FOGSI FOCUS
Midlife Management

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Editor-in-Chief

Jaideep Malhotra

MD FRCOG FRCPI FICS (Obs & Gyn) (FICMCH FIAJAGO FMAS FICOG MASRM FICMU FIUMB)

Professor
Dubrovnik International University
Dubrovnik, Croatia

Managing Director
ART-Rainbow IVF
Agra, Uttar Pradesh, India
President FOGSI–2018

Editor

Jayam Kannan MD DGO

Vice President FOGSI, 2018

Emeritus Professor
Tamil Nadu MGR Medical University
Dubrovnik, Croatia

Member PMNCH WHO Programme Since 2008
Director, Gharbbha Rakshambigai Group of institutions

Co-Editor

Pratik Tambe MD FICOG

ART Consultant and Gynaec Endoscopic Surgeon
Chairperson, FOGSI Endocrinology Committee (2017–19)
Managing Council Member, MOGS (2014 -)
Managing Council Member, MSR (2016 -)
Governing Council Member, AMC (2016–18)
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Mentor, MOGS Youth Council (2014–18)

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Headquarters

Jaypee Brothers Medical Publishers (P) Ltd
4838/24, Ansari Road, Daryaganj
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Phone: +91-11-43574357
Fax: +91-11-43574314
Email: jaypee@jaypeebrothers.com

Overseas Offices

J.P. Medical Ltd
83 Victoria Street, London
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Phone: +44 20 3170 8910
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Email: info@jpmedpub.com

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City of Knowledge, Bld. 235, 2nd Floor, Clayton
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Phone: +1 507-301-0496
Fax: +1 507-301-0499
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Jaypee Brothers Medical Publishers (P) Ltd
17/1-B Babar Road, Block-B, Shaymali
Mohammadpur, Dhaka-1207
Bangladesh
Mobile: +08801912003485
Email: jaypeedhaka@gmail.com

Jaypee Brothers Medical Publishers (P) Ltd
Bhotahity, Kathmandu, Nepal
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Our teachers, mentors, and our patients.

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Contributors

Editor-in-Chief

Jaideep Malhotra
MD FRCOG FRCPI FICS (Obs & Gyn)
(FICMCH FIAJAGO FMAS FICOG MASRM FICMU FIUMB)
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Contributing Authors

Maninder Ahuja DGO FICOG CIMP
Director
Ahuja Health Care Services
Faridabad, Haryana, India

Sasi B Avirneni DGO
Consultant
Department of Obstetrics and Gynecology
BN Hospital
Vijaywada, Andhra Pradesh, India

Charmila Ayyavoo MD DGO DFP FICOG PGDCR
Director
Department of Obstetrics and Gynecology, Aditi Hospital and Parvathy Ayyavoo Fertility Centre
Trichy, Tamil Nadu, India

Rishabh Bora MD
Radiologist
Department of Radiology
Global Rainbow Healthcare
Agra, Uttar Pradesh, India

Sajana Gogineni MS
Head
Department of Obstetrics and Gynecology
PS Institute of Medical Sciences
Vijaywada, Andhra Pradesh, India

Narendra Malhotra MD FICMCH FICOG FICS FMAS FRCOG AFIAPM
Vice President
World Association Perinatal Medicine
President, ISPAT
Agra, Uttar Pradesh, India

Neharika Malhotra MD DRM
Infertility Consultant
Rainbow Hospital
Agra, Uttar Pradesh, India
Joint Secretary, FOGSI–2018

Vaidehi Marathe DGO CIMO FICMCH
Consultant
Department of Obstetrician and Gynecologist
Maher Maternity and Nursing Home
Nagpur, Maharashtra, India

Rajendra Nagarkatti MD FCPS DGO DFP
Hon Consultant and ART Specialist
Department of Obstetrics and Gynecology
Wockhardt Hospital and Bhimsen Joshi Municipal Gen Hosp Mira Bhayander
Thane, Maharashtra, India

Hephziabh K Navamani MD DGO FRCOG FICOG PhD DSc
Professor, Department of Obstetrics and Gynecology, Saveetha Medical College
Chennai, Tamil Nadu, India

MC Patel MB DGO LLM
Gynecologist and Medico Legal Counsellor
Niru Maternity and Nursing Home
Ahmedabad, Gujarat, India

President's Message for South Zone Yuva FOGSI Vijayawada

Jaideep Malhotra
MD FRCOG FRCPI FICS (Obs & Gyn)
(FICMCH FIAJAGO FMAS FICOG MASRM FICMU FIUMB)
Professor
Dubrovnik International University
Dubrovnik, Croatia
Managing Director
ART-Rainbow IVF
Agra, Uttar Pradesh, India
President FOGSI–2018

It gives me immense pleasure to welcome you all for South Zone Yuva FOGSI in Vijayawada this September.

"30 and beyond," a well-chosen theme dealing with all issues of midlife. I congratulate Dr Jayam Kannan and her team for coming up with a wonderfully planned scientific program.

"Continuous learning is a key to success." Learning, wisdom, and success will always go hand in hand.

In this year 2018, we selected four important topics to be covered in our YUVA, topics which have a lot of latest innovations and controversies and topics which need at little more in-depth understanding.

Always remember, knowledge combined with quality, ethics, and dignity will showcase a strong character and "the best is yet to come," so keep on striving.

Vijayawada literally translates to "place of victory", and here in this beautiful city, we are ready with our third YUVA FOGSI to make us understand how to be victorious in midlife and onwards.

All the best for a great conference.

Jaideep Malhotra

Foreword

Jaideep Malhotra
MD FRCOG FRCPI FICS (Obs & Gyn)
(FICMCH FIAJAGO FMAS FICOG MASRM FICMU FIUMB)
Professor
Dubrovnik International University
Dubrovnik, Croatia
Managing Director
ART-Rainbow IVF
Agra, Uttar Pradesh, India
President FOGSI–2018

Dear FOGSIANS,

Greetings,

Heartiest congratulations to each and everyone involved in bringing out this beautiful focus on midlife management.

"Midlife is not a period to disenchant oneself, it is period to turn on our magic in full force."

-Marianne Williamson

Midlife is a central period of a woman's life, where a transition takes place and this transition needs proper guidance and care so that the coming life will be comfortable and healthy. It needs to be understood that a good midlife and old age is a culmination of how one has invested on health during younger days, which most of neglect and take for granted, if this understanding comes earlier in life then most of us will be healthy, wealthy, and wise from our midlife onwards.

Balance and agility are important capabilities often taken for granted. Allow the midlife time to bring in a creative healthy change.

"It's not crisis in midlife, it is an opportunity."

This focus gives us all an insight on all issues of midlife and upgrades our knowledge on how to build it up.

Wish you all a very happy reading.

Jaideep Malhotra

Preface

Respected colleagues and dear friends,

It is with immense pride that we bring to you this FOGSI Focus on Midlife Management.

When women reach the midlife, it is a time of great change in their bodies and minds. Menopause is not the only problem knocking on their door. There are a host of menopause-related gynecological health issues to tackle. There are also several other general health issues that plague women at this time.

You must give everything to make your life as beautiful as the dreams that dance in your imagination.

Roman Payne

India does not have an adequate number of specialists devoted to the field of midