominal ultrasound test.

An abdominal ultrasound uses reflected sound waves to produce a picture of the organs and other structures in the abdomen.

Normal:	The size and shape of the abdominal organs appear normal.
	The liver, spleen, and pancreas appear normal in size and

Abdominal ultrasound

	texture. No abnormal growths are seen. No fluid is found in
	the abdomen.
	The diameter of the aorta is normal, and no aneurysms are
	seen.
	The thickness of the gallbladder wall is normal. The size of
	the bile ducts between the gallbladder and the small intestine
	is normal. No gallstones are seen.
	The kidneys appear as sharply outlined bean-shaped organs.
	No kidney stones are seen. No blockage to the system
	draining the kidneys is present.
Abnormal:	An organ may appear abnormal because of inflammation,
	infection, or other diseases. An organ may be smaller than
	normal because of an old injury or past inflammation. An
	organ may be pushed out of its normal location because of
	an abnormal growth pressing against it. An abnormal growth
	(such as a tumor) may be seen in an organ. Fluid in the
	abdominal cavity may be seen.
	The aorta is enlarged, or an aneurysm is seen.
	The liver may appear abnormal, which may point to liver
	disease (such as cirrhosis or cancer).
	The walls of the gallbladder may be thickened, or fluid may
	be present around the gallbladder, which may point to
	inflammation. The bile ducts may be enlarged because of

lockage (from a gallstone or an abnormal growth in the
ancreas). Gallstones may be seen inside the gallbladder.
The kidneys or the tubes that drain the kidneys (ureters) may
e enlarged because of urine that is not draining properly.
Kidney stones are seen within the kidneys (not all stones can
e seen with ultrasound).
An area of infection (abscess) or a fluid-filled cyst may
ppear as a round, hollow structure inside an organ. The
pleen may be ruptured (if an injury to the abdomen has

Reasons you may not be able to have the test or why the results may not be helpful include: , Stool, air (or other gas), or contrast material (such as barium) in the stomach or intestines , Not being able to remain still during the test , Extreme obesity and Having an open or bandaged wound in the area being viewed.

occurred).

Other tests, such as a computed tomography (CT) scan, may be needed to follow up abnormal ultrasound results. To learn more, see the topic Computed Tomography (CT) Scan of the Body.

X-rays are not recommended during pregnancy because of the risk of damage to the fetus. Because ultrasound is safe during pregnancy, it generally is used instead of an abdominal X-ray if a pregnant woman's abdomen needs to be checked.

In rare cases, gallstones may not be found by ultrasound. Other imaging tests may be done if gallstones are suspected but not seen on the ultrasound:

Gallbladder Scan, Endoscopic Retrograde Cholangiopancreatogram (ERCP) and Ray. Bones or air-filled organs, such as the intestines, do not show up well on an ultrasound and may keep other organs from being seen clearly.Pelvic ultrasound can be done three ways: transabdominal, transrectal, and transvaginal.

Transabdominal ultrasound. A small handheld device called a transducer is passed back and forth over the lower belly. A transabdominal ultrasound is commonly done in women to look for large uterine fibroids (are growths on or in your uterus. Although they are sometimes called fibroid tumors, they aren't cancer. You don't need to do anything about them unless they are causing problems). or other problems.Tran rectal ultrasound. The transducer is shaped to fit into the rectum. A transrectal ultrasound is the most common test to look at the male pelvic organs, such as the prostate and seminal vesicles. Sometimes, a small sample of tissue (biopsy) may be taken with small tools inserted through the rectum during a transrectal ultrasound.Transvaginal ultrasound. The transducer is shaped to fit into a woman's vagina.

A woman may have both transabdominal and transvaginal ultrasounds to look at the whole pelvic area. A transvaginal ultrasound is done to look for problems with fertility. In rare cases, a hysterosonogram is done to look at the inside of the uterus by filling the uterus with fluid during a transvaginal ultrasound. Sometimes, a small sample of tissue (biopsy) may be taken with small tools inserted through the vagina during a transvaginal ultrasound.

In all three types of pelvic ultrasound, the transducer sends the reflected sound waves to a computer, which makes them into a picture that is shown on a video screen. Ultrasound pictures or videos may be saved as a permanent record. For women, pelvic ultrasound may be done to: Find out what is causing pelvic pain , Look for the cause of vaginal bleeding and Look for pelvic inflammatory disease (PID).

Confirm a pregnancy and whether it is in the uterus. Pelvic ultrasound may be used early in pregnancy to check the age of the pregnancy or to find a tubal pregnancy (ectopic pregnancy) or multiple pregnancy. Check uterine fibroids found during a pelvic examination. Pelvic ultrasound may also be done to check the growth of uterine fibroids.Guide a procedure to remove an ovarian follicle for in vitro fertilization.(M. Bazot,2004)

2-2 The ovary.

The ovaries are two almond shaped glands located on either side of the uterus, which develop ova or eggs and produce the hormones estrogen and progesterone. The fallopian tubes transport the eggs from the ovaries to the uterus. It is usually in the fallopian tubes that fertilization takes place. They are almond-shaped and about 3.5 cm (1.5 inches) long. The ovaries are deep in a woman's pelvis, on both sides of the uterus (womb), close to the ends of the Fallopian tubes.

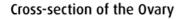
In a fertile woman an egg is usually released once a month from one of her two ovaries. This is called ovulation and usually occurs about 14 days before the first day of menses. Two to five days before and after ovulation is when pregnancy can occur.

If unprotected intercourse takes place during this time, the sperm moves up the uterus into the tubes within minutes. If a single sperm joins with the egg, the egg becomes fertilized. This fertilized egg travels down the tube and attaches to the wall of the uterus, which has increased its blood supply in preparation for pregnancy. If the egg is not fertilized, in about 14 days, the lining of the uterus is shed as menstrual flow.(N. Pierce, 2008)

2-2-1 Anatomy.

2-2-1-1 Structure.

The ovaries are made up of 3 different types of cells:- epithelial cells make up the outer layer covering the ovary (epithelium) and germ cells are inside the ovary. They develop into eggs and stromal cells form the supportive or connective tissues of the ovary (stroma).Each ovary is surrounded by a thin layer of tissue called the capsule.



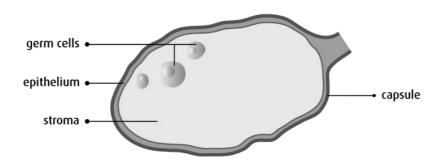
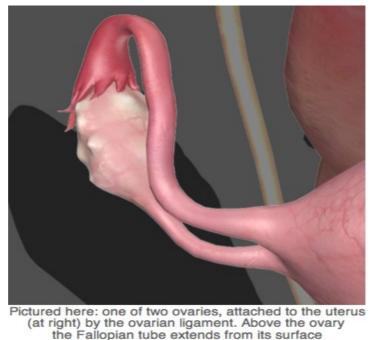


Fig. 2-49 Cross-section of the ovary

The ovaries play two central roles in the female reproductive system by acting as both glands and gonads. Acting as glands, the ovaries produce several female sex hormones including estrogens and progesterone. Estrogen controls the development of the mammary glands and uterus during puberty and stimulates the development of the uterine lining during the menstrual cycle. Progesterone acts on the uterus during pregnancy to allow the embryo to implant and develop in the womb. At birth the ovaries contain anywhere from several hundred thousand to several million circular bundles of cells known as follicles. Each follicle surrounds and supports a single oocyte that has the ability to mature into an ovum, the female gamete. Despite this large number of potential ova, only around 4,000 oocytes survive to puberty and only 400 oocytes mature into ova in a woman's lifetime. During each menstrual cycle around 10-20 follicles and their oocytes begin to develop under the influence of the pituitary hormone follicle-stimulating hormone (FSH). Of these follicles, only one cell completes its development and becomes a mature ovum.



back to the uterus.

Fig. 2-50 Ovary

The uterus, also commonly known as the womb, is a hollow muscular organ of the female reproductive system that is responsible for the development of the embryo and fetus during pregnancy. An incredibly distensible organ, the uterus can expand during pregnancy from around the size of a closed fist to become large enough to hold a full term baby. It is also an incredibly strong organ, able to contract forcefully to propel a full term baby out of the body during childbirth. The uterus is approximately the shape and size of a pear and sits in an inverted position within the pelvic cavity of the torso. It is located along the body's midline posterior to the urinary bladder and anterior to the rectum. The narrow inferior region of the uterus, known as the cervix, connects the uterus to the vagina below it and acts as a sphincter muscle to control the flow of material into and out of the uterus.

The body (or corpus) of the uterus is the wider region of the uterus superior to the cervix. The body is an open and hollow region where the fertilized egg, or zygote, implants itself and develops during pregnancy. The walls of the body are much thicker than those of the cervix as they provide for the protection and support of the developing fetus and contain the muscles that propel the fetus out of the mother's body during childbirth.Superior to the body is a domed region known as the fundus of the uterus. The fallopian tubes extend laterally from the corners of the fundus.

Three distinct tissue layers make up the walls of the uterus:- the perimetrium is the outermost layer that forms the external skin of the uterus. It is a serous membrane continuous with the peritoneum that covers the major organs of the abdominopelvic cavity. The perimetrium protects the uterus from friction by forming a smooth layer of simple squamous epithelium along its surface and by secreting watery serous fluid to lubricate its surface.Deep to the perimetrium layer, the myometrium forms the middle layer of the uterus and contains many layers of visceral muscle tissue. During pregnancy the myometrium allows the uterus to expand and then contracts the uterus during childbirth.Inside the myometrium is the endometrium layer that borders the hollow lumen of the uterus. The endometrium is made of simple columnar epithelial tissue with many associated exocrine glands and a highly vascular connective tissue that provides support to the developing embryo and fetus during pregnancy. Around the time of ovulation the uterus builds a thick layer of vascular endometrial tissue in preparation to receive a zygote, or fertilized egg cell. If the egg cell does not become fertilized by the time it reaches the uterus, it will pass through the uterus and trigger the blood vessels of the endometrium to atrophy and the uterine lining to be shed. The shedding of the egg cell and uterine lining is known as menstruation and occurs approximately every 28 days for most women.

In the case of successful fertilization of the ova, a zygote will implant itself into the endometrial lining, where it begins to develop over many weeks into an embryo and eventually a fetus. As the embryo develops into a fetus, it triggers changes within the endometrium that lead to the formation of the placenta. The placenta provides the developing fetus with vital nutrients and oxygen from the mother's blood, while transferring carbon dioxide and metabolic waste products to the mother's blood for disposal.

At the end of pregnancy, the uterus plays a critical role in the process of childbirth. Prior to delivery, hormones trigger waves of smooth muscle contraction in the myometrium that slowly increase in strength and frequency. At the same time, the smooth muscle tissue of the cervix begins to efface, or thin, and dilate from less than a centimeter in diameter to around ten centimeters at full dilation. Once the cervix is fully dilated, the uterine contractions drastically increase in intensity and duration until the fetus is pushed out of the uterus, through the vagina, and out of the mother's body.

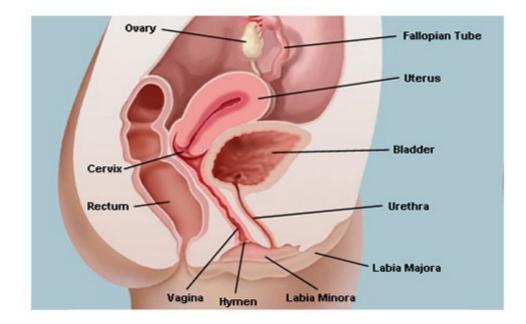


Fig. 2-51 The Ovaries

The ovary is a ductless reproductive gland in which the female reproductive cells are produced. It is one of the paired sexual gonads in females held by a membrane beside the uterus on each side of the lower abdomen. It is needed in reproduction since it is responsible for producing the female reproductive cells or ova. During ovulation, a follicle expels an egg under the stimulation of the luteinizing hormone and the gonadotrophic hormone, also known as the follicle-stimulating hormone. The rest of the follicle or the corpus luteum, secretes the sex hormones estrogen and progesterone, which regulate menstruation and control the development of the sex organs. The sex hormones and the gonadotrophic hormones interact with each other to control the menstrual cycle. When an egg matures, it is released and passes into the fallopian tube towards the uterus. If the ovum is fertilized by the male reproductive cell or sperm, conception happens and pregnancy begins. An ovary is normally firm and smooth and is about the size of an almond.

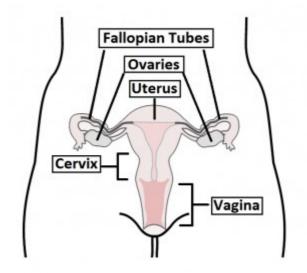


Fig. 2-52 Overview of the female reproductive tract.

In both the males and females, the gonads develop within the mesonephric ridge and descend through the abdomen. However, unlike the testes, the ovaries stop in the pelvis.

The ovaries are paired, oval organs attached to the posterior surface of the broad ligament of the uterus by the mesovarium (a fold of peritoneum, continuous with the outer surface of the ovaries).

Neurovascular structures enter the hilum of the ovary via the mesovarium.

The ovary has 3 components:- **surface:** The surface layer of the ovary is formed by simple cuboidal epithelium, known as germinal epithelium , c**ortex:** The cortex (outer part) of the ovary is largely comprised of a connective tissue stroma. It supports thousands of follicles. Each primordial follicle contains an oocyte surrounded by a single layer of follicular cells and m**edulla**.

The medulla (inner part) is composed of supporting stroma and contains a rich neurovascular network which enters the hilum of ovary from the mesovarium.

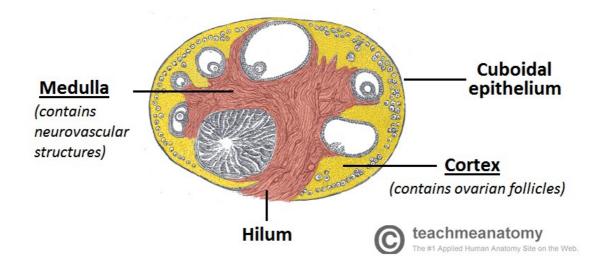


Fig. 2-53 Cross section of an ovary. Shows the three major components of the ovary. Also shows the follicles at various stages of development.

In both the males and females, the gonads develop within the mesonephric ridge and descend through the abdomen. However, unlike the testes, the ovaries stop in the pelvis.

The ovaries are paired, oval organs attached to the posterior surface of the broad ligament of the uterus by the mesovarium (a fold of peritoneum, continuous with the outer surface of the ovaries).

Neurovascular structures enter the hilum of the ovary via the mesovarium.

The ovary has 3 components:- **surface:** The surface layer of the ovary is formed by simple cuboidal epithelium, known as germinal epithelium , **cortex:** The cortex (outer part) of the ovary is largely comprised of a connective tissue stroma. It supports thousands of follicles. Each primordial follicle contains an oocyte surrounded by a single layer of follicular cells and m**edulla:** the medulla (inner part) is composed of supporting stroma and contains a rich neurovascular network which enters the hilum of ovary from the mesovarium.

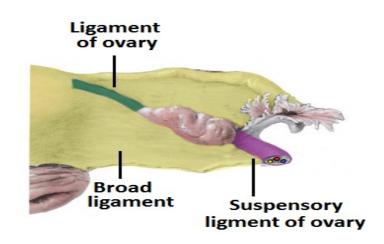


Fig. 2-54 The major ligaments of the ovary.

Two peritoneal ligaments attach to the ovary:- **suspensory ligament** of ovary: fold of peritoneum extending from the mesovarium to the pelvic wall. Contains neurovascular structures and l**igament of ovary**: extends from the ovary to the fundus of the uterus. It then continues from the uterus to the connective tissue of the labium majus, as the round ligament of uterus.

The ovaries receive blood from paired ovarian arteries, which arise directly from the abdominal aorta, below the renal artery.

Venous drainage is achieved by a pair of ovarian veins. The left ovarian vein drains into the left renal vein, and the right ovarian vein drains directly into the inferior vena cava.

Lymph from the ovaries drains into the para-aortic nodes.

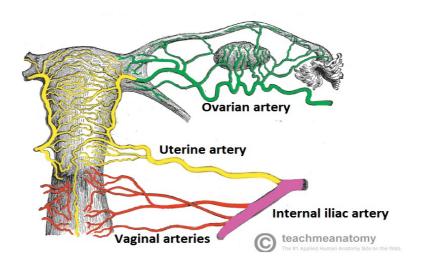


Fig. 2-55 Posterior view of the arterial supply to the female reproductive

tract.

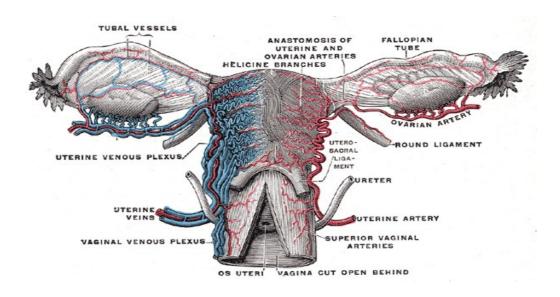


Fig. 2-56 Vessels of the uterus and its appendages, rear view. (Fallopian tubes visible at top right and top left.)

The nerve supply to ovaries runs via the suspensory ligament of the ovary with the vasculature, to enter the ovary at the hilum. The ovaries receive sympathetic and parasympathetic nerve fibres from the ovarian and uterine (pelvic) plexuses, respectively. The uterus and ovaries are the most vital organs of the female reproductive system. These organs work together to produce female sex hormones, produce and develop ova (egg cells), and support the development of a fetus during pregnancy. The uterus, also known as the womb, is a hollow, muscular, pear-shaped organ found in the pelvic region of the abdominopelvic cavity. It is located posterior to the urinary bladder and is connected via the cervix to the vagina on its inferior border and the fallopian tubes along its superior end. Many smooth muscle cells in the walls of the uterus provide it with great extensibility and contractile strength.

The endometrium, or lining of the uterus, consists of a thick layer of epithelial and connective tissues that are shed and regrown periodically during the menstrual cycle. Female hormones encourage the growth of the endometrium to support the potential implantation of an embryo in the event of a successful fertilization of an ovum. At the end of the menstrual cycle, if a fertilized ovum has not implanted into the endometrium, the endometrium is cut off from its blood supply and is shed along with the ovum as menstrual flow. Menstrual flow then exits the body through the cervix and vagina so that the uterus can grow a new endometrium for the next ovum. During pregnancy, the tiny embryo implants itself into the tissues of the endometrium and begins to grow inside of the uterine lining. Tissue from the embryo begins to merge with the tissues of the uterus to form the placenta and umbilical cord that allow for the exchange of respiratory gases, nutrients, and wastes between the mother and the developing embryo. The walls of the uterus extend and grow to accommodate the growing embryo as it enters the fetal stage of development. At the end of pregnancy the cervix dilates and the muscles of the myometrium contract to push the fetus into the birth canal to initiate childbirth. The ovaries are small, oval-shaped, and grayish in color, with an uneven surface. The actual size of an ovary depends on a woman's age and hormonal status; the ovaries, covered by a modified

peritoneum, are approximately 3-5 cm in length during childbearing years and become much smaller and then atrophic once menopause occurs. A cross-section of the ovary reveals many cystic structures that vary in size. These structures represent ovarian follicles at different stages of development and degeneration.

Several paired ligaments support the ovaries. The ovarian ligament connects the uterus and ovary. The posterior portion of the broad ligament forms the mesovarium, which supports the ovary and houses its arterial and venous supply. The suspensory ligament of the ovary (infundibular pelvic ligament) attaches the ovary to the pelvic sidewall. This larger structure also contains the ovarian artery and vein, as well as nerve supply to the ovary.

Blood supply to the ovary is via the ovarian artery; both the right and left arteries originate directly from the descending aorta. The ovarian artery and vein enter and exit the ovary at the hilum. The left ovarian vein drains into the left renal vein, and the right ovarian vein empties directly into the inferior vena cava. Nerve supply to the ovaries runs with the vasculature via the suspensory ligament of the ovary, entering the ovary at the hilum. Supply is through the ovarian, hypogastric, and aortic plexuses.Lymph_ drainage of the ovary is primarily to the lateral aortic nodes; however, the iliac nodes are also involved.

Histologically, the ovary has 2 main sections: the outer cortex and inner medulla. A germinal layer coats the entire ovary, made of cuboidal epithelial cells.The cortex is where the follicles and oocytes are found at various stages of development and degeneration. The cortex is made of tightly packed connective tissue. The stroma of this cortical connective tissue is composed of spindle-shaped fibroblasts that respond to hormonal stimulation in a way different from that of other fibroblasts in the body. The medulla is where the ovarian vasculature is found and is primarily loose stromal tissue.

The ovarian follicles are found within the stroma of the ovarian cortex. A follicle consists of an oocyte surrounded by follicular cells called granulosa cells. Follicles go through stages of development each month, with the goal of their maturation to release the oocyte for the purpose of fertilization and reproduction. If the follicle fails to release the egg, it goes through degeneration.

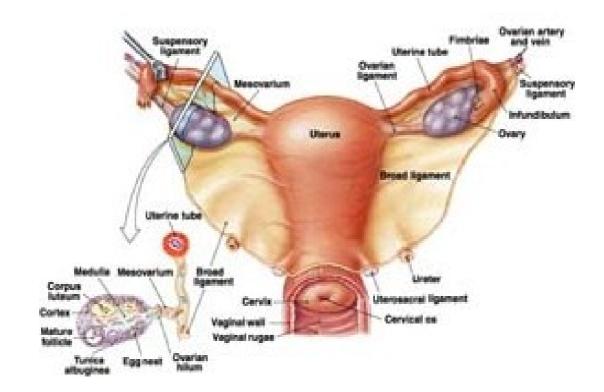


Fig. 2-57 Ovaries.

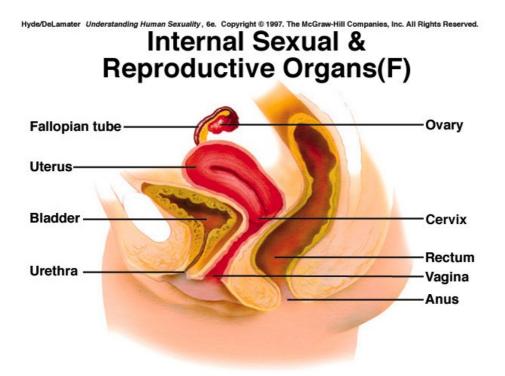


Fig. 2-58 Internal sexual & reproductive organs (A)

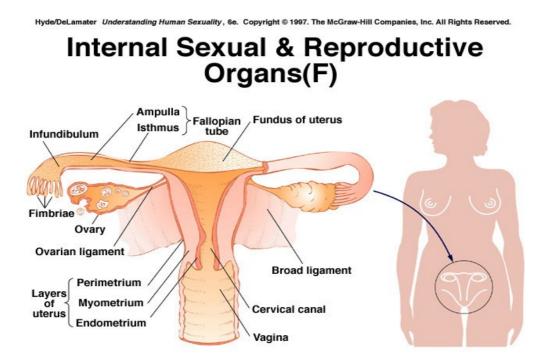


Fig. 2-59 Internal sexual & reproductive organs (B)

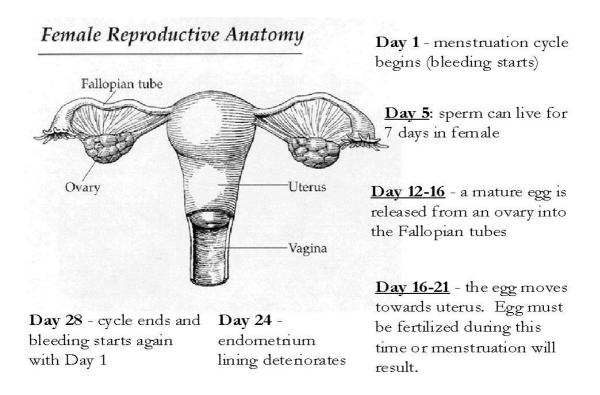


Fig. 2-60 Female reproductive anatomy

Female Reproductive System

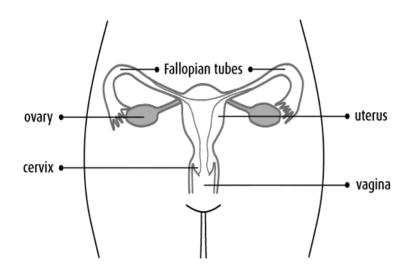


Fig. 2-61 Female reproductive system

2-2-2 Physiology

The ovaries have 2 main functions. They produce mature eggs. They also make the female sex hormones, which control reproduction and sexual development. Estrogen is responsible for the development of secondary sex characteristics, such as the growth of breasts.

Progesterone prepares the body for conception by causing the buildup of the uterine lining (endometrium) and other changes. The ovaries are the main source of estrogen in sexually mature women.

Each month during ovulation, an ovary releases a mature egg. The egg travels down the Fallopian tube to the uterus. If it is fertilized by a sperm, the egg implants into the lining of the uterus and begins to develop into a fetus. If the egg is not fertilized, it is shed from the body along with the lining of the uterus during menstruation. During menopause, the ovaries stop releasing eggs and producing sex hormones. The uterus and ovaries are the most vital organs of the female reproductive system. These organs work together to produce female sex hormones, produce and develop ova (egg cells), and support the development of a fetus during pregnancy. The uterus, also known as the womb, is a hollow, muscular, pear-shaped organ found in the pelvic region of the abdominopelvic cavity. It is located posterior to the urinary bladder and is connected via the cervix to the vagina on its inferior border and the fallopian tubes along its superior end. Many smooth muscle cells in the walls of the uterus provide it with great extensibility and contractile strength.

The endometrium, or lining of the uterus, consists of a thick layer of epithelial and connective tissues that are shed and regrown periodically during the menstrual cycle. Female hormones encourage the growth of the endometrium to support the potential implantation of an embryo in the event of a successful fertilization of an ovum. At the end of the menstrual cycle, if a fertilized ovum has not implanted into the endometrium, the endometrium is cut off from its blood supply and is shed along with the ovum as menstrual flow. Menstrual flow then exits the body through the cervix and vagina so that the uterus can grow a new endometrium for the next ovum.

During pregnancy, the tiny embryo implants itself into the tissues of the endometrium and begins to grow inside of the uterine lining. Tissue from the embryo begins to merge with the tissues of the uterus to form the placenta and umbilical cord that allow for the exchange of respiratory gases, nutrients, and wastes between the mother and the developing embryo. The walls of the uterus extend and grow to accommodate the growing embryo as it enters the fetal stage of development. At the end of pregnancy the cervix dilates and the muscles of the myometrium contract to push the fetus into the birth canal to initiate childbirth.

The ovaries are the female pelvic reproductive organs that house the ova and are also responsible for the production of sex hormones. They are paired organs located on either side of the uterus within the broad ligament below the <u>uterine (fallopian) tubes</u>. The ovary is within the ovarian fossa, a space that is bound by the external iliac vessels, obliterated umbilical artery, and the ureter. The ovaries are responsible for housing and releasing ova, or eggs, necessary for reproduction. At birth, a female has approximately 1-2 million eggs, but only 300 of these eggs will ever become mature and be released for the purpose of fertilization.

The ovary (From Latin: *ovarium*, literally "egg" or "nut") is an ovumproducing reproductive organ, often found in pairs as part of the vertebrate female reproductive system. Ovaries in female individuals are analogous to testes in male individuals, in that they are both gonads and endocrine glands. Endocrine glands are glands of the endocrine system that secrete their products, *hormones*, directly into the blood rather than through a duct. The major glands of the endocrine system include the pineal gland, pituitary gland, pancreas, ovaries, testes, thyroid gland, parathyroid gland, hypothalamus and adrenal glands. The hypothalamus and pituitary gland are neuroendocrine organs. Local chemical messengers, not generally considered part of the endocrine system, include autocrines, which act on the cells that secrete them, and paracrines, which act on a different cell type nearby.

The ability of a target cell to respond to a hormone depends on the presence of receptors, within the cell or on its plasma membrane, to which the hormone can bind.Hormone receptors are dynamic structures. Changes in number and sensitivity of hormone receptors may occur in response to high or low levels of stimulating hormones. Blood levels of hormones reflect a balance between secretion and degradation/excretion. The liver and kidneys are the major organs that degrade hormones; breakdown products are excreted in urine and feces. Hormone half-life and duration of activity are limited and vary from hormone to hormone.(Outwater EK,1997)

2-2-2-1 The major endocrine glands:

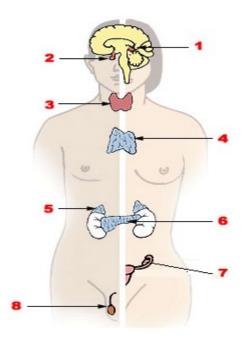


Fig. 2-62 The major endocrine glands

2-2-2-1-1 Pituitary gland (hypophysis)

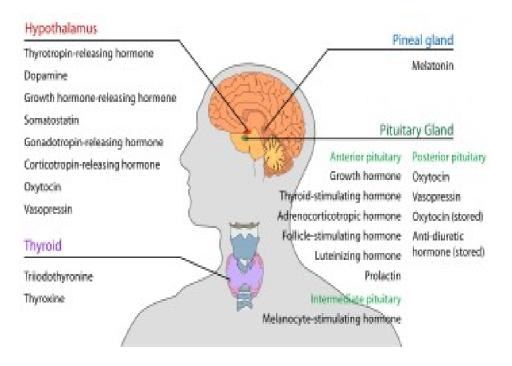


Fig. 2-63 Endocrine glands in the human head and neck and their hormones Pituitary gland

The pituitary gland hangs from the base of the brain by a stalk and is enclosed by bone. It consists of a hormone-producing glandular portion (anterior pituitary) and a neural portion (posterior pituitary), which is an extension of the hypothalamus. The hypothalamus regulates the hormonal output of the anterior pituitary and synthesizes two hormones that it exports to the posterior pituitary for storage and later release.Four of the six adenohypophyseal hormones are tropic hormones that regulate the function of other endocrine organs. Most anterior pituitary hormones exhibit a diurnal rhythm of release, which is subject to modification by stimuli influencing the hypothalamus.

Somatotropic hormone or Growth hormone (GH) is an anabolic hormone that stimulates growth of all body tissues but especially skeletal muscle and bone. It may act directly, or indirectly via insulin-like growth factors (IGFs). GH mobilizes fats, stimulates protein synthesis, and inhibits glucose uptake and metabolism. Secretion is regulated by growth hormone releasing hormone (GHRH) and growth hormone inhibiting hormone (GHIH), or somatostatin. Hypersecretion causes gigantism in children and acromegaly in adults; hyposecretion in children causes pituitary dwarfism.Thyroidstimulating hormone (TSH) promotes normal development and activity of the thyroid gland. Thyrotropin-releasing hormone (TRH) stimulates its release; negative feedback of thyroid hormone inhibits it.

Adrenocorticotropic hormone (ACTH) stimulates the adrenal cortex to release corticosteroids. ACTH release is triggered by corticotropin-releasing hormone (CRH) and inhibited by rising glucocorticoid levels.The gonadotropins—follicle-stimulating hormone (FSH) and luteinizing hormone (LH) regulate the functions of the gonads in both sexes. FSH stimulates sex cell production; LH stimulates gonadal hormone production. Gonadotropin levels rise in response to gonadotropin-releasing hormone (GnRH). Negative feedback of gonadal hormones inhibits gonadotropin release.Prolactin (PRL) promotes milk production in humans females. Its secretion is prompted by prolactin-releasing hormone (PRH) and inhibited by prolactin-inhibiting hormone (PIH).

The neurohypophysis stores and releases two hypothalamic hormones:-Oxytocin stimulates powerful uterine contractions, which trigger labor and delivery of an infant, and milk ejection in nursing women. Its release is mediated reflexively by the hypothalamus and represents a positive feedback mechanism and Antidiuretic hormone (ADH) stimulates the kidney tubules to reabsorb and conserve water, resulting in small volumes of highly concentrated urine and decreased plasma osmolarity. ADH is released in response to high solute concentrations in the blood and inhibited by low solute concentrations in the blood. Hyposecretion results in diabetes insipidus.

2-2-2-1-2 Thyroid gland

The thyroid gland is located in the anterior throat. Thyroid follicles store colloid containing thyroglobulin, a glycoprotein from which thyroid hormone is derived.

Thyroid hormone (TH) includes thyroxine (T4) and triiodothyronine (T3), which increase the rate of cellular metabolism. Consequently, oxygen use and heat production rise.

Secretion of thyroid hormone, prompted by TSH, requires reuptake of the stored colloid by the follicle cells and splitting of the hormones from the colloid for release. Rising levels of thyroid hormone feed back to inhibit the pituitary and hypothalamus. Most T4 is converted to T3 (the more active form) in the target tissues. These hormones act by turning on gene and protein synthesis. Graves' disease is the most common cause of

hyperthyroidism; hyposecretion causes cretinism in infants and myxoedema in adults.

Calcitonin, produced by the parafollicular cells of the thyroid gland in response to rising blood calcium levels, depresses blood calcium levels by inhibiting bone matrix resorption and enhancing calcium deposit in bone.

2-2-1-3 Parathyroid glands

The parathyroid glands, located on the dorsal aspect of the thyroid gland, secrete parathyroid hormone (PTH),^[1] which causes an increase in blood calcium levels by targeting bone, the intestine, and the kidneys. PTH is the antagonist of calcitonin. PTH release is triggered by falling blood calcium levels and is inhibited by rising blood calcium levels.

Hyperparathyroidism results in hypercalcaemia and all its effects and in extreme bone wasting. Hypoparathyroidism leads to hypocalcaemia, evidenced by tetany and respiratory paralysis.

2-2-1-4 Pancreas

The pancreas, located in the abdomen close to the stomach, is both an exocrine and an endocrine gland. The endocrine portion (islets of langerhans) releases insulin and glucagon and smaller amounts of other hormones to the blood. Glucagon, released by alpha (α) cells when glucose level in blood are low, stimulates the liver to release glucose to the blood. Insulin is released by beta (β) cells when blood levels of glucose (and amino acids) are rising. It increases the rate of glucose uptake and metabolism by most body cells. Hyposecretion of insulin results in diabetes mellitus; cardinal signs are polyuria, polydipsia, and polyphagia.

2-2-1-5 Gonads

The ovaries of the female, located in the pelvic cavity, release two main hormones. Secretion of estrogens by the ovarian follicles begins at puberty under the influence of FSH. Estrogens stimulate maturation of the female reproductive system and development of the secondary sexual characteristics. Progesterone is released in response to high blood levels of LH. It works with estrogens in establishing the menstrual cycle. The testes of the male begin to produce testosterone at puberty in response to LH. Testosterone promotes maturation of the male reproductive organs, development of secondary sex characteristics, and production of sperm by the testes.

2-2-1-6 Pineal gland

The pineal gland is located in the diencephalon. Its primary hormone is melatonin, which influences daily rhythms and may have an antigonadotropic effect in humans.

2-2-1-7 Other hormone-producing structures

Many body organs not normally considered endocrine organs contain isolated cell clusters that secrete hormones. Examples include the heart (atrial natriuretic peptide); gastrointestinal tract organs (gastrin, secretin, and others); the placenta (hormones of pregnancy—estrogen, progesterone, and others); the kidneys (erythropoietin and renin); the thymus; skin (cholecalciferol); and adipose tissue (leptin and resistin).

2-2-2 The female cycle.

Each month, the ovaries go through a series of stages, depending on stimulation by the anterior pituitary hormones the follicle stimulating

hormone (FSH) and the luteinizing hormone (LH). A typical female cycle lasts 28 days; however, this can range from 21-35 days. The ovarian cycle has 2 distinct phases: the follicular phase (days 1-14) and the luteal phase (days 14-28). The follicular phase is characterized by follicle development and growth, the goal being that one follicle matures and releases an egg at the time of ovulation, around day 14 of the female cycle. The remaining immature follicles go through stages of degeneration up until day 28, when the cycle repeats itself. The egg that is released is picked up by the fimbriae of the uterine tube, and the egg is transported toward the uterus. If fertilization does not occur, the egg degenerates, and menstruation occurs.

2-2-3 Menstruation.

At the time the ovaries are formed in the fetus, there are approximately 6000000 primordial follicles, which decrease to about 600000 at birth, to 300000 at the first menstrual cycle, to about 10000 at the time of menopause. The average cycle is 28 days and has two distinct phases. The follicular phase starts on day one of the menstrual cycle .The hypothalamus in the brain releases gonadotropin-releasing hormone (GnRH). GnRH signals the pituitary gland to release follicle stimulating hormone (FSH). FSH stimulates the eggs inside the ovaries to grow. About 20 immature eggs response and begin to develop within sacs known as follicles. Follicles provide nourishment to the eggs. As the eggs develop, the ovaries release estrogen. Estrogen signals the pituitary gland to reduce FSH production. Only enough RSH is now released to stimulate one egg to continue developing, the rest of the eggs shrivel away. Estrogen stimulates the lining of the uterus to thicken. The primary follicle contains the contains the egg that has grown the most rapidly. Estrogen continues to rise until it triggers a surge of luteinizing hormone (LH) from the pituitary gland. LH stimulates ovulation. The follicle ruptures and the egg is released along with the

follicular fluid onto the surface of the ovary. The ruptured follicle continues to receive LH. The LH enables the follicle to turn into a small cyst known as the corpus luteum. The corpus luteum produces progesterone. Progesterone :- builds and thickens the endometrium, developing glandular structures and blood vessels that supply nutrients to the developing embryo , it switches off FSH an LH and it raises the basal body temperature (BBT) by half a degree, warming the uterus and fertilized egg. The egg is surrounded by the zona pellucida, a protective shell. The shell is surrounded by a mass of sticky cells called the cumulus oophorus. These sticky cells allow the finger like projections at the end of each fallopian tube, to pick up the egg and sweep it into the tube. The channel from the fimbriae to the uterus is lined with cilia, which together with muscular contractions move the ovum along the tube to the uterus. The journey from the ovary to the uterus take about 6 days. If the egg is not fertilized it will disintegrate and is absorbed

One of the most critical periods of pregnancy is from approximately day 11-16 after mating. The blastocysts, elongate into long (2-3 feet), stringy masses, and they begin to attach to the uterine wall. The greatest potential loss in litter size may occur during this stage of development because of attachment failures. On the average, 17 ova are shed at estrus yet only <u>about</u> <u>12 are accounted</u> for as blastocysts when attachment complete. There is thought to be some factor(s) which limit the number of blastocysts that can attach in a given uterus. Research has shown that overcrowding is not a major limiting factor. <u>Embryonic survival</u> may be related to certain uterine secretions which have not presently been well defined. Environmental stressors such as high temperatures and fighting as a result of mixing or regrouping animals also adversely influence implantation and embryo survival. Generally, the presence of at least four blastocysts are required in order for pregnancy to continue.By days 25-35, the <u>embryo</u> is about 1 to 1 1/2 inches long, and major body systems and appendages are well formed. Each embryo is surrounded by a separate series of <u>fluid-filled membranes</u>, the amnion and chorion, which are comprise the placenta. These membranes help to protect and nourish the growing embryo. Nutrients, waste, gases and certain antibodies cross the membranes between the dam and embryos blood systems. It is the presence or absence of this fluid that is detected by the commonly used <u>"ultrasound" pregnancy diagnosis</u> equipment.

The fetal period begins at approximately day 36. Sexes may be easily determined by external examination and the main systems of the body are more well defined. The fetus can now be called a miniature adult. Fetal orientation is random; some are head to head, some are tail to tail and some are head to tail. At farrowing, about half are born tail first and half are born head first. Embryos which die before day 35-40 are usually reabsorbed by the dam. However, progressive calcification of the skeleton begins to occur from day 36 onward and deaths occurring after this point will result in mummification.

By day 109 the fetus weighs about 1½ to 2 pounds. Hair shafts begin to emerge but remain trapped under a skin layer until close to birth. Throughout gestation, the uterus gradually enlarges from about 2 to 3 pounds at mating to up to 60 pounds, including fetal contents, during the last week. Some females will lose up to 10 to 11% of their body weight at parturition or farrowing.The average gestation length or time from conception until farrowing is 114 days. During gestation, the piglet grows from the union of a microscopic sperm and ovum into a fully formed individual weighing from 3 to 3½ pounds. Several factors can influence ovulation rate age, nutrition and breed .Semen is deposited into the cervix during mating or insemination. Muscular contractions of the cervix stimulate ejaculation of the boar and is the basis of the boar's ejaculatory response to the "gloved hand" or "digital pressure" technique of semen collection.

Thirty to sixty billion sperm are deposited by the boar during natural service or 2 to 6 billion during insemination but only a small fraction of these reach the oviduct and the vicinity of the ova. Even though sperm are motile, they do not propel themselves through the female's tract. Sperm transport results from uterine contractions. These contractions are stimulated by oxytocin released from the pituitary gland. Its release is mediated by the stimuli from mating behavior and copulation. Keep this in mind when inseminating a sow or gilt. Face-to-face contact with a boar, plus tactile stimulus during and after insemination may improve sperm transport. Sperm must reside in the female from 6-10 hours before they are capable of fertilization. This process is called capacitation and it includes both physical and biochemical changes within the sperm.

Fertilization or union of sperm and ova occurs in the upper 1/3 of the oviduct. Fertilization rate is virtually 100% if the female is mated to a fertile boar at the correct time relative to ovulation. About 2 days after fertilization, the <u>blastocysts</u> enter the uterus. They are in the 4-8 cell stage and begin to space themselves equal distances apart in the uterine horns. The blastocysts can <u>migrate</u> from one horn to another during this stage.(P. B. J. VanVierzen,1998)

2-3 Ultrasound appearance of the ovary.

Ultrasound is safe and painless, and produces pictures of the inside of the body using sound waves. Ultrasound imaging, also called ultrasound scanning or sonography, involves the use of a small transducer (probe) and ultrasound gel placed directly on the skin. High-frequency sound waves are transmitted from the probe through the gel into the body. The transducer collects the sounds that bounce back and a computer then uses those sound waves to create an image. Ultrasound examinations do not use ionizing radiation (as used in x-rays), thus there is no radiation exposure to the patient. Because ultrasound images are captured in real-time, they can show the structure and movement of the body's internal organs, as well as blood flowing through blood vessels.

Ultrasound imaging is a noninvasive medical test that helps physicians diagnose and treat medical conditions. A pelvic ultrasound provides pictures of the structures and organs in the lower abdomen and pelvis. A Doppler ultrasound exam may be part of a pelvic ultrasound examination. Doppler ultrasound is a special ultrasound technique that evaluates blood flow through a blood vessel, including the body's major arteries and veins in the abdomen, arms, legs, neck and head (in infants and children).

In women, a pelvic ultrasound is most often performed to evaluate the uterus , cervix , ovaries , fallopian tubes and bladder.Pelvic ultrasound exams are also used to monitor the health and development of an embryo or fetus during pregnancy. Ultrasound examinations can help diagnose symptoms experienced by women such as pelvic pain , abnormal bleeding , other menstrual problems and help identify palpable masses such as ovarian cysts and uterine fibroids.

A transvaginal ultrasound is usually performed to view the endometrium, the lining of the uterus, and the ovaries. Transvaginal ultrasound also provides a good way to evaluate the muscular walls of the uterus, called the myometrium. Sonohysterography allows for a more in-depth investigation of the uterine cavity. Three-dimensional (3-D) ultrasound permits evaluation of the uterus and ovaries in planes that cannot be imaged directly. These exams

are typically performed to detect uterine anomalies , uterine scars , endometrial polyps , fibroids and cancer, especially in patients with abnormal uterine bleeding. Some physicians also use 3-D ultrasound or sonohysterography for patients with infertility. Three-dimensional ultrasound provides information about the outer contour of the uterus and about uterine irregularities.

Doppler ultrasound images can help the physician to see and evaluate blockages to blood flow (such as clots), narrowing of vessels, tumors and congenital vascular malformations. You should wear comfortable, loosefitting clothing for your ultrasound exam. You may need to remove all clothing and jewelry in the area to be examined. You may be asked to wear a gown during the procedure.

ROLE OF ULTRASOUND is To examine the uterus, ovaries cervix vagina and adnexae, Classification of a mass identified on other modalities eg solid, cystic, mixed, Post surgical complications eg abscess, oedema , Guidance of injections, aspiration or biopsy , Assistance with IVFand To identify the relationship of normal anatomy and pathology to each other. INDICATIONS : P/V bleeding/discharge , Menorrhagia , Polymenorrhea , Amenorrhea , Irregular periods , Pelvic pain , F/H uterine or ovarian Cancer , Palpable lump , Infertility- primary or secondary and Anomalies .

LIMITATIONS: - transvaginal scanning is contra-indicated if the patient is not yet sexually active, or cannot provide informed consent, large patient habitus will reduce detail, particularly via the transabdominal approach and excessive bowel gas can obscure the ovaries.

EQUIPMENT SELECTION AND TECHNIQUE: - use of a curvilinear 3-6 MHz probe and a 6-10 MHz endovaginal probe. Low dynamic range.

PATIENT PREPARATION: - If possible, scan the patient in the first 10 days of the cycle. Preferably Day 5-10 for improved diagnostic accuracy in the assessment of the endometrium and ovaries and a full bladder is required . Instruct the patient to drink 1 Litre of water to be finished 1 hour prior to their appointment. They cannot empty their bladder until after the scan.Transabdominal approach is a generalised overview to identify the cervix, uterus and ovaries.

Scan sagitally in the midline immediately above the pubis. In this plane you should be able to assess the uterus, vagina and cervix. Zoom the image to assess and measure the endometrial thickness. Rotate into transverse and angle slightly cranially to be perpendicular to the uterus. Whilst in transverse and slightly right of midline, angle left laterally to identify the left ovary using the full bladder as an acoustic window. Examine this ovary in two planes. Now repeat this for the right ovary.

Endovaginal approach:-before letting the patient empty their bladder, show them the TV probe and explain the procedure. Indicate the length that is inserted which is approximately the length of a standard tampon. Explain there is no speculum used. Explain the importance of a TV scan because it is the gold standard in gynaecological ultrasound because of its superior accuracy and improved diagnostic resolution.

Cover the probe with a latex free Transvaginal sheath and lubricate with sterile gel on the outside.Elevate the patients bottom on a thick sponge/pillow to assist the scan. A gynaecological ultrasound couch which drops down is ideal so that a better angulation is achieved for an anteverted uterus.Ensure the patient is ready and get permission before inserting the probe. If there is some resistance as the probe is being inserted, offer for the patient to help guide the probe in far enough to see the end of the fundus.Keep asking the patient if they are okay.When manouvering the probe to visualise the adnexae, withdraw slightly then angle the probe towards the fornix. This avoids unnecessary patient discomfort against the cervix.



Fig. 2-64 Use the full urinary bladder as an acoustic window to angle across to the ovary.



Fig. 2-65 Axial trans-abdominal image with the ovary lateral to the uterus.

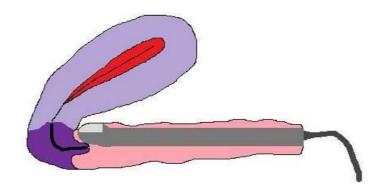


Fig. 2-66Axial trans-vaginal scan plane



Fig. 2-67 Axial trans-vaginal image



Fig. 2-68 Normal transvaginal ovary demonstration normal peripheral follicles.

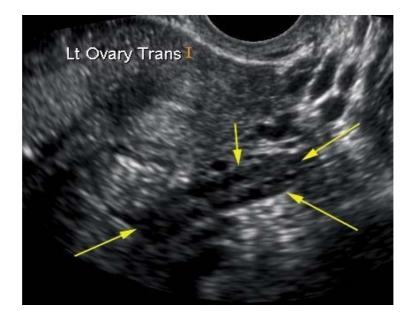


Fig. 2-69 The uterus may be oblique and squash the ovary giving it a flattened ovoid shape.



Fig. 2-70 Uterus with gestation sac and embryo

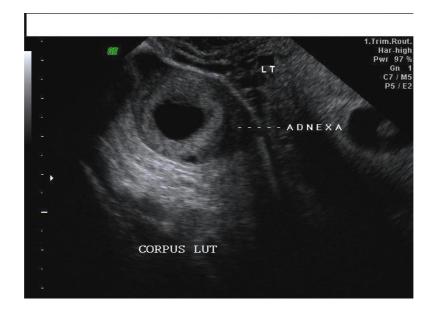


Fig. 2-71 Lt. adnexal cystic mass- Luteal cyst (Lt. ovary)



Fig. 2-72 Rt. ovarian simple cyst

This patient had an early gestation with embryo and intrauterine gestation sac. Sonography of the adnexal regions also showed a cystic lesion of the right ovary, which was thin walled and showed no septae or nodules within it, suggestive of a simple cyst (functional) of the right ovary. However, the left adnexal region showed a thick walled cystic lesion with echogenic walls. This appearance can easily be due to an ectopic pregnancy. Both ectopic gestations and corpus luteal cysts show similar features including the presence of "ring of fire" or ring of vessels around the lesion (on Color Doppler imaging). The left ovary was not seen separate from the left adnexal cyst; also there was no evidence of significant fluid in the cul de sac; besides, the presence of intrauterine pregnancy lead to the diagnosis of a left ovarian Corpus Luteal cyst. Ultrasound images are courtesy of Dr. V. Ganesan, MD, India.

Hemorrhagic cysts of the ovary are the result of bleeding from vascular tissues within the walls of the freshly formed corpus luteum or luteal cyst. The hemorrhagic cyst of ovary can present in various ways, mimicking a number of more ominous diseases or cysts of the ovary. These include ovarian cancers to serous or mucinous cystadenomas. Sometimes, rupture of the hemorrhagic ovarian cyst can result in a medical emergency .



Fig. 2-73 Hemorrhagic cyst of ovary resulting from Ovulation induction



Fig. 2-74 Polycystic ovary



Fig. 2-75 Polycystic ovary with doppler



Fig. 2-76This young nulliparous female patient undwerwent ultrasonography following ovulation induction.

The right ovary shows a typical hemorrhagic cyst formed from the corpus luteum. The first image (top row- left) is a transabdominal ultrasound image showing fine fibrinous strands within the cystic mass in the right ovary. Transvaginal ultrasound and color Doppler images confirm these findings. The uterus shows typical secretory changes in the <u>endometrium</u> suggesting post ovulatory phase.

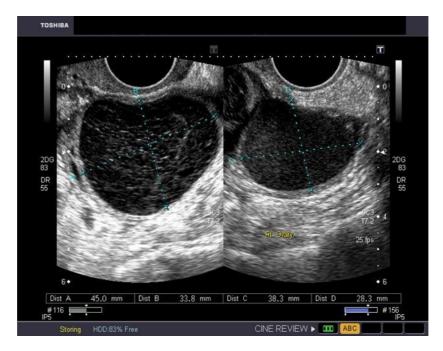


Fig. 2-77 Chocolate cyst

This patient has a co-existing chocolate cyst with a hemorrhagic cyst in the same (right) ovary. The cyst on the left half of the ultrasound image is a hemorrhagic cyst. Note the fine fibrinous strands within the cyst suggesting clot formation. The cyst on the right half of the image is homogenous with fine echoes throughout the ovarian cyst. This is a typical appearance of an endometrioma (chocolate cyst). Ultrasound image is courtesy of Dr. Gunjan Puri, MD, India.

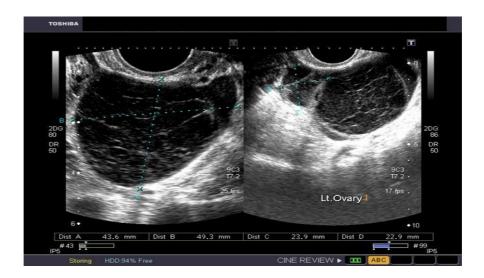


Fig. 2-78 Chocolate cyst



Fig. 2-79 This female patient has a left ovarian hemorrhagic cyst (see ultrasound image above-left). In addition, there is a large collection of free

fluid with particulate matter in the pelvis. The right fallopian tube is thickened with a ring shaped mass. This suggests that there is significant hemorrhage into the pelvis due to a ruptured ectopic pregnancy (right tubal ectopic gestation). The left ovarian hemorrhagic cyst appears intact, ruling out ruptured hemorrhagic cyst. Both above ultrasound images are courtesy of Gunjan Puri, MD, India.

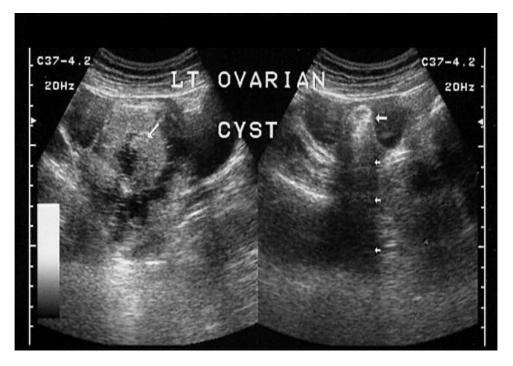
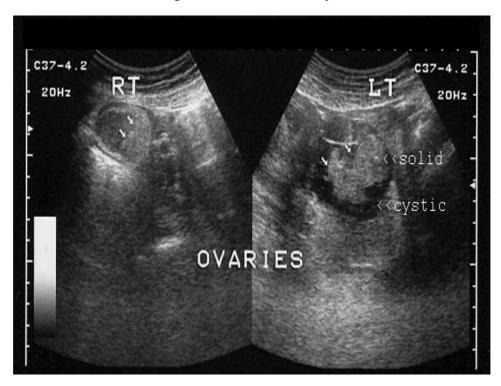


Fig. 2-80 Lt. ovarian cyst



Fig, 2-81 bilateral ovarian complex masses

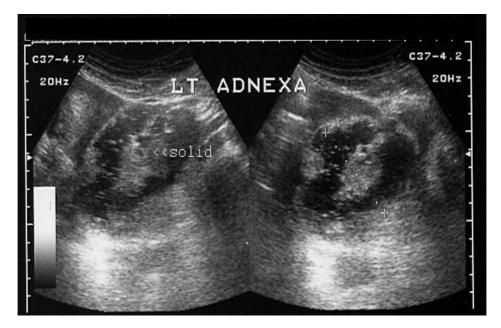


Fig. 2-82solid nodule containing fat and various tissues including hair



Fig. 2-83 Left ovarian dermoid cyst



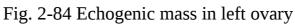




Fig. 2-85 Normal right ovary



Fig. 2-86 Left ovarian dermoid

These ultrasound images show a typical dermoid cyst of the left ovary. Transvaginal images of the left ovary show an echogenic mass of the left ovary with attenuation of the ultrasound beam posteriorly. The echogenic mass contains sebum and other fatty material giving rise to hyperechoic appearance of the lesion. The differential diagnosis in this case includehemorrhagic cyst of the ovary with organized hematoma. Here the hematoma would show acoustic enhancement posterior to the lesion, rather than the attenuation (shadowing) seen in dermoid cyst. Bowel gas can also produce the appearance of an echogenic lesion in the ovary. However, the dirty shadowing seen in bowel gas and also peristalsis would help distinguish bowel gas. Images are courtesy of Dr. Jaydeep Gandhi, MD, India.

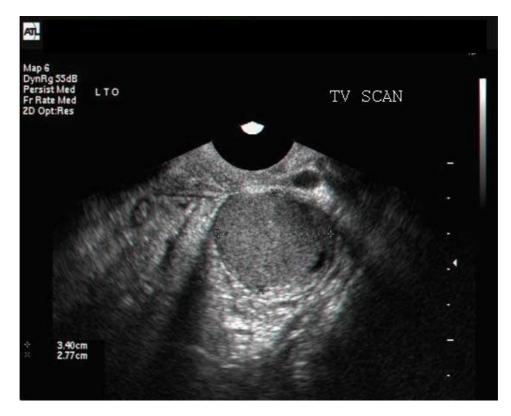


Fig. 2-87 Endometrioma or Endometriotic cyst of ovary or Chocolate cyst of the ovary

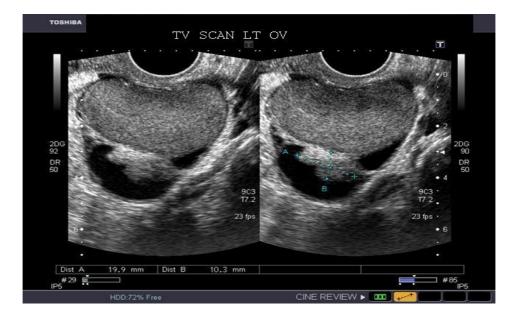


Fig. 2-88 Chocolate cyst



Fig. 2-89 Ultrasound images of chocolate cysts

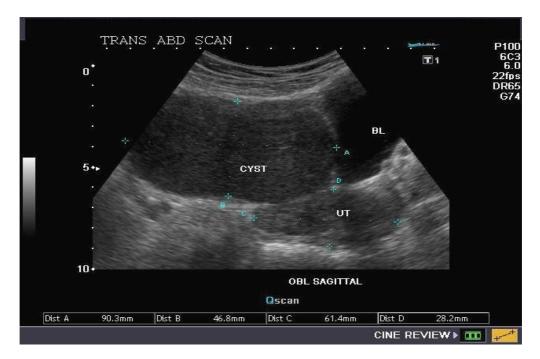


Fig. 2-90 Ovarian cyst

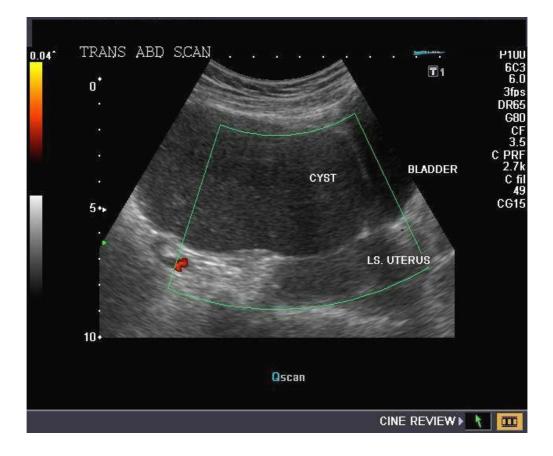


Fig. 2-91 Sonographic images of endometrioma



Fig. 2-92 Ultrasound image of endometrioma

Chocolate cysts or endometrioma of the ovary are caused by bleeding from ectopic endometrial tissue within the ovary. Some researchers believe that normal tissue within the ovaries might undergo changes which results in bleeding within the ovary. All the above ultrasound images (4 different cases) show small to large cystic lesions within the ovaries. The cysts show diffuse, low level echoes within them with poor flow on Doppler imaging. The main differential diagnosis in these cases is hemorrhagic cyst where fine strands are seen coursing within the cyst. Also note that endometriomas show homogenous appearance of the echogenic (altered blood) content within them. Chocolate cysts can be of varying sizes and cause considerable pain, especially during menses. Usually chocolate cysts show absence of septae or calcification and can be mistaken for solid masses. MR imaging can be helpful in clinching the diagnosis of this disease.



Fig. 2-93 Rupture of hemorrhagic ovarian cyst



Fig. 2-94 This female patient presented with pain in the pelvis and tenderness. Transabdominal sonography of the pelvis showed a large amount of free fluid with particulate matter in the cul de sac and around the right adnexal region. The right ovary showed remnants of what appeared to be a ruptured hemorrhagic corpus luteal cyst. Endovaginal imaging showed large amount of fluid with debris posterior to the uterus. The left ovary appeared normal. Lab tests and patient history excluded the possiblity of ectopic pregnancy. It was hence concluded that this was a ruptured right hemorrhagic ovarian cyst with free blood in the pelvis. The rounded echogenic mass seen near the fluid appears to be an organized blood clot.



Fig. 2-95 Ovarian hyperstimulation syndrome (OHSS)



Fig. 2-96 This young adult female patient was examined to evaluate the uterus and ovaries. She was under treatment for infertility and was using gonadotropins. Ultrasound images of the ovaries show grossly enlarged ovaries with large cysts (measuring 2.6 to 3 cms.) in both ovaries. These ultrasound findings are diagnostic of OHSS or ovarian hyperstimulation syndrome.

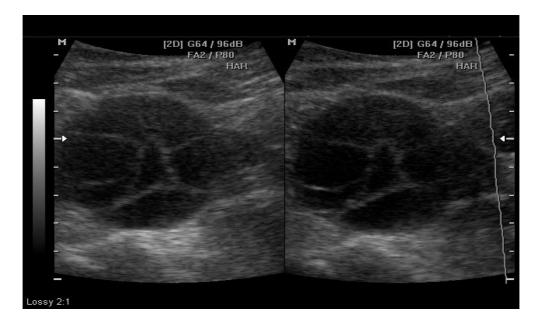


Fig. 2-97 a

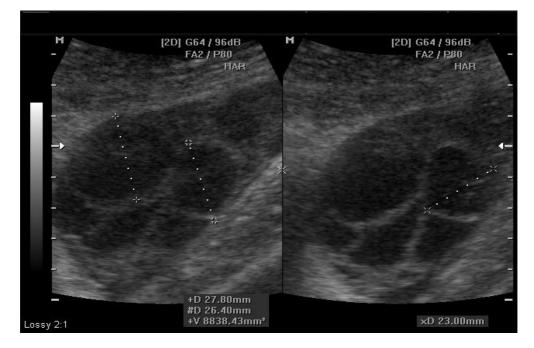


Fig. 2-97 b

The above (Fig. 2-97a &Fig. 2-97b) ultrasound images again show hyperstimulated ovaries. Both ovaries are grossly enlarged and cystic.

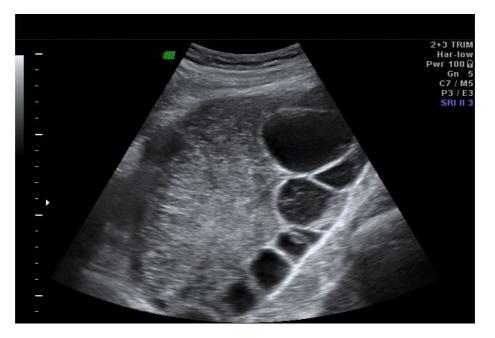


Fig. 2-98 a



Fig. 2-98 b

The above images(Fig. 2-98 a& Fig. 2-98 b) are courtesy of Dr. Dilraj Gandhi, MD, Delhi, India. Grades of OHSS: There are 3 grades of ovarian hyperstimulation based on sonography and clinical features: 1) mild OHSSovaries are less than 5 cms. in diameter and patient has mild abdominal dsicomfort. 2) moderate OHSS- ovaries measure 5 to 10 cms. in diameter 3) severe OHSS- ovaries measure greater than 10 cms. in diameter.

:

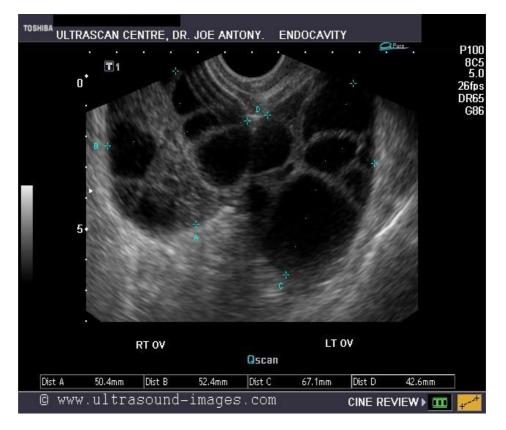


Fig. 2-99 Transvaginal ultrasound images of ovarian hyperstimulation

syndrome

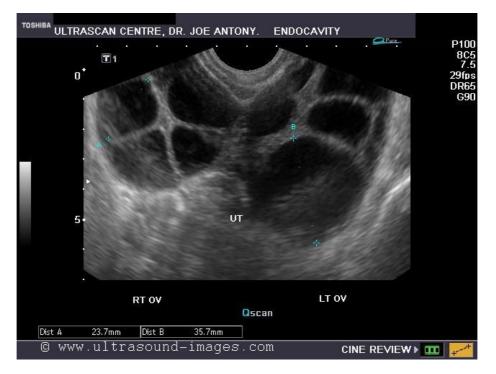


Fig. 2-100 a

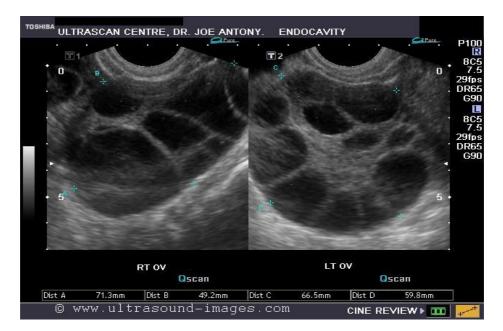


Fig. 2-100 b

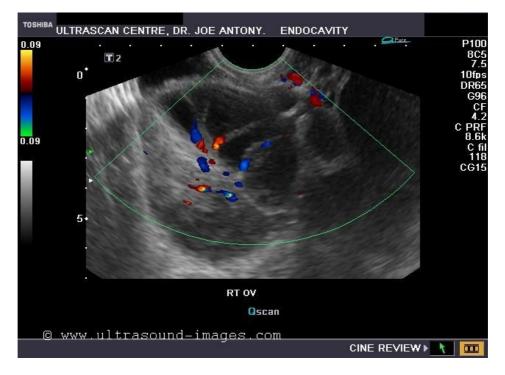


Fig. 2-100 c

(Fig. 2-100 a, Fig. 2-100 b & Fig. 2-100 c)This young adult female patient showed multiple large theca lutein cysts of both ovaries, arranged in spoke-wheel pattern (ultrasound images above) which were the result of use of gonadotropins in the management of infertility. The cysts vary in size from 2 to 4 cms. with the ovaries massively enlarged (each ovary measures up to 7

cms. in size). This can be classified as grade-2 hyperstimulation of the ovaries (ovarian diameter from 5 to 10 cms.). There is not evidence of ascites. The color Doppler image of the ovaries shows vessels passing along the margins of the cysts. One of the complications of such enlarged ovaries in OHSS is torsion and in certain cases rupture of the ovaries, both of which are medical emergencies. Ovarian hyperstimulation syndrome is known to occur more frequently in patients of pre-existing Polycystic ovaries (PCO).



Fig. 2-101 pre-existing Polycystic ovaries (PCO).



Fig. 2-102 a Enlarged ovary



Fig. 2-102 b Enlarged ovary

Ultrasound shows enlarged ovaries on both sides. However, no definite follicles were visualized. The uterus was normal in size. The transvaginal ultrasound images show surprising details of the affected ovaries. The sonographic findings include: a) Enlarged ovaries- the volume of these ovaries ranged from 12 to 15 cc. This is due to stromal proliferation. b) The ovarian stroma (parenchyma) appears echogenic. c) Multiple follicles of small size are seen along the rim of the ovaries. d) The ovarian follicles are less than 10 mm. in size (each of the follicles averaged at 4 to 5 mm. in size). e) There are more than 10 follicles per ovary (here we could count at least 12 to 15 follicles per ovary). The arrangement of the follicles along the rim of the ovary is called a necklace sign and is iagnostic of PCOD or polycystic ovary disease. Usually, clinical findings associated with PCOD include- hirsuitism, obesity, irregular menses and infertility. These conditions associated with polycystic ovaries are together labelled PCOS (polycystic ovarian syndrome).



Fig. 2-103 ovarian torsion



Fig. 2-104 Enlarged lt. ovary



Fig. 2-105 Enlarged lt. ovary

This young girl (6 years age) had severe left pelvic pain. Ultrasound images show an enlarged left ovary with lack of significant blood flow on power Doppler imaging. The right ovary appeared normal. These ultrasound images suggest torsion of the left ovary. This was surgically confirmed, with the left ovary seen to be gangrenous. The normal right ovary is seen as a pink healthy organ (see snapshot) compared to the gangrenous left ovary. These images of torsion of ovary are courtesy of Dr. Jaydeep Gandhi, MD, India.



Fig. 2-106 peritoneal inclusion cyst



Fig. 2-107 Ectobic pregnancy



Fig. 2-108 Ectobic pregnancy

This young adult female patient has a past history of ectopic pregnancy for which she underwent surgery. she presented with symptoms of early pregnancy with pelvic pain. Ultrasound shows presence of intrauterine gestation sac with multiple adhesions within the pelvis with pockets of ascitic fluid. The right ovary appears to be surrounded by multiple adhesions and fluid resulting in an appearance like a spider in a web. These ultrasound image findings are diagnostic of peritoneal inclusion cyst. This is a condition resulting from trauma to the peritoneum usually the result of surgery with resultant accumulation of peritoneal fluid and multiple adhesions. The ovaries appear normal in structure and are well preserved. These ultrasound images of peritoneal inclusions cyst are courtesy of Ajay Garg, MD.

The principal differential diagnosis in such cases of peritoneal inclusion cysts includes ovarian cystic masses such as serous or mucinous cystadenoma of the ovaries. Also, peritoneal inclusion cysts must be differentiated from more ominous conditions such as ovarian malignancies. Careful study of the ovaries, usually via the transvaginal ultrasound scan will help differentiate peritoneal inclusion cysts from ovarian lesions mentioned above. (Ross, E.K.,2013)

2-2-4 Follicle measurements and tracing.

The size of the leading follicles in conjunction with serum hormone levels are used to determine the optimal time for giving the HCG trigger for IVF. Follicles have traditionally been measured manually with two-dimensional (2D) ultrasound by calculating the mean of the 2 largest follicle diameters.Because follicles are often quite irregular in shape, measuring the follicles in the traditional fashion can result in significant inaccuracy. Another issue with manual measurements is that it is time consuming for the staff and the patients.

General Electric (GE) has software (Automated Volume Count, SonoAVC) for three-dimensional (3D) ultrasound machines that can identify follicles and automatically calculate their volumes. It then converts the measured volumes to diameters by using the sphere formula. It is possible that this technology could give more accurate follicle measurements and also could increase the efficiency of the ultrasound monitoring process.

This study was a retrospective review of ultrasound follicle measurements during ovarian stimulation for IVF and the outcome parameters for those cycles. The purpose was to study effectiveness and efficiency of 3D ultrasound assessment of follicle size during ovarian stimulation for IVF using SonoAVC. Clinical pregnancy rates, total number of eggs retrieved, mature eggs retrieved and percentage of mature eggs were compared in 2 groups.

Group 1 included all women using own eggs under age 35 having egg retrievals during the 9 month period of October 2007 through June 2008. Almost all patients in Group 1 had follicles measured manually (2D) with a GE Voluson 730 ProV machine by averaging 2 diameters.Group 2 included all women using own eggs under age 35 that had egg retrievals in the next 9 months (July 2008 through March 2009). Almost all of the patients in Group 2 had follicles measured using the SonoAVC software (3D) and a GE Voluson E8 Expert machine.

23 patients were scanned with both methods (back to back) and the duration of time for scanning and entering data into the chart recorded for each method. Statistical analysis utilized Student's t-test and chi-square.The average time required to do a scan, analyze data and record it in the chart was slightly less with the 3D SonoAVC method (5.6 vs. 6.2 minutes). There were no significant differences in clinical pregnancy rates per egg retrieval or other outcome parameters between the 2 groups. See Table:

	Group 1	Group 2	Р
	(2D)	(3D)	Value
Egg Retrievals	119	126	-
Mean # Oocytes	12.2	11.4	NS
Mean # Metaphase II Oocytes	9.7	9.3	NS
% Metaphase II Oocytes	79.6%	81.5%	NS
Clinical Pregnancy Rate Per Retrieval	70.6%	65.5%	NS

NS = not statistically significant

Follicular size determination during ovarian stimulation for IVF using the SonoAVC system is both effective and efficient.

Because the 3D volumetric method of measuring follicles could be more accurate and can give different diameters compared to manual measurements, studies should be done with SonoAVC (or similar software) to further evaluate the ideal leading follicle size for HCG trigger in order to optimize.Typically, the human ovaries produce a single dominant follicle that results in a single ovulation each menstrual cycle . In any given cycle, the dominant follicle must complete all the steps in folliculogenesis in a timely manner. In this capacity, it survives the negative events that operate to destroy the other follicles by atresia. Recognition that only a few follicles become dominant beautifully demonstrates the fundamental principle that folliculogenesis in mammals is a highly selective process. This chapter considers what is known about the process underlying the expression of the structural and functional organization of developing follicles and how they are controlled.

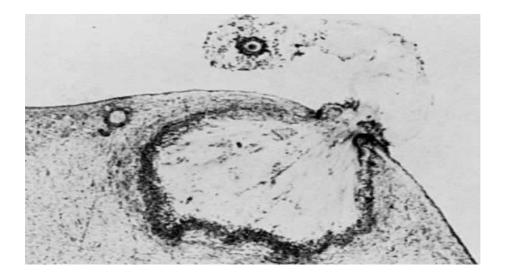


Fig. 2-10. Photomicrograph of ovulation shows the expanded egg-cumulus complex leaving the follicle through the stigma. The remaining cells in the follicle wall (*i.e.* granulosa, membrana and periantral, theca, the theca interna and externa) develop into the corpus luteum.(From Blandau RJ: Growth of the ovarian follicle and ovulation. Prog Gynecol 5:58, 1970.)

2-2-4-1 Folliculogenesis.

Folliculogenesis is the process in which a recruited primordial follicle grows and develops into a specialized graafian follicle with the potential to either ovulate its egg into the oviduct at mid-cycle to be fertilized or to die by atresia. In women, the process is long, requiring almost 1 year for a primordial follicle to grow and develop to the ovulatory stage. During the course of folliculogenesis, growth is achieved by cell proliferation and formation of follicular fluid, whereas development involves cytodifferentiation of all the cells and tissues in the follicle. Only a few follicles in the human ovary survive to complete the cytodifferentiation process, with 99.9% dying by a programmed cell death mechanism called apoptosis.

The mechanisms regulating follicle growth and development are under the control of changing concentrations of ligands (*i.e.* hormones and growth factors). At the endocrine level, folliculogenesis is regulated by a central nervous system, anterior pituitary, and ovary cascade mechanism. Specialized hypothalamic neurons secrete pulses of gonadotropin-releasing hormone (GnRH) into the portal blood vessels, which acts on the gonadotrophs to cause a pulsatile release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which act on ovarian follicle cells to control folliculogenesis. Although GnRH, FSH, and LH are critically important in regulating folliculogenesis, hormones and growth factors, which are themselves products of the follicle, can act locally to modulate (amplify or attenuate) FSH and LH action. This is the autocrine/paracrine system of developing follicles. It is believed that this local regulatory system plays an important role in the complex mechanisms governing the timing of folliculogenesis and whether a follicle becomes dominant or atretic.

2-2-4-2 Chronology.

In women, folliculogenesis is a long process. In each menstrual cycle, the dominant follicle that ovulates its egg originates from a primordial follicle that was recruited to initiate growth almost 1 year earlier. In a broad sense, there are two types of follicles : *preantral* (primordial, primary, secondary, tertiary and *antral* (graafian, small, medium, large, preovulatory. The development of preantral and antral follicles is gonadotropin independent and gonadotropin dependent, respectively.

The rate of preantral follicle development is slow, requiring about 300 days for a recruited primordial follicle to complete the whole preantral period . A long doubling time (about 10 days) for the granulosa cells is responsible for the slow growth rate. After antrum formation in the class 3 follicle (about 0.4 mm in diameter), the rate of growth accelerates. The time interval between antrum formation and the development of a 20-mm preovulatory follicle is about 50 days. The dominant follicle appears to be selected from a cohort of class 5 follicles at the end of the luteal phase of the menstrual cycle. About 15 to 20 days are required for a dominant follicle to grow and develop to the preovulatory stage Atresia can occur in all follicles (preantral and antral) after the class 1 or secondary follicle stage; however, the highest incidence is seen in the antral follicles that are more than 2 mm in diameter .

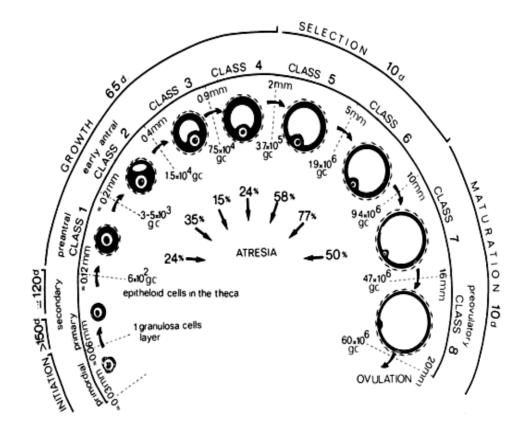


Fig. 2-111 Folliculogenesis

2-2-4-3 The process.Folliculogenesis occurs within the cortex of the ovary. The follicles in the cortex are present in a wide range of sizes representing various stages of folliculogenesis. The goal of folliculogenesis is to produce a single dominant follicle from a pool of growing follicles. There are four major regulatory events involved in this process: recruitment, preantral follicle development, selection, and atresia.

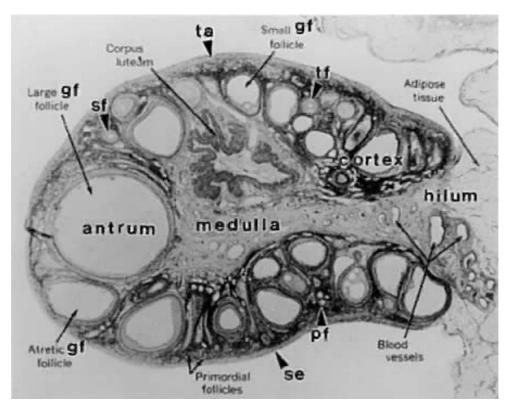


Fig. 2-112 Photomicrograph of an adult primate ovary. Follicular and luteal units are seen in the cortex and large blood vessels and nerves in the medulla. Serous or surface epithelium.

2-2-4-4 The primordial follicle.

All primordial follicles are composed of a small primary oocyte (about 25 μ m in diameter) arrested in the diplotene (or dictyate) stage of meiosis, a single layer of flattened (squamous) granulosa cells, and a basal lamina. The mean diameter of the human primordial follicle is 29 μ m.By virtue of the basal lamina; the granulosa and oocyte exist within a microenvironment in which direct contact with other cells does not occur. The primordial follicles do not have an independent blood supply, it follows that primordial follicles have limited access to the endocrine system.

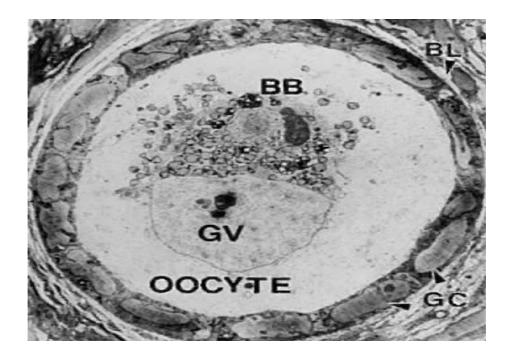


Fig. 2- 113 Electron micrograph of a human primordial follicle shows the flattened granulosa cells (GC), the oocyte with its germinal vesicle (GV) or nucleus, the Balbiani body (BB), with all the oocyte organelles gathered at one pole of the GV, and basal lamina (BL).(From Erickson GF: The ovary: Basic principles and concepts.

2-2-4-5 Recruitment.

The first major event in folliculogenesis is recruitment. Recruitment is the process by which an arrested primordial follicle is triggered to reinitiate development and enter the pool of growing follicles. All primordial follicles (oocytes) present in the human ovaries are formed in the fetus between the sixth and the ninth month of gestation. Because the entire stock of oocytes in primordial follicles is in meiotic prophase, none is capable of dividing mitotically. All oocytes (primordial follicles) capable of participating in reproduction during a woman's life are present in the ovaries at birth. The total number of primordial follicles in the ovaries at any given moment of time is called the ovary reserve (OR). The process of recruitment begins soon after the formation of the primordial follicles in the fetus, and it

continues throughout the life of the female until the pool of primordial follicles is exhausted at the menopause. There is a bi-exponential decrease in OR during aging The number of primordial follicles falls steadily for more than three decades, but when the OR reaches a critical number of about 25,000 at 37.5 ± 1.2 years of age, the rate of loss of primordial follicles accelerates about twofold .This change in OR is associated in an age-related decrease in fecundity, perhaps causal to the age-related increase in FSH that occurs in women after 36 years of age.

2-2-4-6 Mechanism.

The first visible sign that a primordial follicle is being recruited is that some granulosa cells begin to change from a squamous to a cuboidal shape. The first cuboidal cell is seen when the primordial follicle contains 8 granulosa cells, and the process is complete when the granulosa number reaches 19. The shape change is followed by the onset, albeit slow, of DNA synthesis and mitosis in the granulosa cells. A change in shape and acquisition of mitotic potential in the granulosa cells are the hallmarks of recruitment. Such observations suggest that the mechanisms governing recruitment may involve a regulatory response at the level of the granulosa cell. Recruitment is pituitary independent, and it probably is controlled by autocrine/paracrine mechanisms. Whether it is affected by a stimulator or the loss of an inhibitor is uncertain; however, primordial follicles undergo rapid recruitment when removed from the ovary and cultured *in vitro*. These observations support the inhibitor idea.

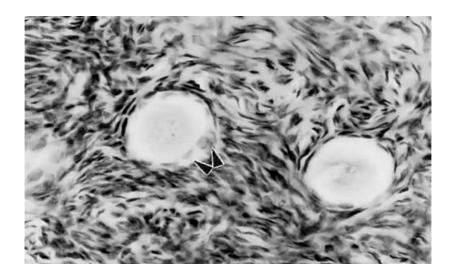
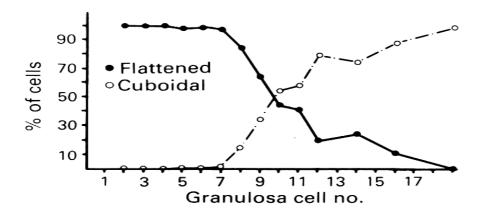


Fig. 2-114 Photomicrograph of nongrowing primordial and a newly recruited follicle in the human ovary.



Fig, 2-115 Relation between granulosa number in the largest cross section of the follicle and the distribution of flattened and cuboidal cells

Several different hypotheses have been put forth to explain the mechanism of recruitment. First, the process appears to occur in primordial follicles nearest the medulla where blood vessels are prominent. This supports the hypothesis that exposure to nutrients or blood-borne regulatory molecules could play a role in the control of recruitment. Second, an internal oocyte clock mechanism has been proposed to control recruitment. In this hypothesis, the clock is related to the time that the oocyte initiates meiosis in the embryo. It is noteworthy that recruitment can be modulated. In rodents, the rate of recruitment can be attenuated by removing the neonatal thymus gland, starvation, or treatment with exogenous opioid peptides. These are important observations, because they argue that ligand-receptor signaling pathways are likely to regulate recruitment. Understanding the regulatory mechanisms underlying recruitment remains a major task in reproductive biology.

2-2-4-7 THE PREANTRAL FOLLICLE.

The early stages of folliculogenesis can be divided into three classes based on the number of layers of granulosa cells, the development of theca tissue, and the expression of a small cavity or antrum. The classes are the primary, secondary, and early tertiary follicles. As the morphologic complexity increases, important cellular and physiologic changes occur in the follicle that renders it competent to respond to gonadotropins. The following sections examine the structure and function changes that accompany preantral follicle growth and development.

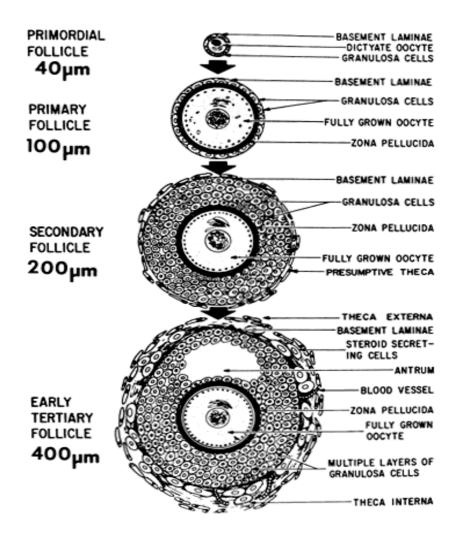


Fig. 2-116 Diagram illustrating the size and histologic organization of early developing human follicles during the gonadotropin-independent period of folliculogenesis

2-2-4-8 Primary Follicle.

A primary follicle consists of one or more cuboidal granulosa cells that are arranged in a single layer surrounding the oocyte. Simultaneous with the shape change and mitotic activities that accompany recruitment, the cuboidal granulosa cells begin to express FSH receptors. The mechanism underlying this critical event in folliculogenesis remains uncertain, but there is evidence in rodents that granulosa-derived activin may play an important role in the expression of FSH receptor by autocrine/paracrine mechanisms . Although the granulosa cells express FSH receptors at this very early stage in folliculogenesis, it is believed that the physiologic levels of plasma FSH during the normal menstrual cycle do not influence granulosa responses because primary follicles lack an independent vascular system. Nevertheless, because there are blood vessels in the vicinity , FSH-induced changes in primary follicle function may occur in response to abnormally high levels of plasma FSH, such as those that occur during ovulation induction or aging.

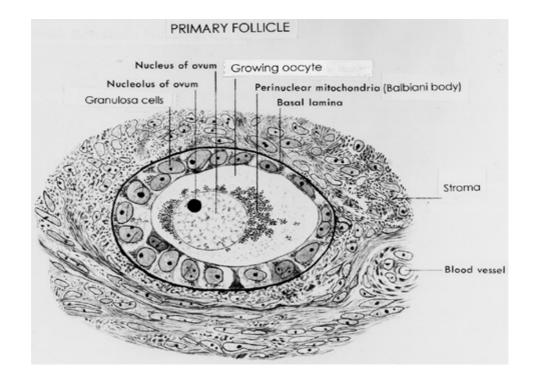
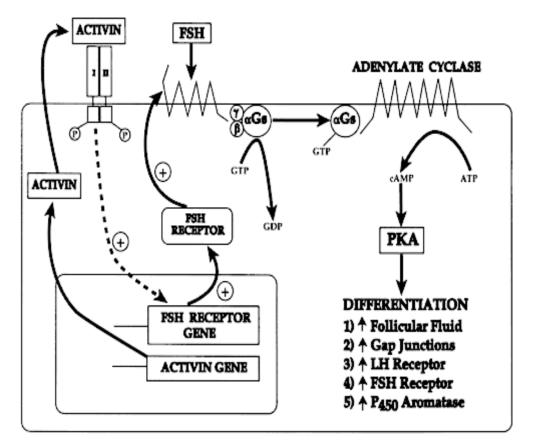


Fig. 2-117 Drawing of a developing primary follicle embedded in the connective tissue or stroma of the ovary cortex. A nucleolus and meiotic chromosomes are evident in the oocyte nucleus. The mitochondria appear aggregated at one pole of the oocyte nucleus



PREANTRAL GRANULOSA CELL

Fig. 2-118 Diagram of the proposed mechanism for the autocrine control of follicle-stimulating hormone receptor expression in granulosa cells of preantral follicles.(From Erickson GF: Dissociation of endocrine and gametogenic ovarian function.

Beginning approximately at the time of recruitment, the oocyte begins to grow and differentiate. This period is marked by a progressive increase in the level of oocyte RNA synthesis. A number of important oocyte genes are turned on at this time. For example, the genes encoding the zona pellucida (ZP) proteins (*i.e.* ZP-1, ZP-2, and ZP-3) are transcribed and translated. The secreted ZP proteins begin to polymerize near the oocyte surface, forming an extracellular matrix coat (the zona pellucida) that eventually encapsulates the egg. The importance of the zona pellucida is emphasized by the fact that the carbohydrate moiety of ZP-3 is the species-specific sperm-binding molecule. It is responsible for initiating the acrosome reaction in capacitated sperm. During primary follicle development, the granulosa cells send processes through the zona layer, where they form gap junctions with the oocyte cell membrane, or oolemma .Gap junctions are intercellular channels composed of proteins called connexins. There are at least 13 members of the connexin family that directly couple adjacent cells to allow the diffusion of ions, metabolites, and other low-molecular-weight signaling molecules such as cAMP and calcium. Connexin 37 (C×37) is an oocyte-derived connexin that forms gap junctions between the oocyte and surrounding granulosa cells. Evidence from C×37-deficient mice assigns C×37 an obligatory role for folliculogenesis, ovulation, and fertility.Large gap junctions are also present between the granulosa cells themselves (Fig. 12). C×43 is a major gap junction protein expressed in the granulosa cells. As a consequence of gap junctions, the primary follicle becomes a metabolically and electrically coupled unit. This communication between the granulosa and oocyte remains throughout folliculogenesis and is responsible for the synchronous expression of important activities (positive and negative).

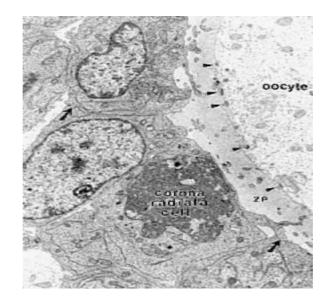


Fig. 2-119 Electron micrograph of the oocyte-corona radiata granulosa cells in a preantral follicle. The granulosa cell processes traversing the zona

pellucida (ZP) make small gap junctions (arrowheads) with the oocyte plasma membrane. Larger gap junctions (*arrows*) are evident between corona radiata cells.

2-2-4-9 Secondary Follicle.

A secondary follicle is a preantral follicle with 2 to 10 layers of cuboidal or low columnar cells that form a stratified epithelium. As seen in, the transition from a primary to a secondary follicle involves the acquisition of a second layer of granulosa cells. This transition is accomplished by the continuing division of the granulosa cells. The mechanisms regulating granulosa mitosis are poorly understood. However, exciting research in rodents has provided compelling evidence for the involvement of an oocytederived growth factor, called growth differentiation factor-9 (GDF-9). GDF-9 is a novel member of the transforming growth factor- β (TGF- β) superfamily. GDF-9 is strongly expressed in the ovary; it is localized only in oocytes of recruited follicles. In GDF-9 deficient mice, follicle growth and development stop at the primary stage; consequently no dominant follicles form, and the females are infertile. Accordingly, GDF-9 is obligatory for folliculogenesis after the primary stage, presumably because it is an obligatory mitogen for granulosa cells. A fundamental concept that emerges from this work is that the oocyte plays a pivotal role in regulating folliculogenesis through its ability to produce novel regulatory ligands, which are crucial for folliculogenesis.

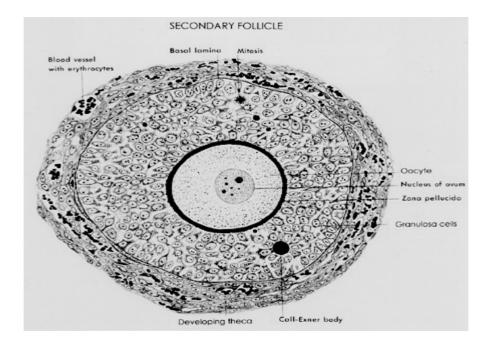


Fig. 2-120 A typical healthy secondary follicle contains a fully grown oocyte surrounded by the zona pellucida, five to eight layers of granulosa cells, a basal lamina, and developing theca tissue with numerous blood vessels

One of the most important changes that occur in the development of a secondary follicle is the acquisition of a theca layer. This tissue, which consists of a layer of stroma-like cells around the basal lamina, subsequently differentiates into the inner theca interna and outer theca externa. Theca development is accompanied by the neoformation of numerous small vessels, presumably through angiogenesis. This is a critical event because blood circulates around the follicle, bringing nutrients and hormones to and waste and secretory products from the secondary follicle. In this regard, some stromal cells in the inner layer express LH receptors. These cells subsequently differentiate into steroidogenic cells called theca interstitial cells (TICs), most likely in response to the plasma LH delivered by the theca vascular system. All the granulosa cells in secondary follicles express FSH receptors. It seems likely that diffusion of plasma FSH into the secondary follicle may evoke FSH-dependent granulosa responses. The outer layer of stroma cells subsequently differentiates into smooth muscle cells called the

theca externa. These smooth muscle cells are innervated by the autonomic nervous system. In the secondary follicle, the oocyte completes its growth. When the follicle is about 200 μ m in diameter, the oocyte has attained its maximum size and grows no more, despite the fact that the human follicle enlarges to a diameter of 2 cm or more (Fig. 14). It is well documented in rodents that granulosa cells play an obligatory role in the growth and differentiation of the oocyte. An important differentiation event that occurs when the oocyte completes its growth is acquisition of the capacity to resume meiosis. Oocytes normally do not resume meiosis during folliculogenesis, and a mechanism must operate to inhibit this process (*i.e.* germinal vesicle breakdown [GVBD]) and the resumption of meiosis. The underlying mechanism for the inhibition remains unknown; however, there is evidence to support the concept that granulosa derived cAMP may play an important role in inhibiting the resumption of meiosis. In such a mechanism, FSH-induces cAMP in the granulosa cells, which diffuses into the oocyte through the C×37 gap junction, where it proceeds to inhibit GVBD.

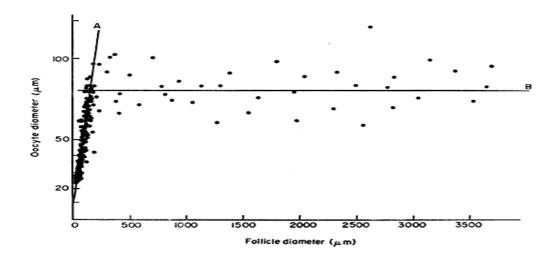


Fig. 2-121 Diagram showing the relation between the size of the oocyte and the size of the follicles in the human infant ovary

2-2-4-10 Tertiary Follicle.

When a preantral follicle completes the secondary stage in development, it contains five distinct structural units: a fully grown oocyte surrounded by a zona pellucida, six to nine layers of granulosa cells, a basal lamina, a theca interna, and a theca externa. The first indication of the onset of tertiary follicle development is the appearance of a cavity in the granulosa cells. In response to an intrinsic stimulus, a cavity begins to form at one pole of the oocyte. This process, called cavitation or beginning antrum formation, is characterized by the accumulation of fluid between the granulosa cells that in time results in the formation of an internal cavity . At completion of cavitation, the basic plan of the Graafian follicle is established, and all the various cell types are in their proper position awaiting the stimuli that will shift them along paths of differentiation and proliferation. Based on evidence from polyoocyte follicles, the specification mechanism of cavitation probably is tightly regulated.

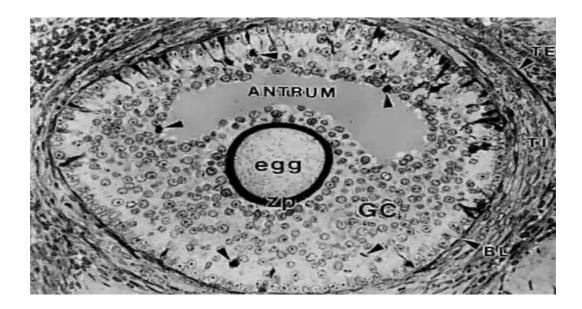


Fig. 2-122 Photomicrograph of an early tertiary follicle.

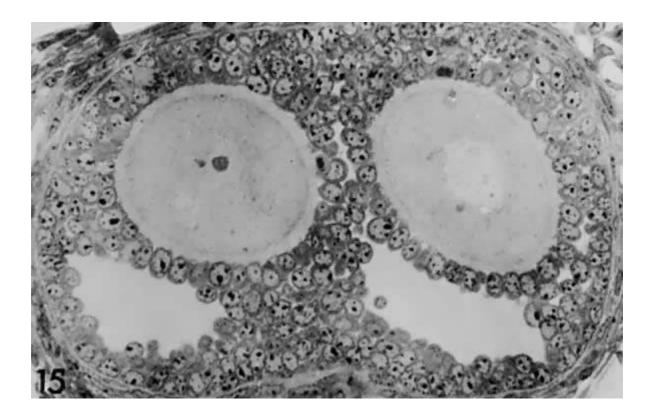


Fig. 2-123 Photomicrograph of a polyovular follicle at the early tertiary stage shows the sites of cavitation or early antrum formation (clear *spaces*) just above oocytes (asterisk). This event, which is under intraovarian control, seems to arise in a specific synchronized manner and establishes the polarity of the follicle.

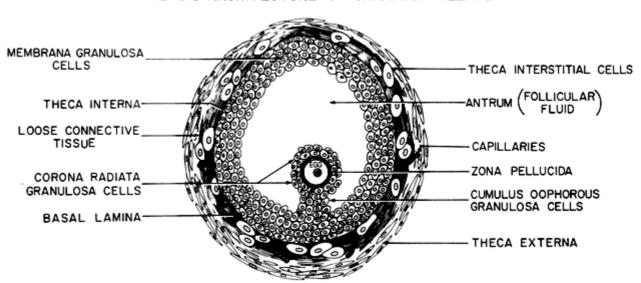
It is well known that cavitation occurs in hypophysectomized animals, demonstrating that pituitary hormones such as FSH are not required for this morphogenetic event. Consistent with this concept is the observation that cavitation occurs in FSH- β -deficient mice. It seems reasonable to conclude that cavitation is controlled by autocrine/paracrine mechanisms. Two growth factors expressed in the follicle itself have been implicated in cavitation: activin and KIT ligand. Treating cultured granulosa cells with activin causes morphogenetic changes that result in the formation of a histologic unit with an antrum-like cavity. Blocking the action of the KIT ligand in the ovary prevents the formation of antral follicles; consequently, there are no ovulations, and the female is infertile. In this regard, evidence supports the

concept that the oocyte gap junctions are also important for cavitation. Gap junctions are intercellular channels composed of proteins called connexins. There are at least 13 members of the connexin family that directly couple adjacent cells, allowing diffusion of ions, metabolites, and other low-molecular-weight signaling molecules such as cAMP, C×37 appears to be an oocyte-derived connexin that forms gap junctions between the oocyte and surrounding granulosa cells. Evidence from C×37-deficient mice assigns to C×37 an obligatory role in Graafian follicle formation, ovulation, and fertility. Collectively, all this evidence suggests that follicle-derived activin, KIT, and C×37 are involved in the autocrine/paracrine mechanisms that control cavitation.

2-2-4-11 THE GRAAFIAN FOLLICLE.

A graafian follicle can be defined structurally as a heterogeneous family of relatively large follicles (0.4 to 23 mm) characterized by a cavity or antrum containing a fluid called follicular fluid or liquor folliculi. The characteristic structural unit of all Graafian follicle is the antrum. For this reason, the term antral follicle is used correctly as a synonym for Graafian follicle. The follicular fluid is the medium in which the granulosa cells and oocyte are found and through which regulatory molecules must pass on their way to and from this microenvironment. Surprisingly, we know almost nothing about the physiologic significance of the antrum and follicular fluid in folliculogenesis. It is clear that follicle development and ovulation occur in birds and amphibians despite the absence of an antrum and follicular fluid. Nonetheless, its presence in all mammalian species testifies to its physiologic importance.

A graafian follicle is a three-dimensional structure with a central antrum surrounded by a variety of different cell types .There are six distinct histologic components in the graafian follicle, including the theca externa, theca interna, basal lamina, granulosa cells, oocyte, and follicular fluid . A graafian follicle does not change its morphologic complexity as growth proceeds. All graafian follicles have this same basic architecture; even though there are dramatic changes in Graafian follicle size, their appearance remains more or less the same.



HISTOLOGIC ARCHITECTURE OF GRAAFIAN FOLLICLE

Fig. 2-124 Diagram of the architecture of a typical class 5 Graafian follicle.

The theca externa is characterized by the presence of smooth muscle cells, which are innervated by autonomic nerves. Although the physiologic significance of the theca externa remains unclear, there is evidence that it contracts during ovulation and atresia. Changes in the contractile activity of the theca externa may be involved in atresia and ovulation; however, this has not been rigorously proved. The corpus luteum retains a theca externa throughout its life, but the significance during luteinization and luteolysis is not known.

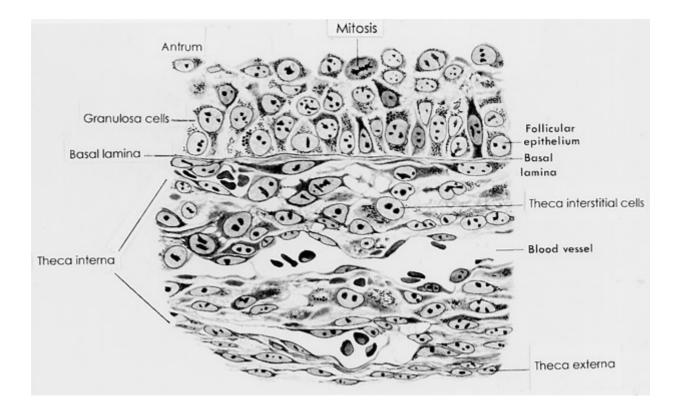


Fig. 2-125 Drawing of the wall of a graafian follicle.

The differentiation of a granulosa cell can be traced to its position within the cellular mass. For example, cells in the membrana domain stop proliferating before those in central domain. The ability of the granulosa cells in the inner domains to continue dividing throughout graafian follicle development suggests they may be precursor cells. The cessation of mitosis in the membrana domain is characterized by the progressive expression of overt differentiation in which they assume the functional phenotype of fully differentiated cells. This process requires the temporal and coordinate expression of genes that form the basis of granulosa cytodifferentiation. The mechanism by which this occurs involves ligand-dependent signaling pathways that are coupled to the activation and inhibition of specific genes. For example, normal differentiation of the membrana granulosa cells requires the activation of specific genes, including those for cytochrome P450 aromatase (P450_{arom}) and the LH receptor, and the inhibition of structural genes in the apoptotic pathways. In contrast, the granulosa cells in

the periantral, cumulus, and corona radiata domains proliferate, but they fail to express the genes that are involved in a terminal differentiation.

All the granulosa cells in the healthy Graafian follicle express FSH receptor, and it has been shown that murine granulosa cells in the membrana and cumulus domains produce cAMP in response to FSH stimulation. These observations argue that post cAMP regulatory events are involved in the aspects of granulosa heterogeneity. The idea that the oocyte plays a key role in causing the different patterns of granulosa cytodifferentiation during Graafian follicle development is supported by studies in rodents. A dialogue takes place between the oocyte and granulosa cells that has a great impact on folliculogenesis. In developing murine graafian follicles, the differential pattern of proliferation and differentiation between the granulosa in the membrana and cumulus domains are under the control of secreted oocyte morphogens. A novel TGF- β family member, GDF-9, was discovered in the mouse. Definitive evidence that GDF-9 is obligatory for folliculogenesis came from studies of GDF-9-deficient mice. In these animals, the absence of GDF-9 resulted in the arrest of follicle growth and development at primary stage and the females are infertile. These data support the idea that GDF-9 secreted by the egg is obligatory for Graafian follicle development, granulosa cytodifferentiation and proliferation, and female fertility. The clinical relevance of this new concept is demonstrated by the presence of GDF-9 mRNA in the human ovary. The current challenges are to elucidate the mechanisms controlling GDF-9 expression and to identify the target cells for GDF-9 and the biologic processes that GDF-9 regulates. The concept that oocyte-derived growth factors control folliculogenesis and fertility could have important implications for human physiology and pathophysiology.

2-2-4-12 Classification.

All graafian follicles can be divided broadly into two groups: healthy and atretic. The main difference between these two groups is whether apoptosis is occurring in the granulosa cells. The development of a graafian follicle (healthy or atretic) follows a progressive course over time. This implies that variability or heterogeneity is a normal consequence of folliculogenesis. A healthy graafian follicle becomes progressively more differentiated with increasing time until it attains the preovulatory stage. The time for this process is about 2 months in women. As this occurs, there is a temporal and spatial pattern of expression of large numbers of genes. In healthy follicles, these genes direct cytodifferentiation, proliferation, and follicular fluid formation. In atretic follicles, the time-dependent changes in gene expression cause the cessation of mitosis and the expression of apoptosis (*i.e.* follicle atresia). During atresia, the oocyte and granulosa cells become committed to express genes that lead to apoptosis. In healthy and atretic graafian follicles, the control mechanisms involve ligand-dependent signaling pathways that inhibit or stimulate the expression of differentiation and apoptosis. Understanding the molecular mechanisms and cellular consequences of the ligand-receptor signaling pathways that control Graafian follicle fate is a major goal of reproductive research.

The process of graafian follicle growth and development can be arbitrarily divided into several stages based on follicle size . It is convenient and important for clinicians and researchers to identify the physiologic function of various types or classes of follicles over the cycle. The healthy human Graafian follicle has a destiny to complete the transition from the small (1 to 6 mm), medium (7 to 11 mm), and large (12 to 17 mm) to the fully differentiated preovulatory state (18 to 23 mm). The atretic Graafian follicle has a destiny to complete the transition from the small to the medium stage (1 to 10 mm) but appears incapable of growing to the large size under

normal physiologic conditions. Because the process of graafian follicle development is asynchronous, it produces a large, heterogeneous population of graafian follicles in the ovaries at any moment in time. Each of these morphologically distinct graafian follicles is a dynamic structure undergoing a flow or progression of developmental change on its way to becoming more differentiated or more atretic. It should be kept in mind that this results in the presence of an extremely heterogeneous pool of graafian follicles. It is the heterogeneity that makes it difficult to come to grips with a simple functional definition for the Graafian follicle.

The size of a graafian follicle is determined largely by the size of the antrum, which is determined by the volume of follicular fluid, which is determined by the bioavailability of FSH in the fluid. FSH is obligatory for Graafian follicle development, and no other ligand by itself has the ability to induce follicular fluid formation. In the absence of FSH, follicular fluid is not produced, and no graafian follicles develop. The proliferation of the follicle cells also contributes to Graafian follicle growth; in healthy follicles, the granulosa and theca cells proliferate extensively (as much as 100-fold), concomitant with the antrum becoming filled with follicular fluid. These events (*i.e.* increased follicular fluid accumulation and cell proliferation) are responsible for the tremendous growth of healthy graafian follicles. In contrast, it is the cessation of mitosis and follicular fluid formation that determines the size of the atretic Graafian follicle.(K. Kinkle,2006)

2-2-4-13 Selection of the dominant follicle.

In each menstrual cycle, the ovaries normally produce a single dominant follicle that participates in a single ovulation. Morphometric analysis of normal human ovaries indicates that the dominant follicle that will ovulate in the subsequent cycle is selected from a cohort of healthy, class 5 follicles measuring 4.7 ± 0.7 mm in diameter at the end of the luteal phase of the menstrual cycle. At the time of selection, each cohort follicle contains a fully grown oocyte, about 1 million granulosa cells, a theca interna containing several layers of TICs, and theca externa composed of smooth muscle cells.

A characteristic feature of a dominant follicle is a high rate of mitosis in the granulosa cells. The evidence suggests that shortly after the mid-luteal phase, the rate of granulosa mitosis increases sharply (about twofold) in the granulosa cells within all cohort follicles. This suggests that luteolysis may be accompanied by a burst of mitosis in the granulosa of the cohort of class 5 follicles. The first indication that one follicle has been selected appears to be that the granulosa cells in the chosen follicle continue dividing at a relatively fast rate while proliferation slows in the granulosa of the other cohort follicles. Because this difference becomes apparent at the end of the luteal phase, it has been argued that selection occurs at the late luteal phase of the menstrual cycle. As a consequence of increased mitosis, the dominant follicle continues to grow rapidly.during the follicular phase, reaching $6.9 \pm$ 0.5 mm at days 1 to 5, 13.7 ± 1.2 mm at days 6 to 10, and 18.8 ± 0.5 mm at days 11 to 14. Conversely, growth proceeds more slowly in the cohort follicles, and with time, atresia becomes increasingly more evident in the nondominant cohort follicles, presumably because of the expression of specific genes in the apoptotic pathway. Rarely does an atretic follicle reach more than 10 mm in diameter, regardless of the stage in the cycle.

2-2-4-14 The process.

There is compelling evidence from laboratory animal and primate experiments, that a secondary rise in plasma FSH must be attained for a follicle to achieve dominance. As shown in Figure 24, the secondary FSH rise in women begins a few days before the progesterone levels fall to basal levels at the end of luteal phase, and the FSH levels remain elevated during the first week of the follicular phase of the cycle. Experiments using monkeys have demonstrated that the dominant follicle undergoes atresia if the secondary rise in FSH is prevented by treatment with exogenous estradiol. An important concept in reproductive biology is that an increase in bioactive FSH is obligatory for follicle selection and fertility. It appears that decreased estradiol production by the corpus luteum is the principal cause for the secondary rise in FSH rather than the fall in corpus luteum-derived inhibin A.

The results from studies of human follicular fluid support the conclusion that the rise in plasma FSH leads to a progressive accumulation of relatively high concentrations of FSH in the microenvironment of one follicle in the cohort; this follicle is destined to become dominant. In developing healthy (dominant) follicles (class 5 to 8 follicles), the mean concentration of follicular fluid FSH increases from about 1.3 mIU/ml (about 58 ng/ml) to about 3.2 mIU/ml (about 143 ng/ml) through the follicular phase.In contrast, the levels of FSH are low or undetectable in the microenvironment of the nondominant cohort follicles.

The entry of FSH into follicular fluid at cavitation is believed to provide the induction stimulus that initiates the process of Graafian follicle growth and development. At the cellular level, it is the FSH receptor on the granulosa cell that is the fundamental player in this process. When an appropriate high

FSH threshold is reached in one Graafian follicle, it is selected to become dominant. In contrast, the small graafian follicles in the cohort with subthreshold levels of FSH become nondominant. The mechanism whereby one small Graafian follicle in a cohort is able to concentrate high levels of FSH in its microenvironment remains one of the mysteries in ovary physiology. An important point is that estradiol produced by the dominant follicle inhibits the secondary rise in FSH by a negative feedback mechanism (Figs. 24 and 26). This is believed to ensure a subthreshold level of FSH in the nondominant cohort follicles, which then leads to atresia. Mitosis in granulosa cells of atretic cohort follicles can be stimulated by treatment with human menopausal gonadotropin (hMG) during the early follicular phase. If FSH levels are increased to threshold levels within the microenvironment, then nondominant follicles may be rescued from atresia. This phenomenon could have implications for the way in which exogenous FSH or hMG triggers the formation of multiple dominant follicles in women undergoing ovulation induction.

2-2-4-15 Autocrinology and paracrinology.

There is no doubt that the ability of the ovary to produce a dominant follicle, which ovulates a fertilizable egg, is under the control of the endocrine system, most notably by the hormones FSH and LH. Anything that interferes directly or indirectly with the normal action of the gonadotropins can be expected to produce a condition leading to apoptosis and infertility.

Research in the past decade has established the concept that FSH and LH signal transduction can be modulated by proteins with growth factor activity. All growth factors are ligands that act locally to amplify or attenuate cellular responses. The autocrine concept is that ligands (*e.g.* hormones, growth factors, neurotrophins, cytokines) produced by a cell act on the cell itself to

modulate cellular activities (*e.g.* growth, differentiation, apoptosis). The paracrine concept is that ligands produced by one cell act on adjacent cells to modify or modulate cell functions.

All five major families of growth factors are expressed within developing follicles of rats and humans. The principle emerging from an enormous amount of *in vivo* and *in vitro* research is that intrinsic growth factors interact with the endocrine system to evoke the physiologic control of all aspects of folliculogenesis, including recruitment, preantral follicle growth, selection, atresia, and ovulation. Two growth factors, oocyte-derived GDF-9 and granulosa-derived IGF-I, are obligatory for folliculogenesis and fertility in female mice.

The probability that new ovarian growth factor systems will be discovered in the future is high. Definitive evidence that local growth factors are obligatory for folliculogenesis and fertility in women is lacking, and the physiologic significance of the autocrine/paracrine concept in human ovaries remains to be established. The current challenges are to understand how specific autocrine/paracrine regulatory molecules control folliculogenesis and how these controls are integrated into the overall physiologic and pathophysiologic mechanisms.

2-2-4-16 Ultrasound monitoring.

Transvaginal ultrasound is preferred and usually mandatory modality for monitoring follicles. Ultrasound monitoring may begin on day 3 of the cycle, to assess a baseline size, as well as exclude if any cyst remains from previous hyperstimulation or otherwise. It's important to count the number of existing follicles, document two/three dimensions of each follicle, and also comment on shape (round/oval/rectangular/triangular), echogenicity (echogenic/hypoechoic/anechoic) and antral edges (smooth/intermediate/rough) if possible.

As the study progresses on day 7, we should start guessing the ovulatory dominant follicle i.e. dominant follicle which is destined to ovulate. Basically, there are three varieties of eligible follicles:- atretic dominant follicle: This follicle is usually largest follicle on day 3, but it is not destined to ovulate. It has an irregular shape, rough edges, and may be little echogenic, ovulatory dominant follicle: This follicle is typically round, with smooth borders, and usually hypoechoic and anovulatory-luteinizing dominant follicle: This dominant follicle grows at a good pace but fails to ovulate, and later becomes a cyst or luteinizes. These are also round and smooth, however anechoic. This subtle recognition of echogenicity difference between hypoechoic and anechoic follicle can help determine whether a follicle is growing to ovulate. Once the follicle reaches 16 mm size, a daily monitoring of follicle is recommended. Next step is documentation of ovulation. Ovulation is sonographically determined by following sonographic signs:- follicle suddenly disappears or regresses in size, irregular margins, intra-follicular echoes. Follicle suddenly becomes more echogenic, free fluid in the pouch of Douglas and increased perifollicular blood flow velocities, on doppler

Ultrasound monitoring in induced cycles, and predicting success of IVF. Most of the IVF studies are conducted after induction of ovaries with help of ovulation inducing agents like Clomiphene citrate. In such induced cycle, primary determinants of success are:- ovarian volume, antral follicle number and ovarian stromal blood flow.

Ovarian volume is easy to measure, although not a good predictor of IVF outcome. Now, it is documented, that a low ovarian volume does not always lead to anovulatory cycle. But, it's important to recognize a polycystic ovarian pattern and differentiate it from post-induction multicystic ovaries. Follicles arranged in the periphery forming a 'necklace sign', echogenic stroma, and more than 10 follicles of less than 9 mm size, signify a polycystic pattern in induced cycle. While, follicles in the center as well as the periphery, are seen in normal induced multicystic ovaries.

Antral follicle number of less than three, usually signify possible failure of assisted reproductive therapy (ART).Ovarian stromal blood flow has been recommended as a good predictor of ART success. Increased peak systolic velocity (>10 cm/sec) is one of such parameters which has been advocated.

Although, its a matter of choice, based on experience of individual IVF specialists, there are certain parameters which may be considered. Minimal criteria⁶ suggested is a follicle size of atleast 15 mm, and serum estradiol level of 0.49 nmol/L. Better prospects are at follicle size of 18 mm, and serum estradiol level of 0.91 nmol/L.

Random HCG administration should be avoided³, to prevent a risk of ovarian hyperstimulation syndrome (OHSS).(Joja I,1998)

2-2-5 Polycystic ovarian syndromes.

2-2-5-1 ovarian cyst.

An ovarian cyst is a fluid-filled sac which develops in an ovary. Most ovarian cysts are non-cancerous (benign) and cause no symptoms. Some cause problems such as pain and irregular bleeding. No treatment may be needed for certain types of ovarian cysts which tend to go away on their own. For other types, an operation may be advised to remove the cyst.Ovarian cysts are fluid-filled sacs in the ovary. They are common and usually form during ovulation. Ovulation happens when the ovary releases an egg each month. Many women with ovarian cysts don't have symptoms. The cysts are usually harmless.

A cyst is a fluid-filled sac. It can form in many places in the body. Ovarian cysts form in or on the ovaries. The most common types of ovarian cysts (called functional cysts) form during the menstrual cycle. They are usually benign (not cancerous).

The two most common types of cysts are: - follicle cysts. In a normal menstrual cycle, the ovaries release an egg each month. The egg grows inside a tiny sac called a follicle. When the egg matures, the follicle breaks open to release the egg. Follicle cysts form when the follicle doesn't break open to release the egg. This causes the follicle to continue growing into a cyst. Follicle cysts often have no symptoms and go away in one to three months and corpus luteum cysts. Once the follicle breaks open and releases the egg, the empty follicle sac shrinks into a mass of cells called corpus luteum. Corpus luteum makes hormones to prepare for the next egg for the next menstrual cycle. Corpus luteum cysts form if the sac doesn't shrink. Instead, the sac reseals itself after the egg is released, and then fluid builds up inside. Most corpus luteum cysts go away after a few weeks. But, they

can grow to almost four inches wide. They also may bleed or twist the ovary and cause pain. Some medicines used to cause ovulation can raise the risk of getting these cysts.

Other types of benign ovarian cysts are less common: - endometriomas are caused by endometriosis. Endometriosis happens when the lining of the uterus grows outside of the uterus, dermoids come from cells present from birth and do not usually cause symptoms and cystadenomas are filled with watery fluid and can sometimes grow large. In some women, the ovaries make many small cysts. This is called polycystic ovary syndrome (PCOS). PCOS can cause problems with the ovaries and with getting pregnant.

Malignant (cancerous) cysts are rare. They are more common in older women. Cancerous cysts are ovarian cancer. For this reason, ovarian cysts should be checked by your doctor. Most ovarian cysts are not cancerous.

Ovarian cysts are common in women with regular periods. In fact, most women make at least one follicle or corpus luteum cyst every month. You may not be aware that you have a cyst unless there is a problem that causes the cyst to grow or if multiple cysts form. About 8% of premenopausal women develop large cysts that need treatment. Ovarian cysts are less common after menopause. Postmenopausal women with ovarian cysts are at higher risk for ovarian cancer.

At any age, see your doctor if you think you have a cyst. See your doctor also if you have symptoms such as bloating, needing to urinate more often, pelvic pressure or pain, or abnormal (unusual) vaginal bleeding. These can be signs of a cyst or other serious problem.

The most common causes of ovarian cysts include:- hormonal problems. Functional cysts usually go away on their own without treatment. They may be caused by hormonal problems or by drugs used to help you ovulate, endometriosis. Women with endometriosis can develop a type of ovarian cyst called an endometrioma. The endometriosis tissue may attach to the ovary and form a growth. These cysts can be painful during sex and during your period, pregnancy. An ovarian cyst normally develops in early pregnancy to help support the pregnancy until the placenta forms. Sometimes, the cyst stays on the ovary until later in the pregnancy and may need to be removed and severe pelvic infections. Infections can spread to the ovaries and fallopian tubes and cause cysts to form.

Most ovarian cysts are small and don't cause symptoms. If a cyst does cause symptoms, you may have pressure, bloating, swelling, or pain in the lower abdomen on the side of the cyst. This pain may be sharp or dull and may come and go. If a cyst ruptures, it can cause sudden, severe pain. If a cyst causes twisting of an ovary, you may have pain along with nausea and vomiting.

Less common symptoms include:- pelvic pain , dull ache in the lower back and thighs , problems emptying the bladder or bowel completely , pain during sex , unexplained weight gain , pain during your period , unusual (not normal) vaginal bleeding , breast tenderness and needing to urinate more often.

If you have symptoms of ovarian cysts, talk to your doctor. Your doctor may do a pelvic exam to feel for swelling of a cyst on your ovary. If a cyst is found, your doctor will either watch and wait or order tests to help plan treatment.

Tests include: - *ultrasound* test uses sound waves to create images of the body. With ultrasound, your doctor can see the cyst's shape, size, location

and mass (whether it is fluid-filled, solid, or mixed), *pregnancy test* to rule out pregnancy, *hormone level tests* to see if there are hormone-related problems and *blood test*.

If you are past menopause, your doctor may give you a test to measure the amount of cancer-antigen 125 (CA-125) in your blood. The amount of CA-125 is higher with ovarian cancer. In premenopausal women, many other illnesses or diseases besides cancer can cause higher levels of CA-125.If your doctor told you that you have an ovarian cyst and you have any of the following symptoms, get medical help right away:- pain with fever and vomiting , sudden, severe abdominal pain , faintness, dizziness, or weakness and rapid breathing.

These symptoms could mean that your cyst has broken open, or ruptured. Sometimes, large, ruptured cysts can cause heavy bleeding. The National Institutes of Health estimates that 5% to 10% of women have surgery to remove an ovarian cyst. Only 13% to 21% of these cysts are cancerous. Your cyst may require surgery if you are past menopause or if your cyst:- does not go away after several menstrual cycles , gets larger , looks unusual on the ultrasound and causes pain

If your cyst does not require surgery, your doctor may:- talk to you about pain medicine. Your doctor may recommend over-the-counter medicine or prescribe stronger medicine for pain relief , prescribe hormonal birth control if you have cysts often. Hormonal birth control, such as the pill, vaginal ring, shot, or patch, help prevent ovulation. This may lower your chances of getting more cysts. If your cyst requires surgery, your doctor will either remove just the cyst or the entire ovary. Surgery can be done in two different ways:- laparoscopy or laparotomy.Some ovarian cysts can become cancerous. But most ovarian cysts are not cancerous. The risk for ovarian cancer increases as you get older. Women who are past menopause with ovarian cysts have a higher risk for ovarian cancer. Talk to your doctor about your risk for ovarian cancer. Screening for ovarian cancer is not recommended for most women. This is because testing can lead to "false positives." A false positive is a test result that says a woman has ovarian cancer when she does not.

Most ovarian cysts do not affect the chances of getting pregnant. Sometimes, though, the illness causing the cyst can make it harder to get pregnant. Two conditions that cause ovarian cysts and affect fertility are:-endometriosis, which happens when the lining of the uterus grows outside of the uterus. Cysts caused by endometriosis are called endometriomas and polycystic ovary syndrome (PCOS), one of the leading causes of infertility (problems getting pregnant). Women with PCOS often have many small cysts on their ovaries.

Ovarian cysts are common during pregnancy. Typically, these cysts are benign (not cancerous) and harmless. Ovarian cysts that continue to grow during pregnancy can rupture or twist or cause problems during childbirth. Your doctor will monitor any ovarian cyst found during pregnancy.

2-2-5-2 Polycystic ovaries.

Are characterized by hormone dysfunction and multiple (over 10) ovarian cysts. It is associated with infertility.

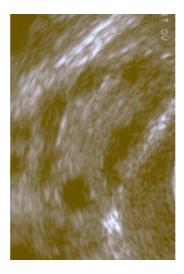


Fig. 2-126 Ultrasound image of a polycystic ovary

2-2-5-2 ovarian torsion.

Ovarian torsion is an ovarian cyst that has grown in size to the point at which it turns over on itself, twisting the suspensory ligament of the ovary and cutting off blood supply. The typical presentation of a woman with ovarian torsion is intense, severe, sudden-onset pain in the right or left lower quadrant. Ultrasound evaluation reveals decreased or absent Doppler flow to the ovary on the affected side. The diagnosis of ovarian torsion warrants emergency surgery to reverse the torsion, hopefully in time to avoid necrosis of the tissue.

2-2-6 ovarian masses

Ovarian <u>masses</u> is detected physically in the same manner as an ovarian cyst, by bimanual or pelvic examination. Confirmation is then obtained by ultrasound and further workup as necessary.Ovarian tumours are another serious disorder. The most common cancers arise from epithelial components or germ cells. 90% of ovarian cancers are derived from epithelium, these are termed ovarian adenocarcinomas. Most germ cell tumours are teratomas, which comprise cells from all 3 germ cell layers and are usually benign.Suspicion of an ovarian carcinoma on ultrasound examination includes characteristics such as complex, multiloculated, septated masses. The tumor marker CA-125 may be tested serologically, and an elevated level may support the diagnosis of ovarian cancer. This tumor marker is not always helpful, as it can be elevated in noncancerous conditions such as endometriosis, peritonitis, pregnancy, and liver disease. Ovarian cancer is an aggressive disease that is often not detected until late stages.

2-2-6-1 Cystic and semi-cystic ovarian masses.

Tumors can form in the ovaries, just as they form in other parts of the body. If tumors are non-cancerous, they are said to be benign. If they are cancerous, they are called malignant. The three types of ovarian tumors are:epithelial cell tumors start from the cells on the surface of the ovaries. These are the most common type of ovarian tumors, germ cell tumors start in the cells that produce the eggs. They can either be benign or cancerous. Most are benign and stromal tumors originate in the cells that produce female hormones.

Doctors aren't sure what causes ovarian cancer. They have identified, though, several risk factors, including:- age specifically women who have gone through menopause , smoking , obesity , not having children or not breastfeeding (however, using birth control pills seems to lower the risk) , taking fertility drugs (such as Clomid) , hormone replacement therapy and family or personal history of ovarian, breast, or colorectal cancer (having the BRCA gene can increase the risk)

Often, ovarian cysts don't cause any symptoms. You may not realize you have one until you visit your health care provider for a routine pelvic exam.

Ovarian cysts can, however, cause problems if they twist, bleed, or rupture.If you have any of the symptoms below, it's important to have them checked out. That's because they can also be symptoms of ovarian tumors. Ovarian cancer often spreads before it is detected.

Symptoms of ovarian cysts and tumors include:- pain or bloating in the abdomen , difficulty urinating, or frequent need to urinate , dull ache in the lower back , pain during sexual intercourse , painful menstruation and abnormal bleeding , weight gain , nausea or vomiting and loss of appetite, feeling full quickly

The obstetrician/gynecologist or your regular doctor may feel a lump while doing a routine pelvic exam. Most ovarian growths are benign. But a small number can be cancerous. That's why it's important to have any growths checked. Postmenopausal women in particular should get examined. That's because they face a higher risk of ovarian cancer.

Tests that look for ovarian cysts or tumors include:- ultrasound which uses sound waves to create an image of the ovaries , other imaging tests. Computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) are highly detailed imaging scans. The doctor can use them to find ovarian tumors and see whether and how far they have spread , hormone levels. The doctor may take a blood test to check levels of several hormones. These may include luteinizing hormone (LH), follicle stimulating hormone (FSH), estradiol, and testosterone , laparoscopy and CA-125. If the doctor thinks the growth may be cancerous, he might take a blood test to look for a protein called CA-125. Levels of this protein tend to be higher in some -- but not all -- women with ovarian cancer. This test is mainly used in women over age 35, who are at slightly higher risk for ovarian cancer. If the diagnosis is ovarian cancer, the doctor will use the diagnostic test results to determine whether the cancer has spread outside of the ovaries. If it has, the doctor will also use the results to determine how far it has spread. This diagnostic procedure is called staging. This helps the doctor plan your treatment.

Most ovarian cysts will go away on their own. If you don't have any bothersome symptoms, especially if you haven't yet gone through menopause, your doctor may advocate "watchful waiting." The doctor won't treat you. But the doctor will check you every one to three months to see if there has been any change in the cyst. Birth control pills may relieve the pain from ovarian cysts. They prevent ovulation, which reduces the odds that new cysts will form.

Surgery is an option if the cyst doesn't go away, grows, or causes you pain. There are two types of surgery: - laparoscopy uses a very small incision and a tiny, lighted telescope-like instrument. The instrument is inserted into the abdomen to remove the cyst. This technique works for smaller cysts and laparotomy involves a bigger incision in the stomach. Doctors prefer this technique for larger cysts and ovarian tumors. If the growth is cancerous, the surgeon will remove as much of the tumor as possible. This is called debulking. Depending on how far the cancer has spread, the surgeon may also remove the ovaries, uterus, fallopian tubes, omentum fatty tissue covering the intestines and nearby lymph nodes.

Other treatments for cancerous ovarian tumors include:- chemotherapy drugs given through a vein (IV), by mouth, or directly into the abdomen to kill cancer cells. Because they kill normal cells as well as cancerous ones, chemotherapy medications can have side effects, including nausea and vomiting, hair loss, kidney damage, and increased risk of infection. These side effects should go away after the treatment is done and r<u>adiation</u> -- highenergy X-rays that kill or shrink cancer cells. Radiation is either delivered from outside the body, or placed inside the body near the site of the tumor. This treatment also can cause side effects, including red skin, nausea, diarrhea, and fatigue. Radiation is not often used for ovarian cancer. Surgery, chemotherapy, and radiation may be given individually or together. It is possible for cancerous ovarian tumors to return. If that happens, you will need to have more surgery, sometimes combined with chemotherapy or radiation.

2-2-6-2 Solid ovarian masses.

Cystadenofibroma is a subset of epithelial ovarian neoplasms that are usually benign. A lesion with a solid portion that exhibits intense contrast enhancement is the prominent feature of cystadenofibroma that mimics malignancy. The presence of rims, plaques, or nodules that have low signal intensity on T2-weighted images and that range from 2 mm to 4 cm in a multiloculated cystic ovarian mass can suggest the diagnosis . The lowsignal-intensity foci correspond to intratumoral regions of dense fibrous tissue .



Fig. 2-127 38-year-old woman with ovarian mucinous cystadenofibroma. <u>CT scan shows large cystic mass with enhancing solid portion (*arrows*).</u>

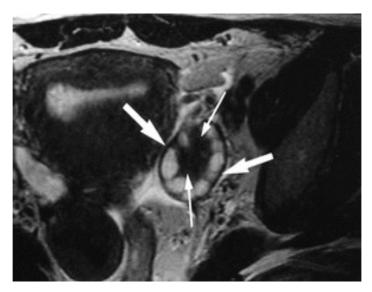


Fig. 2-128 43-year-old woman with ovarian serous cystadenofibroma. Axial T2-weighted (TR/TE, 2,000/80) (A), axial T1-weighted (600/15) (B), and axial contrast-enhanced T1-weighted (C) MR images show cystic lesion with solid nodular area (*thin arrows*) surrounded by thickened septa and wall with moderate enhancement (*thick arrows*).

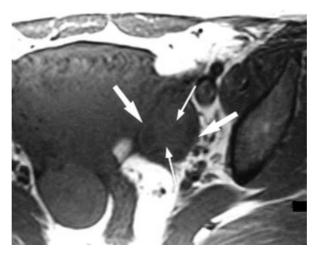


Fig. 2-129 43-year-old woman with ovarian serous cystadenofibroma. Axial T2-weighted (TR/TE, 2,000/80) (A), axial T1-weighted (600/15) (B), and axial contrast-enhanced T1-weighted (C) MR images show cystic lesion

with solid nodular area (*thin arrows*) surrounded by thickened septa and wall with moderate enhancement (*thick arrows*).

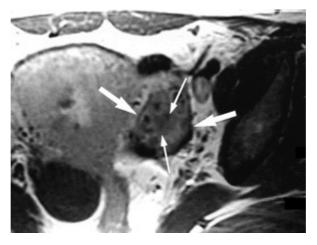


Fig. 2-130 43-year-old woman with ovarian serous cystadenofibroma. Axial T2-weighted (TR/TE, 2,000/80) (A), axial T1-weighted (600/15) (B), and axial contrast-enhanced T1-weighted (C) MR images show cystic lesion with solid nodular area (*thin arrows*) surrounded by thickened septa and wall with moderate enhancement (*thick arrows*).

To our knowledge, the imaging findings of ovarian adenofibroma have not been described in the English-language literature. In a case we encountered, this lesion appeared as a multiloculated cystic mass with enhancing septa and solid portions on MR images,

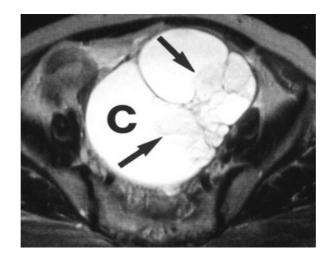


Fig. 2-131 62-year-old woman with ovarian clear cell adenofibroma. Axial T2-weighted (TR/TE, 2,000/80) (A), axial T1-weighted (600/15) (B), and axial contrast-enhanced T1-weighted (C) MR images show large cystic mass with enhancing multiple septa and solid portions (*arrows*). C = cystic portions of mass.

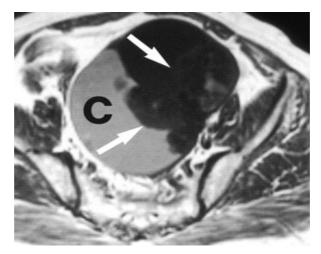


Fig. 2-132 62-year-old woman with ovarian clear cell adenofibroma. Axial T2-weighted (TR/TE, 2,000/80) (A), axial T1-weighted (600/15) (B), and axial contrast-enhanced T1-weighted (C) MR images show large cystic mass with enhancing multiple septa and solid portions (*arrows*). C = cystic portions of mass.

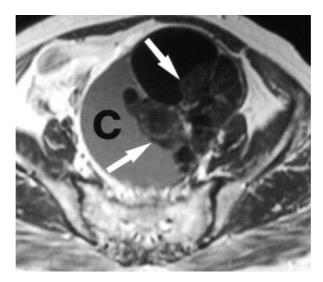


Fig. 2-133 62-year-old woman with ovarian clear cell adenofibroma. Axial

T2-weighted (TR/TE, 2,000/80) (A), axial T1-weighted (600/15) (B), and axial contrast-enhanced T1-weighted (C) MR images show large cystic mass with enhancing multiple septa and solid portions (*arrows*). C = cystic portions of mass.

Benign transitional cell (Brenner) tumors of the ovary compose approximately 2% of epithelial ovarian neoplasms. Brenner tumors are often discovered incidentally at surgery or pathologic examination. Extensive amorphous calcification in a solid mass or a solid component in a multilocular cystic mass is a characteristic finding. Low signal intensity on T2-weighted MR images may result from the abundant fibrous stroma. (Kimura, K.,1996)



Fig. 2-134 68-year-old woman with Brenner tumor. Radiograph shows dense calcification (*arrows*) in pelvis.

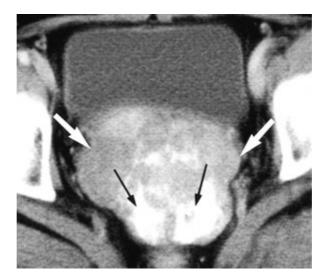


Fig. 2-135 68-year-old woman with Brenner tumor. CT scan shows solid pelvic mass (*white arrows*) with calcifications (*black arrows*).



Fig. 2-136 68-year-old woman with Brenner tumor. Axial T2-weighted (TR/TE, 2,000/80) (C), axial T1-weighted (600/15) (D), and axial contrastenhanced T1-weighted (E) MR images show enhancing ovarian solid mass (*arrows*). Low signal intensity on T2-weighted image is due to abundant fibrous stroma.

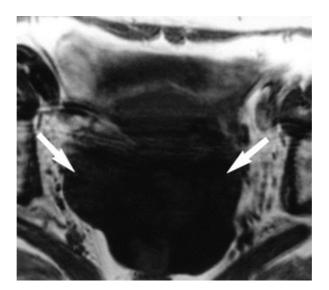


Fig 2-137 68-year-old woman with Brenner tumor. Axial T2-weighted (TR/TE, 2,000/80) (C), axial T1-weighted (600/15) (D), and axial contrastenhanced T1-weighted (E) MR images show enhancing ovarian solid mass (*arrows*). Low signal intensity on T2-weighted image is due to abundant fibrous stroma.

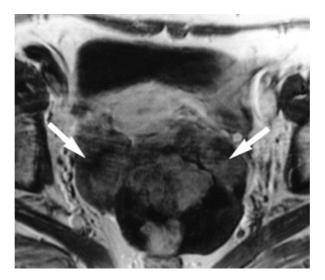


Fig. 2-138 68-year-old woman with Brenner tumor. Axial T2-weighted (TR/TE, 2,000/80) (C), axial T1-weighted (600/15) (D), and axial contrast-enhanced T1-weighted (E) MR images show enhancing ovarian solid mass (*arrows*). Low signal intensity on T2-weighted image is due to abundant fibrous stroma.

<u>2-3 Feamle infertility.</u>

<u>Female infertility refers to</u> infertility in female humans. It affects an estimated 48 million women with the highest prevalence of infertility affecting people in South Asia, Sub-Saharan Africa, North Africa/Middle East, and Central/Eastern Europe and Central Asia. Infertility is caused by many sources, including nutrition, diseases, and other malformations of the uterus. Infertility affects women from around the world, and the cultural and social stigma surrounding it varies.Fertility awareness is a type of natural family planning based on a woman's physical signs of ovulation, such as changes in cervical mucus consistency and basal (resting) body temperature. Keeping track of these symptoms may be helpful if a couple is trying to become pregnant or trying to avoid pregnancy.

If a woman is trying to become pregnant, having sex during the 5 days before she ovulates and the day she ovulates increases her chances of success.If a woman is trying to avoid pregnancy, avoiding sex until several days after she has ovulated helps prevent pregnancy (the human egg is typically fertile for only 12 to 24 hours after ovulation).Because intercourse before ovulation can lead to pregnancy, and ovulation does not always occur at the same time every month, fertility awareness is not the most reliable method of avoiding pregnancy.

2-3-1 Definition

There is no unanimous definition of female infertility, because the definition depends on social and physical characteristics which may vary by culture and situation. NICE guidelines state that: "A woman of reproductive age who has not conceived after 1 year of unprotected

vaginal sexual intercourse, in the absence of any known cause of infertility, should be offered further clinical assessment and investigation along with her partner. It is recommended that a consultation with a fertility specialist should be made earlier if the woman is aged 36 years or over, or there is a known clinical cause of infertility or a history of predisposing factors for infertility. According to the World Health Organization (WHO), infertility can be described as the inability to become pregnant, maintain a pregnancy, or carry a pregnancy to live birth. A clinical definition of infertility by the WHO and ICMART is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. Infertility can further be broken down into primary and secondary infertility. Primary infertility refers to the inability to give birth either because of not being able to become pregnant, or carry a child to live birth, which may include miscarriage or a stillborn child. ^{[5][6]} Secondary infertility refers to the inability to conceive or give birth when there was a previous pregnancy or live birth.

2-3-1-1 Prevalence

Female infertility varies widely by geographic location around the world. In 2010, there was an estimated 48.5 million infertile couples worldwide, and from 1990 to 2010 there was little change in levels of infertility in most of the world. In 2010, the countries with the lowest rates of female infertility included the South American countries of Peru, Ecuador and Bolivia, as well as in Poland, Kenya, and Republic of Korea. The highest rate regions included Eastern Europe, North Africa, the Middle East, Oceania, and Sub-Saharan Africa. The prevalence of primary infertility has increased since 1990, but secondary infertility has decreased overall. Rates decreased (although not prevalence) of female infertility in high-income, Central/Eastern Europe, and Central Asia regions.Sub-Saharan Africa has had decreasing levels of primary infertility from 1990 to 2010. Within the Sub-Saharan region, rates were lowest in Kenya, Zimbabwe, and Rwanda, while the highest rates were in Guinea, Mozambique, Angola, Gabon, and Cameroon along with Northern Africa near the Middle East. According to a 2004 DHS report, rates in Africa were highest in Middle and Sub-Saharan Africa, with East Africa's rates close behind.

In Asia, the highest rates of combined secondary and primary infertility was in the South Central region, and then in the Southeast region, with the lowest rates in the Western areas. The prevalence of female infertility in the Latin America/Caribbean region is typically lower than the global prevalence. However, the greatest rates occurred in Jamaica, Suriname, Haiti, and Trinidad and Tobago. Central and Western Latin America has some of the lowest rates of prevalence. The highest regions in Latin America and the Caribbean was in the Caribbean Islands and in less developed countries.

2-3-2 Causes and factors

Causes or factors of female infertility can basically be classified regarding whether they are acquired or genetic, or strictly by location.Although factors of female infertility can be classified as either acquired or genetic, female infertility is usually more or less a combination of nature and nurture. Also, the presence of any single risk factor of female infertility (such as smoking, mentioned further below) does not necessarily cause infertility, and even if a woman is definitely infertile, the infertility cannot definitely be blamed on any single risk factor even if the risk factor is present.

2-3-2-1 Acquired

According to the American Society for Reproductive Medicine (ASRM), Age, Smoking, Sexually Transmitted Infections, and Being Overweight or Underweight can all affect fertility. In broad sense, acquired factors practically include any factor that is not based on a genetic mutation, including any intrauterine exposure to toxins during fetal development, which may present as infertility many years later as an adult.

2-3-2-2 Age and female fertility

A woman's fertility is affected by her age. The average age of a girl's first period (menarche) is 12-13 (12.5 years in the United States, 12.72 in Canada, 12.9 in the UK), but, in postmenarchal girls, about 80% of the cycles are anovulatory in the first year after menarche, 50% in the third and 10% in the sixth year. A woman's fertility peaks in the early and mid 20s, after which it starts to decline, with this decline being accelerated after age 35. However, the exact estimates of the chances of a woman to conceive after a certain age are not clear, with research giving differing results. The chances of a couple to successfully conceive at an advanced age depend on many factors, including the general health of a woman and the fertility of the male partner.

2-3-2-3 Tobacco smoking

See also: Women and smoking § Unique gender differences and health

effects for Females. Tobacco smoking is harmful to the ovaries, and the degree of damage is dependent upon the amount and length of time a woman smokes or is exposed to a smoke-filled environment. Nicotine and other harmful chemicals in cigarettes interfere with the body's ability to create estrogen, a hormone that regulates folliculogenesis and ovulation. Also, cigarette smoking interferes with folliculogenesis, embryo transport, endometrial receptivity, endometrial angiogenesis, uterine blood flow and the uterine myometrium. Some damage is irreversible, but stopping smoking can prevent further damage. Smokers are 60% more likely to be infertile than non-smokers. Smoking reduces the chances of IVF producing a live birth by 34% and increases the risk of an IVF pregnancy miscarrying by 30%. Also, female smokers have an earlier onset of menopause by approximately 1-4 years.

2-3-2-4 Sexually transmitted infections

Sexually transmitted infections are a leading cause of infertility. They often display few, if any visible symptoms, with the risk of failing to seek proper treatment in time to prevent decreased fertility.

2-3-2-5 Body weight and eating disorders

Twelve percent of all infertility cases are a result of a woman either being underweight or overweight. Fat cells produce estrogen, in addition to the primary sex organs. Too much body fat causes production of too much estrogen and the body begins to react as if it is

on birth control, limiting the odds of getting pregnant. Too little body fat causes insufficient production of estrogen and disruption of the menstrual cycle. Both under and overweight women have irregular cycles in which ovulation does not occur or is inadequate. Proper nutrition in early life is also a major factor for later fertility. A study in the US indicated that approximately 20% of infertile women had a past or current eating disorder, which is five times higher than the general lifetime prevalence rate. A review from 2010 concluded that overweight and obese subfertile women have a reduced probability of successful fertility treatment and their pregnancies are associated with more complications and higher costs. In hypothetical groups of 1000 women undergoing fertility care, the study counted approximately 800 live births for normal weight and 690 live births for overweight and obese anovulatory women. For ovulatory women, the study counted approximately 700 live births for normal weight, 550 live births for overweight and 530 live births for obese women. The increase in cost per live birth in anovulatory overweight and obese women were, respectively, 54 and 100% higher than their normal weight counterparts, for ovulatory women they were 44 and 70% higher, respectively.

2-3-2-6 Chemotherapy

Chemotherapy poses a high risk of infertility. Chemotherapies with high risk of infertility include procarbazine and other alkylating drugs such as cyclophosphamide, ifosfamide, busulfan, melphalan, chlorambucil and chlormethine. Drugs with medium risk include doxorubicin and platinum analogs such as cisplatin and carboplatin. On the other hand, therapies with low risk of gonadotoxicity include plant derivatives such as vincristine and vinblastine, antibiotics such as bleomycin and dactinomycin and antimetabolites such as methotrexate, mercaptopurine and 5-fluorouracil.

Female infertility by chemotherapy appears to be secondary to premature ovarian failure by loss of primordial follicles. This loss is not necessarily a direct effect of the chemotherapeutic agents, but could be due to an increased rate of growth initiation to replace damaged developing follicles. Antral follicle count decreases after three series of chemotherapy, whereas follicle stimulating hormone (FSH) reaches menopausal levels after four series. Other hormonal changes in chemotherapy include decrease in inhibin B and anti-Müllerian hormone levels.Women may choose between several methods of fertility preservation prior to chemotherapy, including cryopreservation of ovarian tissue, oocytes or embryos.

2-3-2-7 Other acquired factors

Adhesions secondary to surgery in the peritoneal cavity is the leading cause of acquired infertility. A meta-analysis in 2012 came to the conclusion that there is only little evidence for the surgical principle that using less invasive techniques, introducing less foreign bodies or causing less ischemia reduces the extent and severity of adhesions. Diabetes mellitus. A review of type 1 diabetes came to the result that, despite modern treatment, women with diabetes are at increased risk of female infertility, such as reflected by delayed puberty and menarche, menstrual irregularities (especially oligomenorrhoea), mild hyperandrogenism, polycystic ovarian syndrome, fewer live born children and possibly earlier menopause. Animal models indicate that abnormalities on the molecular level caused by diabetes include defective leptin, insulin and kisspeptin signalling. Significant liver or kidney disease. Thrombophilia. Cannabis smoking, such as of marijuana causes disturbances in the endocannabinoid system, potentially causing infertility. Radiation, such as in radiation therapy. The radiation dose to the ovaries that generally causes permanent female infertility is 20.3 Gy at birth, 18.4 Gy at 10 years, 16.5 Gy at 20 years and 14.3 Gy at 30 years.^[30] After total body irradiation, recovery of gonadal function occurs in 10–14% of cases, and the number of pregnancies observed after hematopoietic stem cell transplantation involving such as procedure is lower than 2%.

2-3-2-8 Genetic factors

There are many genes wherein mutation causes female infertility, as shown in table below. Also, there are additional conditions involving female infertility which are believed to be genetic but where no single gene has been found to be responsible, notably Mayer-Rokitansky-Küstner-Hauser Syndrome (MRKH). Finally, an unknown number of genetic mutations cause a state of subfertility, which in addition to other factors such as environmental ones may manifest as frank infertility.Chromosomal abnormalities causing female infertility include Turner syndrome.Some of these gene or chromosome abnormalities cause intersexed conditions, such as androgen insensitivity syndrome.

Genes wherein mutation causes female infertility

Gene	Encoded protein	Effect of deficiency
BMP15	Bone morphogenetic	Hypergonadotrophic ovarian
	protein 15	failure (POF4)

BMPR1B	Bone morphogenetic protein receptor 1B	Ovarian dysfunction, hypergonadotrophic hypogonadism and acromesomelic chondrodysplasia
CBX2; M33	Chromobox protein homolog 2 ; Drosophila polycomb class	Autosomal 46,XY, male-to- female sex reversal (phenotypically perfect
CHD7	Chromodomain-helicase- DNA-binding protein 7	females) CHARGE syndrome and Kallmann syndrome (KAL5)
DIAPH2	Diaphanous homolog 2	Hypergonadotrophic, premature ovarian failure (POF2A)
FGF8	Fibroblast growth factor 8	Normosmic hypogonadotrophic hypogonadism and Kallmann syndrome (KAL6)
FGFR1	Fibroblast growth factor receptor 1	Kallmann syndrome (KAL2)
HFM1		Primary ovarian failure [[]
FSHR	FSH receptor	Hypergonadotrophic hypogonadism and ovarian hyperstimulation syndrome
FSHB	Follitropin subunit beta	Deficiency of follicle- stimulating hormone, primary amenorrhoea and infertility

FOXL2	Forkhead box L2	Isolated premature ovarian failure (POF3) associated with BPES type I; FOXL2 402C> G mutations associated with human
FMR1	Fragile X mental retardation	granulosa cell tumours Premature ovarian failure n (POF1) associated with premutations
GNRH1	Gonadotropin releasing hormone	Normosmic hypogonadotrophic hypogonadism
GNRHR	GnRH receptor	Hypogonadotrophic hypogonadism
KAL1	Kallmann syndrome	Hypogonadotrophic hypogonadism and insomnia, X-linked Kallmann syndrome (KAL1)
KISS1R ; GPR54	KISS1 receptor	Hypogonadotrophic hypogonadism
LHB	Luteinizing hormone beta polypeptide	Hypogonadism and pseudohermaphroditism
LHCGR	LH/choriogonadotrophin receptor	Hypergonadotrophic hypogonadism (luteinizing hormone resistance)
DAX1	Dosage-sensitive sex reversal, adrenal hypoplasia	X-linked congenital adrenal hypoplasia with

		hypogonadotrophic
	critical region, on	hypogonadism; dosage-
	chromosome X, gene 1	sensitive male-to-female sex
		reversal
		46,XY male-to-female sex
		reversal and streak gonads and
NR5A1;		congenital lipoid adrenal
SF1	Steroidogenic factor 1	hyperplasia; 46,XX gonadal
		dysgenesis and 46,XX primary
		ovarian insufficiency
DODID	Premature ovarian failure	Hypergonadotrophic, primary
POF1B	1B	amenorrhea (POF2B)
		Normosmic
	D 11	hypogonadotrophic
PROK2	Prokineticin	hypogonadism and Kallmann
		syndrome (KAL4)
PROKR2	Prokineticin receptor 2	Kallmann syndrome (KAL3)
	Den en die familie manhau	46,XX, female-to-male sex
RSPO1	R-spondin family, member 1	reversal (individuals contain
		testes)
		Mutations lead to 46,XY
SRY	Sex-determining region Y	females; translocations lead to
		46,XX males
		Autosomal 46,XY male-to-
SOX9	SRY-related HMB-box gene 9	female sex reversal
		(campomelic dysplasia)
STAG3	Stromal antigen 3	Premature ovarian failure ^[36]

		Normosmic
TAC3	Tachykinin 3	hypogonadotrophic
		hypogonadism
		Normosmic
TACR3	Tachykinin receptor 3	hypogonadotrophic
		hypogonadism
7D1	zona pellucida glycoprotein	Dysfunctional zona pellucida
ZP1	1	formation ^[37]

By location

2-3-2-9 Hypothalamic-pituitary factors.

Hypothalamic dysfunction and hyperprolactinemia.

2-3-2-10 Ovarian factors

Chemotherapy (as detailed previously) with certain agents have a high risk of toxicity on the ovaries , many genetic defects (as also detailed previously) also disturb ovarian function , polycystic ovary syndrome (also see infertility in polycystic ovary syndrome) , anovulation. Female infertility caused by anovulation is called "anovulatory infertility", as opposed to "ovulatory infertility" in which ovulation is present , diminished ovarian reserve, also see Poor Ovarian Reserve , premature_menopause , menopause , luteal dysfunction , gonadal dysgenesis and ovarian cancer.

2-3-2-11 Tubal (ectopic)/peritoneal factors

Endometriosis (also see endometriosis and infertility), pelvic adhesions, Pelvic inflammatory disease (PID, usually due to chlamydia), t<u>ubal</u>

occlusion , tubal dysfunction and Previous ectopic pregnancy. A randomized study in 2013 came to the result that the rates of intrauterine pregnancy 2 years after treatment of ectopic pregnancy are approximately 64% with radical surgery, 67% with medication, and 70% with conservative surgery.^[43] In comparison, the cumulative pregnancy rate of women under 40 years of age in the general population over 2 years is over 90%.^[2]

2-3-2-12 Uterine factors

Uterine malformations, Uterine fibroids, a<u>sherman's Syndrome</u>, t<u>mplantation failure</u> without any known primary cause. It results in negative pregnancy test despite having performed e.g. embryo transfer and previously, a bicornuate uterus was thought to be associated with infertility but recent studies have not confirmed such an association.

2-3-2-13 Cervical factors

Cervical stenosis , antisperm antibodies and non-receptive cervical mucus[.]

2-3-2-14 Vaginal factors

Vaginismus and vaginal obstruction.

2-3-3 Diagnosis

Diagnosis of infertility begins with a medical history and physical exam. The healthcare provider may order tests, including the following:Lab tests:- hormone testing, to measure levels of female hormones at certain times during a menstrual cycle , day 2 or 3 measure of FSH and estrogen, to assess ovarian reserve , measurements of thyroid function (a thyroid stimulating hormone (TSH) level of between 1 and 2 is considered optimal for conception) , measurement of progesterone in the second half of the cycle to help confirm ovulation and a<u>nti-Müllerian hormone</u> to estimate ovarian reserve.

2.3.4 Examination and imaging

An endometrial biopsy, to verify ovulation and inspect the lining of the uterus , laparoscopy, which allows the provider to inspect the pelvic organs , fertiloscopy, a relatively new surgical technique used for early diagnosis (and immediate treatment) , Pap smear, to check for signs of infection , pelvic exam, to look for abnormalities or infection , a postcoital test, which is done soon after intercourse to check for problems with sperm surviving in cervical mucous (not commonly used now because of test unreliability) , hysterosalpingography or sonosalpingography, to check for tube patency and Sonohysterography to check for uterine abnormalities.There are genetic testing techniques under development to detect any mutation in genes associated with female infertility.^[34]

Initial diagnosis and treatment of infertility is usually made by obstetrician/gynecologists or women's health nurse practitioners. If initial treatments are unsuccessful, referral is usually made to physicians who are fellowship trained as reproductive endocrinologists. Reproductive endocrinologists are usually obstetrician/gynecologists with advanced training in reproductive endocrinology and infertility (in North America). These physicians treat reproductive disorders affecting not only women but also men, children, and teens.

Usually reproductive endocrinology & infertility medical practices do not see women for general maternity care. The practice is primarily focused on helping their women to conceive and to correct any issues related to recurring pregnancy loss.

2-3-5 Prevention

Acquired female infertility may be prevented through identified interventions:*Maintaining a healthy lifestyle*. Excessive exercise, consumption of caffeine and alcohol, and smoking have all been associated with decreased fertility. Eating a well-balanced, nutritious diet, with plenty of fresh fruits and vegetables, and maintaining a normal weight, on the other hand, have been associated with better fertility prospects.

Treating or preventing existing diseases. Identifying and controlling chronic diseases such as diabetes and hypothyroidism increases fertility prospects. Lifelong practice of safer sex reduces the likelihood that sexually transmitted diseases will impair fertility; obtaining prompt treatment for sexually transmitted diseases reduces the likelihood that such infections will do significant damage. Regular physical examinations (including pap smears) help detect early signs of infections or abnormalities.

Not delaying parenthood. Fertility does not ultimately cease before menopause, but it starts declining after age 27 and drops at a somewhat greater rate after age 35. Women whose biological mothers had unusual or abnormal issues related to conceiving may be at particular risk for some conditions, such as premature menopause, that can be mitigated by not delaying parenthood.

Egg freezing. A woman can freeze her eggs preserve her fertility. By using egg freezing while in the peak reproductive years, a woman's oocytes are cryogenicaly frozen and ready for her use later in life, reducing her chances of female infertility.

Social stigma 2-3-6

Social stigma due to infertility is seen in many cultures throughout the world in varying forms. Often, when women cannot conceive, the blame is put on them, even when approximately 50% of infertility issues come from the man . In addition, many societies only tend to value a woman if she is able to produce at least one child, and a marriage can be considered a failure when the couple cannot conceive. The act of conceiving a child can be linked to the couple's consummation of marriage, and reflect their social role in society. This is seen in the "African infertility belt", where infertility is prevalent in Africa which includes countries spanning from Tanzania in the east to Gabon in the west In this region, infertility is highly stigmatized and can be considered a failure of the couple to their societies. This is demonstrated in Uganda and Nigeria where there is a great pressure put on childbearing and its social implications. This is also seen in some Middle Eastern societies including Egypt and Pakistan.

Wealth is sometimes measured by the number of children a woman has, as well as inheritance of property. Children can influence financial security in many ways. In Nigeria and Cameroon, land claims are decided by the number of children. Also, in some Sub-Saharan countries women may be neglected inheritance if she did not bear and children In some African and Asian countries a husband can neglect his infertile wife of food, shelter and other basic necessities like clothing. In Cameroon, a woman may lose access to land from her husband and left on her own in old age.

In many cases, a woman who cannot bear children is excluded from social and cultural events including traditional ceremonies. This stigmatization is seen in Mozambique and Nigeria where infertile women have been treated as outcasts to society. This is a humiliating practice which devalues infertile women in society. In the Macua tradition, pregnancy and birth are considered major life events for a woman, with the ceremonies of nthaa´ra and ntha´ara no mwana, which can only be attended by women who have been pregnant and have had a baby.

The effect of infertility can lead to social shaming from internal and social norms surrounding pregnancy, which affects women around the world. When pregnancy is considered such an important event in life, and considered a "socially unacceptable condition", it can lead to a search for treatment in the form of traditional healers and expensive Western treatments. The limited access to treatment in many areas can lead to extreme and sometimes illegal acts in order to produce a child.

2-3-7 Marital role

Men in some countries may find another wife when their first cannot produce a child, hoping that by sleeping with more women he will be able to produce his own child. This can be prevalent in some societies, including Cameroon, Nigeria, Mozambique, Egypt, Botswana, and Bangladesh, among many more where polygamy is more common and more socially acceptable.In some cultures, including Botswana and Nigeria, women can select a woman with whom she allows her husband to sleep with in hopes of conceiving a child. Women who are desperate for children may compromise with her husband to select a woman and accept duties of taking care of the children to feel accepted and useful in society.

Women may also sleep with other men in hopes of becoming pregnant. This can be done for many reasons including advice from a traditional healer, or finding if another man was "more compatible". In many cases, the husband was not aware of the extra sexual relations and would not be informed if a woman became pregnant by another man. This is not as culturally acceptable however, and can contribute to the gendered suffering of women who have fewer options to become pregnant on their own as opposed to men.

Men and women can also turn to divorce in attempt to find a new partner with whom to bear a child. Infertility in many cultures is a reason for divorce, and a way for a man or woman to increase his/her chances of producing an heir. When a woman is divorced, she can lose her security that often comes with land, wealth, and a family. This can ruin marriages and can lead to distrust in the marriage. The increase of sexual partners can potentially result with the spread of disease including HIV/AIDS, and can actually contribute to future generations of infertility.

2-3-8 Domestic abuse

The emotional strain and stress that comes with infertility in the

household can lead to the mistreatment and domestic abuse of a woman. The devaluation of a wife due to her inability to conceive can lead to domestic abuse and emotional trauma such as victim blaming. Women are sometimes or often blamed as the cause of a couples' infertility, which can lead to emotional abuse, anxiety, and shame. In addition, blame for not being able to conceive is often put on the female, even if it is the man who is infertile. Women who are not able to conceive can be starved, beaten, and may be neglected financially by her husband as if she had no child bearing use to him. The physical abuse related to infertility may result from this and the emotional stress that comes with it. In some countries, the emotional and physical abuses that come with infertility can potentially lead to assault, murder, and suicide.^[63]

2-3-9 Mental and psychological impact

Many infertile women tend to cope with immense stress and social stigma behind their condition, which can lead to considerable mental distress The long-term stress involved in attempting to conceive a child and the social pressures behind giving birth can lead to emotional distress that may manifest as mental disease. Women who suffer from infertility might deal with psychological stressors such as denial, anger, grief, guilt, and depression. There can be considerable social shaming that can lead to intense feelings of sadness and frustration that potentially contribute to depression and suicide. (Legendre G,2012)

Chapter three

Methodology

Chapter three Methodology

3-1 Material

The data of this study collected by Aloka SSD 500 with convex 3.5 MHRz and endovaginal probs.

3-2 Population of the study

This study consisted of female complaining from primary infertility with different clinical symptoms and manifestation, visited the ultrasound clinic for examination.

3-3 Sample and size of the study

The data of this study collected from 300 patients selected conveniently

3-4 Design of the study

This study is a corss-sectional, descriptive study

3-5 Method of data collection

3-5-1 Techniques

A pelvic ultrasound is a noninvasive diagnostic exam that produces images that are used to assess organs and structures within the female pelvis. A pelvic ultrasound allows quick visualization of the female pelvic organs and structures including the uterus, cervix, vagina, fallopian tubes and ovaries.

Ultrasound uses a transducer that sends out ultrasound waves at a frequency too high to be heard. The ultrasound transducer is placed on the skin, and the ultrasound waves move through the body to the organs and structures within. The sound waves bounce off the organs like an echo and return to the transducer. The transducer processes the reflected waves, which are then converted by a computer into an image of the organs or tissues being examined. The sound waves travel at different speeds depending on the type of tissue encountered - fastest through bone tissue and slowest through air. The speed at which the sound waves are returned to the transducer, as well as how much of the sound wave returns, is translated by the transducer as different types of tissue.

An ultrasound gel is placed on the transducer and the skin to allow for smooth movement of the transducer over the skin and to eliminate air between the skin and the transducer for the best sound conduction. Transvaginal ultrasound is a test used to look at a woman's reproductive organs, including the uterus, ovaries, and <u>cervix</u>.

Transvaginal means across or through the vagina. The ultrasound probe will be placed inside the vagina. You will lie down on a table with your knees bent. Your feet may be held in stirrups. You will be given a probe, called a transducer, to place into the vagina. The probe is covered with a condom and a gel. The probe sends out sound waves, which reflect off body structures. A computer receives these waves and uses them to create a picture.

The ultrasound technician or doctor can see the picture on a TV monitor. The health care provider will move the probe around the area to see the pelvic organs. In some cases, a special transvaginal ultrasound method called saline infusion sonography (SIS) may be needed to more clearly view the uterus.

You will be asked to undress, usually from the waist down. A transvaginal ultrasound is done with your bladder empty or partly filled.

The test is usually painless, although some women may have mild discomfort from the pressure of the probe. Only a small part of the probe is placed into the vagina.Transvaginal ultrasound may be done for the following problems: Abnormal findings on a physical exam, such as cysts, fibroid tumors, or other growths , Abnormal vaginal bleeding and menstrual problems , Certain types of infertility , Ectopic pregnancy , Pelvic pain and Transvaginal ultrasound is also used during pregnancy.

The pelvic structures or fetus is normal. An abnormal result may be due to many conditions. Some problems that may be seen include: Birth defects, Cancers of the uterus, ovaries, vagina, and other pelvic structures, Infection, including pelvic inflammatory disease , Growths in or around the uterus and ovaries (such as cysts or fibroids) and Twisting of the ovaries. There are no known harmful effects of transvaginal ultrasound on humans. Unlike traditional x-rays, there is no radiation exposure with this test.

A special type of transvaginal ultrasound is called a saline infusion sonography (SIS). This procedure involves inserting sterile salt water into the uterus before the ultrasound to help identify any possible masses. The saline solution stretches the uterus slightly, providing a more detailed picture of the inside of the uterus than a conventional ultrasound.

3-6 Protocols

The following points should be considered for all ultrasound examinations:the clinical details provided are sufficient to carry out the examination requested and the correct examination has been requested , relevant information is available from the case notes, previous investigations and other sources , the role of the ultrasound examination is understood in the clinical context for the patient , informed consent is obtained before proceeding with the examination , the necessity for the presence of a chaperone and/or an interpreter , a systematic scanning approach that can be modified according to the individual patient , the implications should the examination be incomplete , the need to extend the ultrasound examination, and/or proceed to additional imaging techniques .where necessary in accordance with locally agreed protocol , the after care of the patient , the potential risks involved in the procedure to the patient and appropriate national and local Health and Safety regulations including infection control.

The sonographer should:- Recognise his/her scope of practice and work within its boundaries ensure that a locally agreed written scheme of work is in place accept properly delegated responsibility, in accordance with local practice and guidelines An ultrasound examination should not be carried out unless a valid request has been received. The request should include such clinical details as are relevant to the examination, clear identification of the person requesting the examination and to whom the report should be directed.

The sonographer should be responsive to:- potential bio-effects of ultrasound and the need to minimise dose at all times , potential hazards arising from the particular ultrasound equipment , relative risks for each application , conditions where current recommendations contra-indicate the use of certain types of ultrasound equipment and current guidelines regarding replacement of ultrasound equipment. The sonographer is expected to:- have detailed knowledge of ultrasound equipment in order to ensure that it is appropriate for purpose , manipulate the equipment correctly so that patient diagnosis and management are not compromised , ensure that an agreed quality assurance programme is in place that incorporates the regular and inspection of ultrasound machines and auxiliary equipment.

The stated aim of quality assurance procedures applied to ultrasound equipment is to ensure consistent and acceptable levels of performance of the imaging system and image recording facilities. Most quality assurance protocols focus on the consistency. The acceptability of image quality may not be apparent from measurable changes in the parameters tested. The issue of what constitutes unacceptable equipment performance is still very difficult to assess objectively. In the absence of nationally accepted performance standards for ultrasound equipment, local and subjective evaluation is required.

We usually get better images during transabdominal ultrasound if the bladder is partially filled, so to help your examination we ask you to drink water prior to the assessment. Please empty your bladder 1 hour before your appointment, drink 2 glasses of water and try not to empty your bladder again until after your appointment. A full bladder moves bowel out from the pelvis into the abdomen, helping visualisation of the uterus and ovaries.

The bladder should not be so full that it causes pain. If your bladder is very full and painful, you should empty a small amount so you are more comfortable. You will be able to empty your bladder after the transabdominal ultrasound is completed and before the transvaginal ultrasound begins.

A pelvic ultrasound can be performed at any time during the menstrual cycle. Your referring doctor will let you know if it is more appropriate to

have your pelvic ultrasound at a particular time during your cycle. Most pelvic conditions can be adequately assessed at any time of the menstrual cycle.

The best time to have your pelvic scan is usually just after your period has finished. The timing of your scan may be more important if your doctor is concerned about an endometrial problem such as endometrial polyps (growths of the endometrium). The endometrial lining becomes thin just after the period has ceased, making polyps easier to view.

You will be asked to remove your clothes and put on a gown or cover for the procedure. Depending on your doctor's instructions and the reasons for the ultrasound, you might need to either have your bladder empty or partially filled. When your bladder is full, it actually lifts the intestines away and allows for a clearer picture of your pelvic organs. You can have this procedure performed during your period or if you're spotting, but if you are wearing a tampon, you will have to take it out before the ultrasound.

3-7 Data analysis:-

The collected data will be analyzed through statistical procedures, which include quantitative and descriptive analysis such as percentage, mean and standard deviation to obtain the results of this study.

Chapter four Results

Chapter four Results The main objective of this study was to investigate the potential of endovaginal probe in exploring the factors behind the primary infertility in Sudanese females. The study consisted of 300 female suffers from primary infertility visits the ultrasound clinic for diagnosis purposes.

Diagnosis	Frequency
Polycystic ovarian syndrome	122
Normal ovary	149
Follicle size	17
Cyst	12
total	300

Table 4-1 a frequency distribution table, shows the distribution of ultrasound diagnosis of ovaries using Transvaginal probe

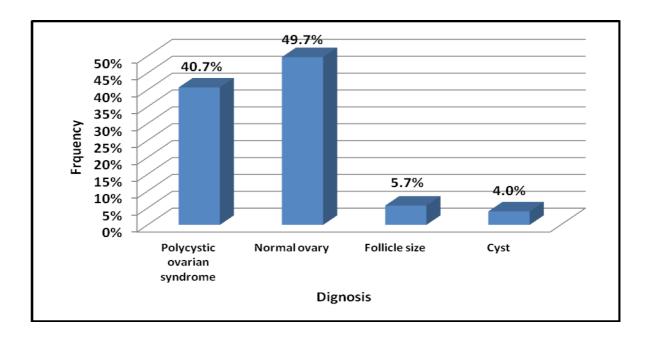


Table 4-1 a bar plot, shows the % distribution of ovaries diagnosis by ultrasound using Transvaginal probe

Remarks of infertility	Frequency
Fibroid	40
Male factor	83
Tube blocked	26

|--|

Table 4-2 a frequency distribution table, shows the distribution of infertility remarks for normal ovaries ultrasound scan outcome using Transvaginal probe

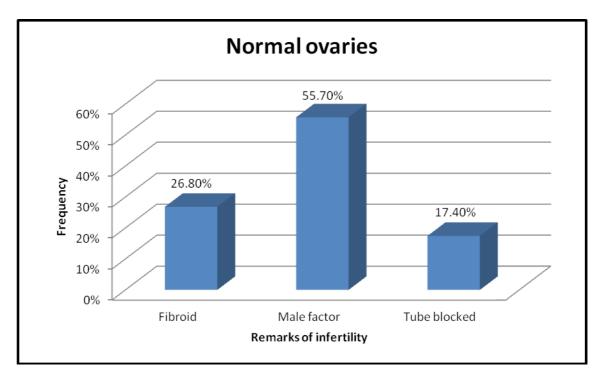
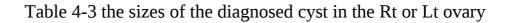


Figure 4-2 a bar plot, shows the distribution of infertility remarks % for normal ovaries ultrasound scan outcome using Transvaginal probe.

Size of Cyst in	Size of Cyst in
Lt ovary	Rt. ovary
13.32	9
18.92	10.5
22.1	26
25	30.25
40.95	39.69
64	81



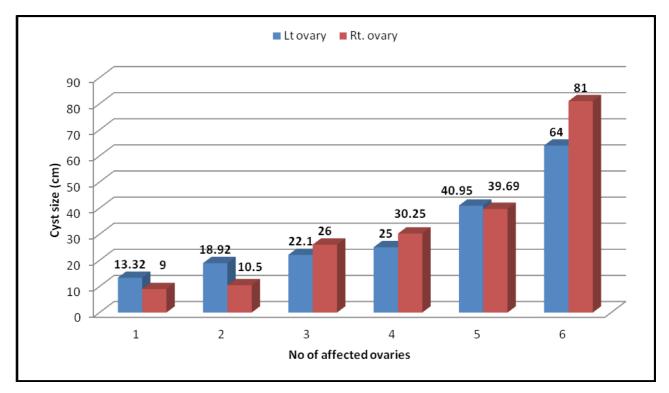


Figure 4-3 a bar plot show the sizes distribution of cyst in the Rt or Lt ovary diagnosed using transvaginal probe

Follicle size (cm)	Frequency
13-14	1
15-16	4
16-17	5
18-19	6

Table 4-4 a frequency distribution table, shows the distribution of follicles sizes for female in induction treatment using Transvaginal probe

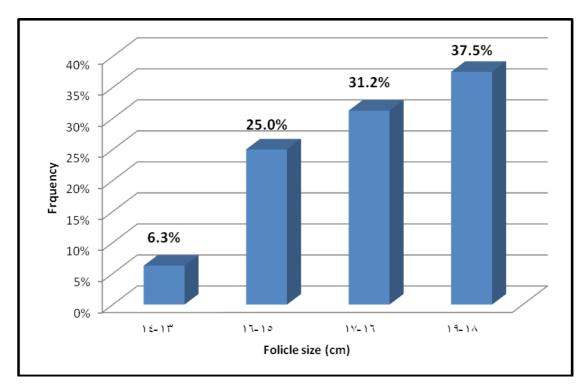


Figure 4-4 a bar plot shows % distribution of follicles sizes for female in induction treatment using Transvaginal probe

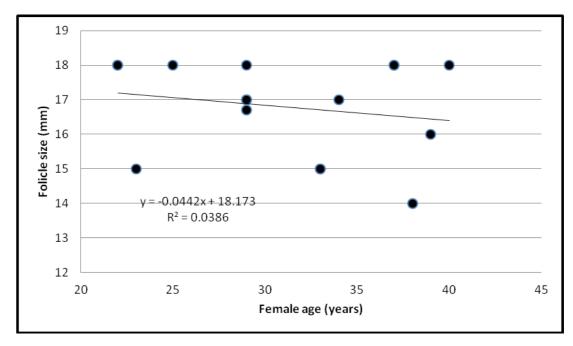


Figure 4-5 scatter plot shows the relationship between the female age and the size of the follicles in the induction treatment, follicle size decreases by 0.044 mm/year of age.

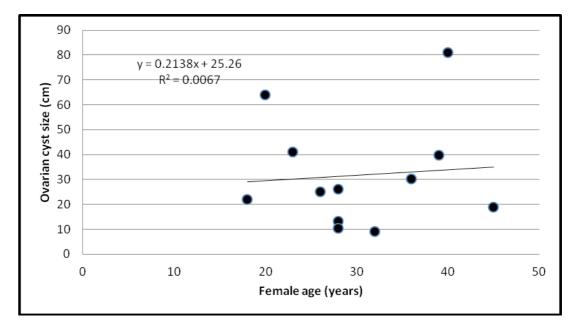


Figure 4-6 scatter plot shows the relationship between the female age and the size of the ovarian cyst, cyst size increases by 0.21 cm/year of age.

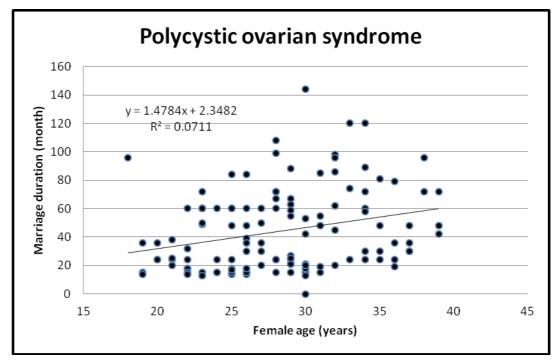


Figure 4-7 scatter plot shows the relationship between the female age and marriage duration in female with polycystic ovarian syndrome, marriage duration increases by 1.5 month/year of age.

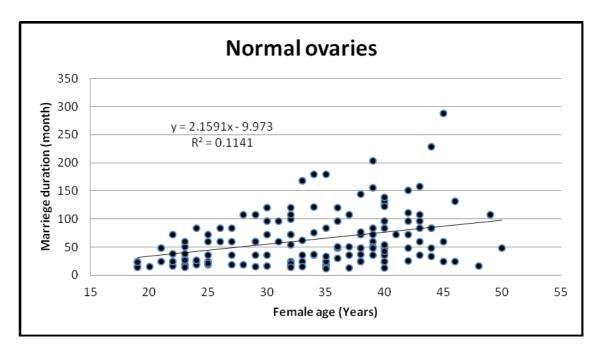


Figure 4-8 scatter plot shows the relationship between the female age and marriage duration in female with normal ovaries and other remarks of infertility, marriage duration increases by 2.2 month/year of age.

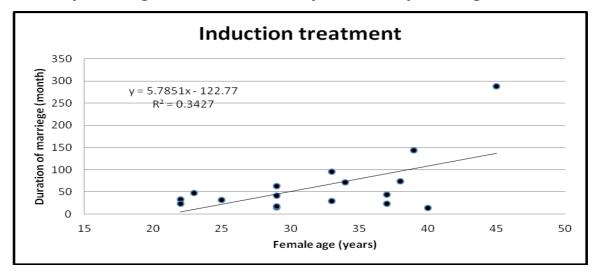


Figure 4-9 scatter plot shows the relationship between the female age and marriage duration in female with normal ovaries and under induction treatment for infertility, marriage duration increases by 5.8 month/year of age.

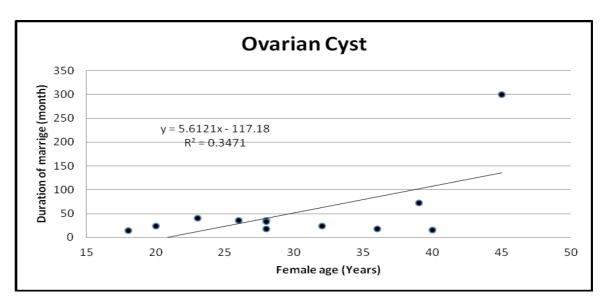


Figure 4-10 scatter plot shows the relationship between the female age and marriage duration in female with ovarian cyst, marriage duration increases by 5.6 month/year of age.

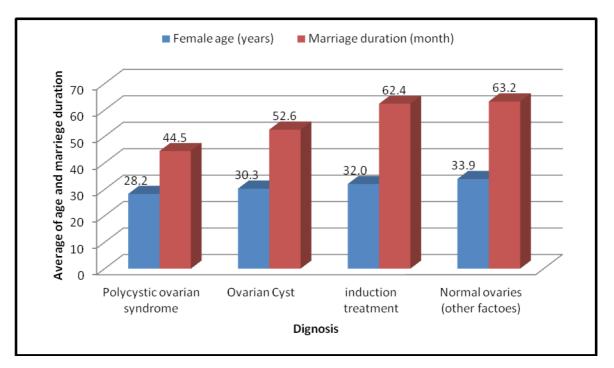


Figure 4-11 a bar blot shows the distribution of female infertility problems in respect average female age and marriage duration. With the lowest average age and marriage duration recorded by polycystic disease and relatively highest average female age and marriage duration scored by group with normal ovaries with others infertility factors.

Chpater five Discussion, conclusion and recommendation

Chpater five Discussion, conclusion and recommendation

5-1 Discussion

The main objective of this study was to investigate the potential of endovaginal probe in exploring the factors behind the primary infertility in Sudanese females. The study consisted of 300 female suffers from primary infertility visits the ultrasound clinic for diagnosis purposes. The mean age of the female enrolled in this study was 31.4±7.2 years which is range from 18 to 50 years old. Their mean marriage duration period was 55.2±45 month, which is ranged from 12 to 300 month. The diagnosis of these cases using endovaginal probe reveals that 122 (40.7%) females suffering from polycystic ovarian syndrome, 149 (49.7%) had normal ovaries but with other infertility remarks, 12 (4%) had ovarian cyst and 17 (5.7%) had no obvious reasons fro infertility and they are under stimulation (induction) treatment of ovulation (Table and Figure 4-1). This result implicate that the most obvious reasons for infertility were might not attributed to ovaries problems directly, although direct ovaries abnormality has mostly 40% of the underlying problem which represented mostly by polycystic ovarian syndrome and in small scale by ovarian cyst.

The presence of polycystic ovarian syndrome can be mostly observed clinically and confirmed by ultrasound or laboratory test. But other causes which is attributed to other factors than ovaries makes the ultrasound one of the potential tool for exploring the causes of primary infertility. The results of this study as mentioned earlier emphasizes that almost 50% of primary infertility attributed to other factors than ovarian problem (i.e. normal ovaries). This study concerning the category of normal ovaries found that in 83 cases (55.7%) out of 149 the causes of infertility were male problem and in 26.8% were attributed to the presence of fibroid and in 17.4% of this category attributed to blocked tubes. This result dictate that, investigation of infertility problems should start by excluding ovarian problem, then both partner should be enrolled in the investigation after that since after the exclusion of ovarian problem the causes might be anywhere including the male partner (Figure and Table (4-2).

The presence of ovarian cysts were unilaterally 6 in each ovary fro 12 females with average size of 30.7 and 32.7 cm for the Lt and Rt ovary respectively with minor increases of the ovarian cyst in the Rt one (Figure and Table 4-3). Also as mentioned before there is 17 female in induction treatment their follicular size ranged 14 to 18 mm (Figure and Table 4-4). The size of the follicles indicates the success of induction treatment and this size taken for several days for fertilization reasons. In this study it has been noticed that the size of the follicle regardless the day of scanning inversely proportion with the female age where the size of the follicle decreases by

0.044 mm/year. This means younger females will have optimum follicle size in a shorter period than older in respect to the decreases coefficient mentioned earlier (Figure 4-5). Also it has been found that the ovarian cyst in respect to female age had a direct relationship i.e. as the age of the female increase the cyst size increases; where it increases by 0.21cm/year. This means older women developed larger ovarian cyst than the youngest one (Figure 4-6).

Concerning the relationship of the female age with the duration of marriage in connection with the causes of infertility like in polycystic ovarian syndrome, those with normal ovaries but with other factors of infertility problem, those in induction treatment without known causes and ovarian cyst; in all of these situation the duration of marriage period directly increases with the female age which is equal to 1.5 month/year, 2.2 month/year, 5.8/year and 5.6/year for the mentioned causes respectively (Figure 4-7 to 4-10). This results implicate that the polycystic ovarian syndrome discovered very early within a few months while ovarian cyst take respectively longer time to be prevail mostly as the results of treatment or irregular cycle and so one. In case of polycystic ovarian syndrome the average marriage duration to average female age was 28.2 month to 44.2 years old. While for normal ovaries (other factors of infertilities) it was ≈ 40 month to 63.3 year. These results in summary indicates that the increases in female age in (average) connection with the increases of marriage duration in month (average) characterizes the pattern of the infertility problem ascendingly from polycystic ovarian syndrome (28.2 month, 44.5 years), ovarian cyst (30.3 month, 52.6 years), no obvious cause (32.0 month, 62.4 years) and normal ovaries with other infertility causes (32.9 month, 63,2 years) Figure 4-11.

5-2 Conclusion

This study was intended to explore and emphasis the ability of the endovaginal probe to investigate the causes of primary infertility in Sudanese females. The infertility problem considers one of the major health conditions, mostly can be treated if the underlying causes were diagnosed as soon as possible. Endovaginal ultrasound is considered as one of the important tool in revealing the mystery behind the primary infertility in most cases weather the problem confined to the ovary or other reproductive system regions including the husband.

Three hundred females were enrolled in this study all of them suffering from primary infertility for variable periods of time. All female underwent endovaginal ultrasound exam under by expert gynecologist with the presence and contribution of the researcher in the examination. The duration of marriage in moth and the age of the patient were recorded including the diagnosis, clinical remarks and size of the follicles and cyst if present.

The result of this study showed that ≈50% had normal ovaries but with other infertility remarks, which includes: fibroid, male factor and blocked tubes, with the male factor represent the dominant factor in this category (55.7%). The results also highlights that the increases of female age (average) in relation to the increases of marriage duration (average) together portrayed the pattern of the infertility problem in ascending fashion from polycystic ovarian syndrome, ovarian cyst, unknown obvious cause and normal ovaries with other infertility causes.

5-3 Recommendatios

• All infertility investigation must be carried out using endovaginal probe

- The duration of marriage and female age should be taken as indicator for infertility problems.
- The size of the follicles in induction treatment should be related to the age of the female, which gives a good estimate of the time needed to reach a proper size.
- For further studies a large sample could be used where each category of primary infertility factor can be represented by sufficient data to generate an empirical equation that included the period of marriage, female age and the causes of infertility.

References

- Aarnio M, Sankila R, Pukkala E, et al. Cancer risk in mutation carriers of DNA-mismatch-repair genes. Int J Cancer. 1999; 81:214-8.
 [PubMed Abstract]
- AJR Am J Roentgenol ,emergencies. 2000; 174:651–656.
- American Cancer Society. (2011, December 5). *Ovarian Cancer*.
 Atlanta, GA:
- American Cancer Society. Ovarian Cancer: <u>Can Ovarian Cancer Be</u>
 <u>Found Early?</u> Atlanta, GA: American Cancer Society 2006.
- American College of Obstetricians and Gynecologists. ACOG
 Committee Opinion: The role of the generalist obstetrician in the early detection of ovarian cancer. Obstet Gynecol 2002; 100:1413-6.
 [PubMed Abstract]
- American College of Obstricians and Gynecologists Practice Bulletin: Alternatives to hysterectomy in the management of leiomyomas.
 Number 96, August 2008.Obstet Gynecol

- AndZiskin, M. C.372 G ter Haar Proc. IMechE Vol. 224 Part H: J.
 Engineering in Medicine JEIM613 F IMechE 2010 And Zachary, J.
 F. and umbilicoplacental hemodynamics during early
- Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in Series unselected for family history: a combined analysis of 22 studies. Am J Hum Genet. 2003; 72:1117-30. [PubMed Abstract]
- Atiomo WU, Pearson S, Shaw S et-al. Ultrasound criteria in the diagnosis of polycystic ovary syndrome (PCOS). Ultrasound Med Biol. 2000;26 (6): 977-80. <u>Ultrasound Med Biol (link)</u> <u>Pubmed citation</u>
- Azziz R, Carmina E, Dewailly D et-al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil. Steril. 2009;91 (2): 456-88.
 <u>doi:10.1016/j.fertnstert.2008.06.035</u> - <u>Pubmed citation</u>
- Balen A. Polycystic ovary syndrome and cancer. Hum. Reprod.
 Update. 7 (6): 522-5. <u>doi:10.1093/humupd/7.6.522</u> <u>Pubmed citation</u>
- Balen AH, Laven JS, Tan SL et-al. Ultrasound assessment of the polycystic ovary: international consensus definitions. Hum. Reprod. Update. 9 (6): 505-14. <u>doi:10.1093/humupd/dmg044</u> <u>Pubmed</u>
 <u>citation</u>
- Balen and K. Michelmore, "What is polycystic ovary syndrome? Are national views important?" Human Reproduction, vol. 17, no. 9, pp. 2219–2227, 2002. View at Google Scholar · View at Scopus
- Bell R, Petticrew M, Luengo S, Sheldon TA. Screening for ovarian cancer: a systematic review. Health Technology Assessment. 1998;
 2:1-84. [PubMed Abstract]

- Bergfeldt K, Rydh B, Granath F, et al. Risk of ovarian cancer in breast-cancer patients with a family history of breast or ovarian cancer: a population-based cohort study. Lancet. 2002; 360:891-4.
 [PubMed Abstract]
- Brinton, LA, Lamb EJ, Moghissi KS, et al. Ovarian cancer risk associated with varying causes of infertility. Fertil Steril. 2004; 82:405-14. [PubMed Abstract]
- Brown DL, Zou KH, Tempany CM, et al. Primary versus secondary ovarian malignancy: imaging findings of adnexal masses in the Radiology Diagnostic Oncology Group Study.Radiology 2001; 219:213–218.
- Buys SS, Partridge E, Greene MH, et al. Ovarian cancer screening in the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial: findings from the initial screen of a randomized trial. Am J Obstet Gynecol. 2005; 193:1630-9. [PubMed Abstract]
- C. A. Gougoutas, E. S. Siegelman, J. Hunt, and E. K. Outwater,
 "Pelvic endometriosis: various manifestations and MR imaging findings," American Journal of Roentgenology, vol. 175, no. 2, pp. 353–358, 2000. View at Google Scholar · View at Scopus
- Chernecky CC, Berger BJ (2013). Laboratory Tests and Diagnostic
 Procedures, 6th ed. St. Louis: Saunders.
- Chi DS, Eisenhauer EL, Zivanovic O, Sonoda Y, Abu-Rustum NR,
 Levine DA, Guile MW, Bristow RE, Aghajanian C, Barakat
- Christopher T: Computing the mechanical index. J Ultrasound Med 1999; 18:63– 8

- <u>Cohen JG, White M, Cruz A, et al</u>; In 2014, can we do better than
 CA125 in the early detection of ovarian cancer? World J Biol Chem.
 2014 Aug 26;5(3):286-300. doi: 10.4331/wjbc.v5.i3.286.
- Coleman RL, Ramirez PT, Gershenson DM. Neoplastic diseases of the ovary: Screening, benign and malignant epithelial and germ cell neoplasms, sex-cord stromal tumors. In: Lentz GM, Lobo RA, Gershenson DM, Katz VL, eds.Comprehensive Gynecology
- Dalecki D: Mechanical bioeffects of ultrasound. Annu Rev Biomed Eng 2004; 6:229 – 48.
- Deane C, Lees C: Doppler obstetric ultrasound: A graphical display of temporal changes in safety indices. Ultrasound Obstet Gynecol 2000; 15:418–23
- Dodge JE, Covens AL, Lacchetti C, et al; Preoperative identification of a suspicious adnexal mass: a systematic review and meta-analysis.
 Gynecol Oncol. 2012 Jul;126(1):157-66. doi: 10.1016/j.ygyno.2012.03.048. Epub 2012 Apr 6.
- Doody C, Porter H, Duck FA, Humphrey VF: In vitro heating of human fetal vertebra by pulsed diagnostic ultrasound.
 Ultrasound Med Biol 1999; 25:1289–94.
- Dunlop MG, Farrington SM, Carothers AD, et al. Cancer risk associated with germline DNA mismatch repair gene mutations. Hum Mol Genet. 1997; 6:105-10. [PubMed Abstract]
- E. Bouic-Pagès, H. Perrochia, S. Mérigeaud, P. Y. Giacalone, and P. Taourel, "Corrélations anatomopathologiques: IRM des tumeurs ovariennes primitives," Journal de Radiologie, vol. 90, no. 7-8, pp. 787–802, 2009. View at Publisher · View at Google Scholar

- E. K. Outwater and D. G. Mitchell, "Magnetic resonance imaging techniques in the pelvis," Magnetic Resonance Imaging Clinics of North America, vol. 2, no. 2, pp. 161–188, 1994. View at Google Scholar · View at Scopus
- E. Outwater, M. L. Schiebler, R. S. Owen, and M. D. Schnall,
 "Characterization of hemorrhagic adnexal lesions with MR imaging: blinded reader study," Radiology, vol. 186, no. 2, pp. 489–494, 1993. View at Google Scholar · View at Scopus
- E. S. Siegelman and E. K. Outwater, "Tissue characterization in the female pelvis by means of MR imaging," Radiology, vol. 212, no. 1, pp. 5–18, 1999. View at Google Scholar · View at Scopus
- Edmondson RJ, Monaghan JM. The epidemiology of ovarian cancer.
 Int J Gynecol Cancer. 2001; 11:423-9. [PubMed Abstract]
- F. Minutoli, A. Blandino, M. Gaeta, M. Lentini, and I. Pandolfo,
 "Twisted ovarian fibroma with high signal intensity on T1-weighted MR image: a new sign of torsion of ovarian tumors?" European Radiology, vol. 11, no. 7, pp. 1151–1154, 2001. View at Publisher · View at Google Scholar · View at Scopus
- Fischbach FT, Dunning MB III, eds. (2009). Manual of Laboratory and Diagnostic Tests, 8th ed. Philadelphia: Lippincott Williams and Wilkins.
- Ford D, Easton DF, Stratton M, et al. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. Am J Hum Genet. 1998; 62:676-89. [PubMed Abstract]
- Fowlkes JB, Bioeffects Committee of the American Institute of Ultrasound in Medicine: American Institute of Ultrasound in

Medicine consensus report on potential bioeffects of diagnostic ultrasound: Executive summary. J Ultrasound Med 2008; 27:503–15

- Franks S. Controversy in clinical endocrinology: diagnosis of polycystic ovarian syndrome: in defense of the Rotterdam criteria. J. Clin. Endocrinol. Metab. 2006;91 (3): 786-9. <u>doi:10.1210/jc.2005-2501</u> <u>Pubmed citation</u>
- Funt SA, Hann LE. Detection and characterization of adnexal masses.
 Radiol Clin North Am 2002; 40:591–608.
- G. M. Kalish, M. D. Patel, M. L. D. Gunn, and T. J. Dubinsky,
 "Computed tomographic and magnetic resonance features of gynecologic abnormalities in women presenting with acute or chronic abdominal pain," Ultrasound Quarterly, vol. 23, no. 3, pp. 167–175,
 2007. View at Publisher · View at Google Scholar · View at PubMed · View at Scopus
- Garel L, Dubois J, Grignon A, Filiatrault D, Van Vliet G. US of the pediatric female pelvis: a clinical perspective. Radiographics 2001; 21:1393–1407.
- Gertig DM, Hunter DJ, Cramer DW, et al. Prospective study of talc
 use and ovarian cancer. J Natl Cancer Inst. 2000; 92:249-52. [PubMed
 Abstract]
- Ghossain MA, Buy JN, Ligneres C, et al. Epithelial tumors of the ovary: comparison of MR and CT findings. *Radiology* 1991; 181:863
 –870 [CrossRef] [Medline]
- <u>Goh W, Bohrer J, Zalud I</u>; Management of the adnexal mass in pregnancy. Curr Opin Obstet Gynecol. 2014 Apr;26(2):49-53. doi: 10.1097/GCO.000000000000048.

- Goodwin SC, Spies JB, Worthington-Kirsch R et al.
 Uterine artery embolization for treatment of leiomyomata: long-term outcomes from the FIBROID registry.Obstet Gynecol
- Grimes DA, Jones LB, Lopez LM, et al; Oral contraceptives for functional ovarian cysts. Cochrane Database Syst Rev. 2014 Apr 29;4:CD006134. doi: 10.1002/14651858.CD006134.pub5.
- Hernon M, McKenna J, Busby G, et al; The histology and management of ovarian cysts found in children and adolescents BJOG. 2010 Jan;117(2):181-4.
- Horder MM, Barnett SB, Vella GJ, Edwards MJ, Wood AK: In vivo heating of the guinea-pig fetal brain by pulsed ultra- sound and estimates of thermal index. Ultrasound Med Biol 1998; 24:1467–74
- Horowitz, N.S. (2011). <u>Management of adnexal masses in pregnancy</u>. *Clinical Obstetrics & Gynecology*; 54: 519–527
 <u>http://drjoea.googlepages.com/ovary</u>

http://emedicine.medscape.com/article/1343572-overview (free article and grades of OHSS)

http://emedicine.medscape.com/article/255865-diagnosis

http://emedicine.medscape.com/article/255865-overview

http://emedicine.medscape.com/article/403435-media

- <u>http://en.wikipedia.org/wiki/Main_Page</u>
- http://images.medicinenet.com/images/medicinenet/header/medicinen et_logo.png

http://nscfa.web.its.manchester.ac.uk/images/Fetal/Publications/anten atal_working_standards.pdf

http://radiopaedia.org/articles/ovarian-hyperstimulation-syndrome-1(free images/ radiology of OHSS)

- Image: http://teachmeanatomy.info/
- Image: http://techterms.com
- <u>http://www.advancedfertility.com/</u>

http://www.ajronline.org/cgi/reprint/173/5/1301.pdf (free article and images)

- http://www.babble.com/
 http://www.babycentre.co.uk/a7432/polycystic-ovary-syndromepcos#ixzz3Z3yVBipL
- http://www.babycentre.co.uk/a7432/polycystic-ovary-syndromepcos#ixzz3Z3zH4wfQ
- l http://www.bma.org.uk/ap.nsf/Content/Hubethicsconsentandcapacity
- http://www.cancer.ca/en/?region=on
- http://www.cancerresearchuk.org/home/

http://www.drspock.com/article/0,1510,5335,00.html

http://www.emedicinehealth.com/ovarian_cysts/article_em .htm

- http://www.glowm.com/
- Ihttp://www.innerbody.com/

http://www.jultrasoundmed.org/cgi/reprint/21/8/879 (free article and images)

http://www.jultrasoundmed.org/content/21/8/879.full.pdf(f ree article on hemorrhagic cysts of ovary)

- http://www.mayoclinic.org/~/media/images/mayologo.ashx
- Ihttp://www.medscape.com
- http://www.merckmanuals.com/professional
- http://www.mskcc.org/
- http://www.ncbi.nlm.nih.gov/pubmed
- http://www.nlm.nih.gov/medlineplus/medlineplus.html
- http://www.patient.co.uk/
- http://www.radiologyinfo.org/
- l http://www.rcog.org.uk/resources/Public/pdf/CGA_No6.pdf
- l http://www.rcr.ac.uk/index.asp?PageID=310&PublicationID=73
- 1 http://www.thefreedictionary.co/
- http://www.uptodate.com/index
- http://www.womenshealth.gov/index.html
- https://www.womentowomen.com/
- Imaoka, A. Wada, Y. Kaji et al., "Developing an MR imaging strategy for diagnosis of ovarian masses," Radiographics, vol. 26, no. 5, pp. 1431–1448, 2006. View at Publisher · View at Google Scholar · View at PubMed · View at Scopus
- J. A. Spencer and S. Ghattamaneni, "MR imaging of the sonographically indeterminate adnexal mass," Radiology, vol. 256, no. 3, pp. 677–694, 2010. View at Publisher · View at Google Scholar · View at PubMed · View at Scopus

- J. A. Spencer, R. Forstner, T. M. Cunha, and K. Kinkel, "ESUR guidelines for MR imaging of the sonographically indeterminate adnexal mass: an algorithmic approach," European Radiology, vol. 20, no. 1, pp. 25–35, 2010. View at Publisher · View at Google Scholar · View at Scopus
- J. Acoust. Soc. Am., 2004, 113, 2912–2926.15 Tarantal, A. F. and Canfield, D. R.
- J. M. Hawnaur, K. Reynolds, and C. McGettigan, "Magnetic resonance imaging of actinomycosis presenting as pelvic malignancy," The British Journal of Radiology, vol. 72, pp. 1006–1011, 1999. View at Google Scholar · View at Scopus
- J. Ultrasound Med. , 2008, 27 , 565–592. 21 Fatemi, M., Ogburn, P.
 L., and Greenleaf, J. F.J. Thermal Biol.
- J.E.E. Fleming, I.H. Spencer and M. Nicholson ., in Clinical
 Diagnostic Ultrasound, Baxter G M, Paul L P Allan and Patricia
 Morley, Eds. Blackwell Publishing. 2nd Edition, 1999.
- Jacobs IJ, Skates SJ, MacDonald N, et al. Screening for ovarian cancer: a pilot randomized controlled trial. Lancet. 1999; 353:1207-10. [PubMed Abstract]
- Jarvela IY, Sladkevicius P, Kelly S, Ojha K, Nargund G, Campbell S.
 Three-dimensional sonographic and power Doppler characterization of ovaries in late follicular phase.
- Joja I, Asakawa T, Mitsumori A, et al. Struma ovarii: appearance on MR images. *Abdom Imaging* 1998; 23:652 –656 [CrossRef] [Medline]
- Joja I, Okuno K, Tsunoda M, et al. Sclerosing stromal tumor of the ovary: US, MR, and dynamic MR findings. *J Comput Assist Tomogr* 2001; 25:201 –206 [CrossRef] [Medline]

- K. Kinkel, K. A. Frei, C. Balleyguier, and C. Chapron, "Diagnosis of endometriosis with imaging: a review," European Radiology, vol. 16, no. 2, pp. 285–298, 2006. View at Publisher · View at Google Scholar · View at PubMed · View at Scopus
- K. Tamai, T. Koyama, T. Saga et al., "MR features of physiologic and benign conditions of the ovary," European Radiology, vol. 16, no. 12, pp. 2700–2711, 2006. View at Publisher · View at Google Scholar · View at PubMed · View at Scopus
- K. Togashi, K. Nishimura, I. Kimura et al., "Endometrial cysts: diagnosis with MR imaging," Radiology, vol. 180, no. 1, pp. 73–78, 1991. View at Google Scholar · View at Scopus
- Kaakaji Y, Nghiem HV, Nodell C, Winter TC. Sonography of obstetric and gynecologic emergencies, part II: gynecologic emergencies. AJR Am J Roentgenol 2000; 174:651–656.
- Katz VL. Benign gynecologic lesions: vulva, vagina, cervix, uterus, oviduct, ovary, ultrasound imaging of pelvic structures. In: Lentz GM, Lobo RA, Gershenson DM, Katz VL, eds.Comprehensive Gynecology
- Kauff ND, Mitra M, Robson ME, et al. Risk of Ovarian Cancer in BRCA1 and BRCA2 Mutation Negative Hereditary Breast Cancer Families. Journal of the National Cancer Institute. 2005; 97:1382-4.
 [PubMed Abstract]
- Kerlikowske K, Brown JS, Grady DG. Should women with familial ovarian cancer undergo prophylactic oophorectomy? Obstet Gynecol. 1992; 80:700-7. [PubMed Abstract]

- Kimura, K. Togashi, S. Kawakami et al., "Polycystic ovaries: implications of diagnosis with MR imaging," Radiology, vol. 201, no.
 2, pp. 549–552, 1996. View at Google Scholar · View at Scopus
- Kjaer SK, Mellemkjaer L, Brinton LA, Johansen C, Gridley G, Olsen JH. Tubal sterilization and risk of ovarian, endometrial and cervical cancer. A Danish population-based follow-up study of more than 65,000 sterilized women. Int J Epidemiol. 2004; 33:596-602.
 [PubMed Abstract]
- Legendre G, Catala L, Moriniere C, et al; Relationship between ovarian cysts and infertility: what surgery and when? Fertil Steril.
 2014 Mar;101(3):608-14. doi: 10.1016/j.fertnstert.2014.01.021.
- Levine D, Brown DL, Andreotti RF, et al; Management of asymptomatic ovarian and other adnexal cysts imaged at US: Society Radiology. 2010 Sep;256(3):943-54. Epub 2010 May 26.
- Lu Y, Tsuda K, Filly RA. US characterization of ovarian masses: a meta-analysis. Radiology 2000; 217:803–811.
- M. Bazot, I. Thomassin, R. Hourani, A. Cortez, and E. Darai,
 "Diagnostic accuracy of transvaginal sonography for deep pelvic endometriosis," Ultrasound in Obstetrics and Gynecology, vol. 24, no.
 2, pp. 180–185, 2004. View at Publisher · View at Google Scholar · View at PubMed · View at Scopus
- M. E. Heilbrun, J. Olpin, and A. Shaaban, "Imaging of benign adnexal masses: characteristic presentations on ultrasound, computed tomography, and magnetic resonance imaging," Clinical Obstetrics and Gynecology, vol. 52, no. 1, pp. 21–39, 2009. View at Publisher · View at Google Scholar · View at PubMed · View at Scopus

- Management of epithelial ovarian cancer; Scottish Intercollegiate
 Guidelines Network SIGN (Nov 2013)
- Management of Suspected Ovarian Masses in Premenopausal
 Women; Royal College of Obstetricians and Gynaecologists (December 2011)
- Margaret B McNay and John E.E. Fleming. "Forty Years of Obstetric Ultrasound 1957-1997: From A-scope to Three Dimensions".
 Ultrasound in Med. & Biol., Vol. 25, No. 1, pp. 3 - 56, 1999.
- Martini, F. H., Timmons, M. J., & Tallitsch, R. B. (2012). *Human Anatomy*. (7th Edition). San Francisco: Pearson Benjamin Cummings.
- McCartney CR, Eagleson CA, Marshall JC. Regulation of gonadotropin secretion: implications for polycystic ovary syndrome.
 Semin. Reprod. Med. 2002;20 (4): 317-26. <u>doi:10.1055/s-2002-36706</u>
 <u>Pubmed citation</u>
- MHRA Device Bulletin DB2006(05) "Managing Medical Devices: Guidance for healthcare and social services organizations", Nov.
 2006. Available at www.mhra.gov.uk/Home Publications Safety guidance Device Bulletins
- Moon WJ, Koh BH, Kim SK, et al. Brenner tumor of the ovary: CT and MR findings. *J Comput Assist Tomogr* 2000; 24:72 –76
 [CrossRef] [Medline]
- N. Pierce, P. Narayanan, A. Sahdev, R. Reznek, and A. Rockall,
 "Ovarian lesions pose diagnostic dilemmas," Diagnostic Imaging
 Europe, vol. 24, no. 3, pp. 14–18, 2008. View at Google Scholar .
- National Cancer Institute. (2012, March 2). Ovarian Epithelial
 CancerTreatment (PDQ®) Patient Version. Bethesda, MD: National
 Cancer Institute.

- Ness RB, Cramer DW, Goodman MT, et al. Infertility, fertility drugs, and ovarian cancer: a pooled analysis of case-control studies. Am J Epidemiol. 2002; 155:217-24. [PubMed Abstract]
- NIH consensus conference (1995). Ovarian cancer: screening, treatment, and follow-up. NIH Consensus Development Panel on Ovarian Cancer. *JAMA*; 273: 491–497. <u>Retrieved from 2013 article</u>.
- O'Brien WD Jr: Ultrasound-biophysics mechanisms. Prog Biophys Mol Biol 2007; 93:212–55 NSC (2007) Informed Consent n-invasive low-intens Neuroimage
- <u>Obeidat BR, Amarin ZO, Latimer JA, et al</u>; Risk of malignancy index in the preoperative evaluation of pelvic masses. Int J Gynaecol Obstet. 2004 Jun;85(3):255-8.
- Outwater EK, Siegelman ES, Talerman A, Dunton C. Ovarian fibromas and cystadenofibromas: MRI features of the fibrous component. *J Magn Reson Imaging* 1997; 7:465 –471 [CrossRef]
 [Medline]
- P. B. J. Van Vierzen, L. F. A. G. Massuger, S. H. J. Ruys, and J. O. Barentsz, "Borderline ovarian malignancy: ultrasound and fast dynamic MR findings," European Journal of Radiology, vol. 28, no. 2, pp. 136–142, 1998. View at Publisher · View at Google Scholar · View at Scopus
- P. J. Woodward and M. Gilfeather, "Magnetic resonance imaging of the female pelvis," Seminars in Ultrasound CT and MRI, vol. 19, no. 1, pp. 90–103, 1998. View at Publisher · View at Google Scholar · View at Scopus

- Pagana KD, Pagana TJ (2010). Mosby's Manual of Diagnostic and Laboratory Tests, 4th ed. St. Louis: Mosby Elsevier.
- Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. Cancer.
 2005; 104:2807-16. [PubMed Abstract]
- Deradigm. Gynecol Oncol. 2009 Jul;114(1):26-31. Epub 2009 Apr 23.
- <u>Patel MD</u>; Pitfalls in the sonographic evaluation of adnexal masses.
 Ultrasound Q. 2012 Mar;28(1):29-40. doi:
 10.1097/RUQ.0b013e31823c22a4.
- Petricoin EF, Ardekani AM, Hitt BA, et al. Use of proteomic patterns in serum to identify ovarian cancer. Lancet. 2002; 359:572-7.
 [PubMed Abstract]
- R. D. Bellah and N. T. Griscom, "Torsion of normal uterine adnexa before menarche: CT appearance," American Journal of Roentgenology, vol. 152, no. 1, pp. 123–124, 1989. View at Google Scholar · View at Scopus
- R. N. Low and J. S. Sigeti, "MR imaging of peritoneal disease: comparison of contrast-enhanced fast multiplanar spoiled gradientrecalled and spin-echo imaging," American Journal of Roentgenology, vol. 163, no. 5, pp. 1131–1140, 1994. View at Google Scholar · View at Scopus
- R. N. Troiano and S. McCarthy, "Magnetic resonance imaging evaluation of adnexal masses," Seminars in Ultrasound CT and MRI, vol. 15, no. 1, pp. 38–48, 1994. View at Google Scholar · View at Scopus.

- RCOG (2004) Obtaining valid consent. Clinical Governance Advice
 No 6. London, Royal College of Obstetricians .
- Ries LAG, Harkins D, Krapcho M, et al. (eds). <u>SEER Cancer</u> <u>Statistics Review</u>, 1975-2003, National Cancer Institute. Bethesda, MD.
- Risch HA, McLaughlin JR, Cole DE, et al. Prevalence and penetrance of germline BRCA1 and BRCA2 mutations in a population series of 649 women with ovarian cancer. Am J Hum Genet. 2001; 68: 700-710. [PubMed Abstract]
- Rodriguez MI, Warden M, Darney PD. Intrauterine progestins, progesterone antagonists, and receptor modulators: a review of gynecologic applications.Am J Obstet Gynecol.
- Ross, E.K. (2013). <u>Incidental Ovarian Cysts: When to Reassure,</u> <u>When to Reassess, When to Refer</u>. *Cleveland Clinic Journal of Medicine;* 80(8): 503–514. Retrieved from 2013 article.
- Rossing MA, Tang MC, Flagg EW, Weiss LK. Wicklund KG. A casecontrol study of ovarian cancer in relation to infertility and the use of ovulation-inducing drugs. Am J Epidemiol. 2004 Dec 1;160(11):1070-8. [PubMed Abstract]
- Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA. 2002; 288:321-33. [PubMed Abstract]
- RR. Improved progression-free and overall survival in advanced ovarian cancer as a result of a change in surgical

- Rubin SC, Blackwood MA, Bandera C, et al. BRCA1, BRCA2 and hereditary nonpolyposis colorectal cancer gene mutations in an unselected ovarian cancer population: relationship to family history and implications for genetic testing. Am J Obstet Gynecol. 1998; 178: 670-677. [PubMed Abstract]
- S. A. A. Sohaib and R. H. Reznek, "MR imaging in ovarian cancer," Cancer Imaging, vol. 7, pp. S119–S129, 2007. View at Publisher ·
 View at Google Scholar · View at PubMed · View at Scopus
- S. E. Rha, J. Y. Byun, S. E. Jung et al., "CT and MR imaging features of adnexal torsion," Radiographics, vol. 22, no. 2, pp. 283–294, 2002.
 View at Google Scholar · View at Scopus
- S. H. Kim, D. M. Yang, and K. A. Kim, "Unusual causes of tuboovarian abscess: CT and MR imaging findings," Radiographics, vol. 24, no. 6, pp. 1575–1793, 2004. View at Google Scholar · View at Scopus
- S. K. Stevens, H. Hricak, and Z. Campos, "Teratomas versus cystic hemorrhagic adnexal lesions: differentiation with proton-selective fatsaturation MR imaging," Radiology, vol. 186, no. 2, pp. 481–488, 1993. View at Google Scholar · View at Scopus
- Sato S, Yokoyama Y, Sakamoto T, Futagami M, Saito Y. Usefulness of mass screening for ovarian carcinoma using transvaginal ultrasonography. Cancer 2000; 89:582–588.
- Shankar H, Pagel PS. Potential adverse ultrasound-related biological effects: a critical review. Anesthesiology. 2011 Nov;115(5):1109-24.
- Shapiro HM. Practical flow cytometry. New York: Alan R. Liss, 1988.

- <u>Smorgick N, Maymon R</u>; Assessment of adnexal masses using ultrasound: a practical review. Int J Womens Health. 2014 Sep 23;6:857-63. doi: 10.2147/IJWH.S47075. eCollection 2014.
- <u>Solnik MJ, Alexander C</u>; Ovarian incidentaloma. Best Pract Res Clin Endocrinol Metab. 2012 Feb;26(1):105-16. doi: 10.1016/j.beem.2011.07.002.
- Stein IF, Leventhal ML. Amenorrhoea associated with bilateral polycystic ovaries. Am J Obstet Gynecol 1935;29:181–91
- Stevens SK, Hricak H, Stern JL. Ovarian lesions: detection and characterization with gadolinium-enhanced MR imaging at 1.5 T. *Radiology* 1991; 181:481 –488 [Medline]
- Stratton JF, Pharoah P, Smith SK, Easton D, Ponder BA. A systematic review and meta-analysis of family history and risk of ovarian cancer.
 Br J Obstet Gynaecol. 1998; 105:493-9. [PubMed Abstract]
- Struewing JP, Hartge P, Wacholder S, et al. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. N Engl J Med. 1997; 336:1401-8. [PubMed]
 <u>Abstract</u>]
- T. A. Tukeva, H. J. Aronen, P. T. Karjalainen, P. Molander, T.
 Paavonen, and J. Paavonen, "MR imaging in pelvic inflammatory disease: comparison with laparoscopy and US," Radiology, vol. 210, no. 1, pp. 209–216, 1999. View at Google Scholar · View at Scopus
- Thomassin-Naggara, G. Dubernard, C. Lafont, J. Chopier, E. Daraï, and M. Bazot, "Imaging in pelvic inflammatory disease," Journal de Radiologie, vol. 89, no. 1, pp. 134–141, 2008. View at Publisher · View at Google Scholar · View at Scopus.

- Ueda J, Furukawa T, Higashino K, et al. Ovarian fibroma of high signal intensity on T2-weighted MR image. *Abdom Imaging* 1998; 23:657 –658 [CrossRef] [Medline].
- Van Nagell JR Jr, DePriest PD, Reedy MB, et al. The efficacy of transvaginal sonographic screening in asymptomatic women at risk for ovarian cancer. Gynecol Oncol. 2000; 77:350-6. [PubMed]
 <u>Abstract</u>]
- Y. O. Tanaka, T. Yoshizako, M. Nishida, M. Yamaguchi, K.
 Sugimura, and Y. Itai, "Ovarian carcinoma in patients with endometriosis: MR imaging findings," American Journal of Roentgenology, vol. 175, no. 5, pp. 1423–1430, 2000. View at Google Scholar · View at Scopus
- Y. Y. Jeong, E. K. Outwater, and H. K. Kang, "From the RSNA refresher courses: imaging evaluation of ovarian masses,"
 Radiographics, vol. 20, no. 5, pp. 1445–1470, 2000. View at Google Scholar · View at Scopus
- Yamashita Y, Torashima M, Hatanaka Y, et al. Adnexal masses: accuracy of characterization with transvaginal US and precontrast and postcontrast MR imaging. *Radiology* 1995; 194:557 –565 [Medline].

Appendix A

A-1 Form for recording results

DATA SHEET

NO..., Female Age:-.....years, Marriage Age:-.....Months

DIGNOSING	OVARY	TRANSABDOMINAL	ENDOVAG
		U/S	U/S
Normal			
Follicle Measurements	Rt. Ovary		
	Lt. Ovary		
Cyst	Rt. Ovary		
	Lt. Ovary		
Polycystic			

Dermoid Cyst	Rt. Ovary	
	Lt. Ovary	
Cystic Tertomas	Rt. Ovary	
	Lt. Ovary	
Fibromas	Rt. Ovary	
	Lt. Ovary	
Cystadenomas	Rt. Ovary	
	Lt. Ovary	
Solid Ovarian	Rt. Ovary	
Masses	Lt. Ovary	
Ovarian Cancer	Rt. Ovary	
	Lt. Ovary	

A-2 Master data sheet

No.	Female Age	Marriage	Diagnosis	Remarks
	(years)	Age		
		(months)		
1.	39	48	pcos	
2.	39	72	pcos	
3.	39	42	pcos	
4.	38	96	pcos	
5.	38	72	pcos	
6.	37	30	pcos	
7.	37	36	pcos	
8.	37	48	pcos	
9.	37	30	pcos	

10.	36	24	pcos	
11.	36	19	pcos	
12.	36	36	pcos	
13.	36	79	pcos	
14.	35	24	pcos	
15.	35	30	pcos	
16.	35	81	pcos	
17.	35	48	pcos	
18.	34	72	pcos	
19.	34	24	pcos	
20.	34	60	pcos	
21.	34	30	pcos	
22.	34	89	pcos	
23.	34	58	pcos	
24.	34	120	pcos	
25.	33	120	pcos	
26.	33	24	pcos	
27.	33	74	pcos	
28.	32	20	pcos	
29.	32	98	pcos	
30.	32	96	pcos	
31.	32	45	pcos	
32.	32	62	pcos	
33.	32	86	pcos	
34.	31	15	pcos	
35.	31	19	pcos	

36.	31	48	pcos	
37.	31	85	pcos	
38.	31	55	pcos	
39.	30	15	pcos	
40.	30	18	pcos	
41.	30	13	pcos	
42.	30	42	pcos	
43.	30	21	pcos	
44.	30	20	pcos	
45.	30	53	pcos	
46.	30		pcos	-
47.	30	144	pcos	
48.	29	21	pcos	
49.	29	27	pcos	
50.	29	15	pcos	
51.	29	24	pcos	
52.	29	21	pcos	
53.	29	55	pcos	
54.	29	67	pcos	
55.	29	63	pcos	
56.	29	25	pcos	
57.	29	59	pcos	
58.	29	88	pcos	
59.	28	24	pcos	
60.	28	15	pcos	
61.	28	99	pcos	

62.	28	24	pcos	
63.	28	72	pcos	
64.	28	67	pcos	
65.	28	60	pcos	
66.	28	108	pcos	
67.	28	72	pcos	
68.	27	36	pcos	
69.	27	60	pcos	
70.	27	30	pcos	
71.	27	20	pcos	
72.	27	50	pcos	
73.	26	39	pcos	
74.	26	15	pcos	
75.	26	60	pcos	
76.	26	14	pcos	
77.	26	48	pcos	
78.	26	30	pcos	
79.	26	15	pcos	
80.	26	18	pcos	
81.	26	36	pcos	
82.	26	84	pcos	
83.	25	24	pcos	
84.	25	18	pcos	
85.	25	60	pcos	
86.	25	48	pcos	
87.	25	14	pcos	

88.	25	15	pcos
89.	25	84	pcos
90.	25	17	pcos
91.	25	60	pcos
92.	24	60	pcos
93.	24	15	pcos
94.	24	24	pcos
95.	24	15	pcos
96.	23	13	pcos
97.	23	15	pcos
98.	23	60	pcos
99.	23	49	pcos
100.	23	60	pcos
101.	23	50	pcos
102.	23	60	pcos
103.	23	72	pcos
104.	23	13	pcos
105.	22	18	pcos
106.	22	18	pcos
107.	22	60	pcos
108.	22	15	pcos
109.	22	24	pcos
110.	22	32	pcos
111.	22	14	pcos
112.	21	20	pcos
113.	21	24	pcos

114.	21	38	pcos	
115.	21	25	pcos	
116.	20	24	pcos	
			peos	
117.	20	24	pcos	
118.	20	36	pcos	
119.	19	36	pcos	
120.	19	15	pcos	
121.	19	14	pcos	
122.	18	96	pcos	
123.	50	48	Normal	Fibroid
124.	48	16	Normal	Fibroid
125.	46	24	Normal	Fibroid
126.	46	132	Normal	Fibroid
127.	45	24	Normal	Fibroid
128.	45	60	Normal	Fibroid
129.	45	288	Normal	Fibroid
130.	44	84	Normal	Fibroid
131.	44	48	Normal	Fibroid
132.	44	33	Normal	Fibroid
133.	43	36	Normal	Fibroid
134.	43	84	Normal	Fibroid
135.	42	72	Normal	Fibroid
136.	42	96	Normal	Fibroid
137.	42	48	Normal	Fibroid
138.	41	72	Normal	Fibroid
139.	40	36	Normal	Fibroid
140.	40	48	Normal	Fibroid
141.	40	96	Normal	Fibroid
142.	40	138	Normal	Fibroid
143.	40	122	Normal	Fibroid
144.	40	13	Normal	Fibroid
145.	40	96	Normal	Fibroid
146.	40	24	Normal	Fibroid

47.	39	36	Normal	Fibroid
48.	39	60	Normal	Fibroid
49.	39	51	Normal	Fibroid
50.	39	48	Normal	Fibroid
51.	38	48	Normal	Fibroid
52.	38	77	Normal	Fibroid
53.	38	48	Normal	Fibroid
54.	38	37	Normal	Fibroid
55.	38	144	Normal	Fibroid
56.	37	13	Normal	Fibroid
57.	36	51	Normal	Fibroid
58.	34	180	Normal	Fibroid
59.	33	24	Normal	Fibroid
60.	33	15	Normal	Fibroid
61.	32	14	Normal	Fibroid
62.	27	36	Normal	Fibroid
63.	44	84	Normal	Male factor
64.	44	228	Normal	Male factor
65.	43	96	Normal	Male factor
66.	43	158	Normal	Male factor
67.	43	108	Normal	Male factor
68.	40	132	Normal	Male factor
69.	40	42	Normal	Male factor
70.	39	156	Normal	Male factor
71.	39	84	Normal	Male factor
72.	39	204	Normal	Male factor
73.	38	72	Normal	Male factor
74.	38	24	Normal	Male factor
75.	37	36	Normal	Male factor
76.	37	50	Normal	Male factor
77.	37	108	Normal	Male factor
78.	36	48	Normal	Male factor
79.	36	96	Normal	Male factor
80.	36	120	Normal	Male factor
81.	36	48	Normal	Male factor

182.	35	15	Normal	Male factor
183.	35	18	Normal	Male factor
184.	35	24	Normal	Male factor
185.	35	12	Normal	Male factor
186.	35	33	Normal	Male factor
187.	35	180	Normal	Male factor
188.	34	121	Normal	Male factor
189.	34	75	Normal	Male factor
190.	33	62	Normal	Male factor
191.	33	168	Normal	Male factor
192.	33	168	Normal	Male factor
193.	32	54	Normal	Male factor
194.	32	18	Normal	Male factor
195.	32	72	Normal	Male factor
196.	32	21	Normal	Male factor
197.	32	120	Normal	Male factor
198.	32	108	Normal	Male factor
199.	31	96	Normal	Male factor
200.	30	16	Normal	Male factor
201.	30	96	Normal	Male factor
202.	30	72	Normal	Male factor
203.	30	36	Normal	Male factor
204.	30	120	Normal	Male factor
205.	29	36	Normal	Male factor
206.	29	15	Normal	Male factor
207.	29	108	Normal	Male factor
208.	29	60	Normal	Male factor
209.	29	60	Normal	Male factor
210.	28	18	Normal	Male factor
211.	28	108	Normal	Male factor
212.	27	19	Normal	Male factor
213.	27	60	Normal	Male factor
214.	27	84	Normal	Male factor
215.	26	60	Normal	Male factor
216.	26	84	Normal	Male factor

217.	25	72	Normal	Male factor
218.	25	18	Normal	Male factor
219.	25	21	Normal	Male factor
220.	25	36	Normal	Male factor
221.	25	60	Normal	Male factor
222.	24	24	Normal	Male factor
223.	24	18	Normal	Male factor
224.	24	27	Normal	Male factor
225.	24	84	Normal	Male factor
226.	23	18	Normal	Male factor
227.	23	29	Normal	Male factor
228.	23	27	Normal	Male factor
229.	23	14	Normal	Male factor
230.	23	38	Normal	Male factor
231.	23	51	Normal	Male factor
232.	23	60	Normal	Male factor
233.	22	72	Normal	Male factor
234.	22	16	Normal	Male factor
235.	22	38	Normal	Male factor
236.	22	24	Normal	Male factor
237.	22	24	Normal	Male factor
238.	21	48	Normal	Male factor
239.	21	24	Normal	Male factor
240.	21	48	Normal	Male factor
241.	20	15	Normal	Male factor
242.	19	15	Normal	Male factor
243.	19	14	Normal	Male factor
244.	19	24	Normal	Male factor
245.	19	23	Normal	Male factor
246.	49	108	Normal	Tube blocked
247.	43	60	Normal	Tube blocked
248.	42	111	Normal	Tube blocked
249.	42	151	Normal	Tube blocked
250.	42	25	Normal	Tube blocked
251.	40	84	Normal	Tube blocked
252.	40	24	Normal	Tube blocked
253.	40	36	Normal	Tube blocked
254.	40	126	Normal	Tube blocked
255.	40	48	Normal	Tube blocked

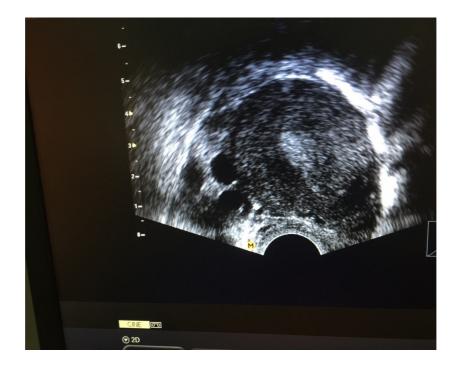
256.	40	54	Normal	Tube blocked
257.	39	72	Normal	Tube blocked
258.	38	24	Normal	Tube blocked
259.	36	30	Normal	Tube blocked
260.	36	48	Normal	Tube blocked
261.	35	84	Normal	Tube blocked
262.	35	24	Normal	Tube blocked
263.	35	14	Normal	Tube blocked
264.	34	36	Normal	Tube blocked
265.	34	37	Normal	Tube blocked
266.	33	36	Normal	Tube blocked
267.	32	24	Normal	Tube blocked
268.	32	99	Normal	Tube blocked
269.	32	72	Normal	Tube blocked
270.	31	60	Normal	Tube blocked
271.	25	24	Normal	Tube blocked
272.	38	74	Follicle measurement	18mm
273.	37	44	Follicle measurement	18mm
274.	29	18	Follicle measurement	18mm
275.	29	41	Follicle measurement	18mm
276.	23	48	Follicle measurement	18mm
277.	22	33	Follicle measurement	18mm
278.	45	288	Follicle measurement	18 mm
279.	37	24	Follicle measurement	17mm
280.	33	96	Follicle measurement	17mm
281.	29	63	Follicle measurement	17mm
282.	22	24	Follicle measurement	17 mm
283.	40	14	Follicle measurement	16mm
284.	29	15	Follicle measurement	16.7mm
285.	34	72	Follicle measurement	15mm
286.	33	30	Follicle measurement	15mm

287.	25	32	Follicle measurement	15 mm
288.	39	144	Follicle measurement	14mm
289.	45	300	Cyst	Lt. ovary
				4.4x4.3cm
290.	40	16	Cyst	Rt. ovary 9x9cm
291.	39	72	Cyst	Rt. ovary
				6.3x6.3cm
292.	36	18	Cyst	Rt. ovary
				5.5x5.5cm
293.	32	24	Cyst	Rt. ovary 3x3cm
294.	28	36	Cyst	Lt. ovary
				3.7x3.6cm
295.	28	33	Cyst	Rt. ovary
				3.5x3cm
296.	28	18	Cyst	Rt. ovary 5.2x5
				cm
297.	26	36	Cyst	Lt. ovary 5x5cm
298.	23	40	Cyst	Lt. ovary
				6.5x6.3cm
299.	20	24	Cyst	Lt. ovary 8x8cm
300.	18	14	Cyst	Lt. ovary
				4.8x4.6cm

Appendix B Ultrasound images



Fig. B-1 Lt. ovary



Fig, B-2 Normal Lt. ovary & uterus



Fig. B-3 Follicle measuring 1.44cm

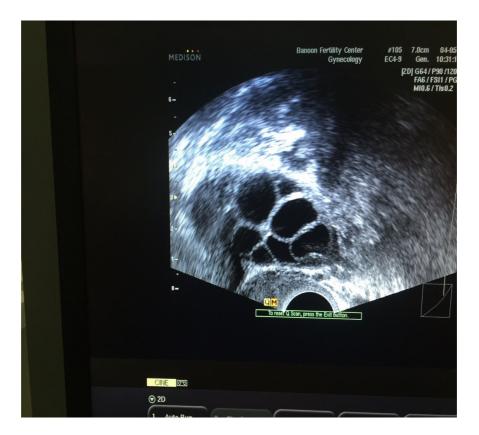


Fig. B-4 polyscestic ovary



Fig. B-5 Two follicles one measuring 1.92cm the other measuring 1.48cm



Fig. B-6 Follicle measuring 1.44cm



Fig. B-7 Follicle measuring 1.44cm



Fig. B-8 Lt. ovary



Fig. B-9 Fibroid



Fig. B-10 A folliclemeasuring 1.23cm



Fig. B-11 Follicle measuring 1.25 cm



Fig. B-12 Follicle measuring 1.43cm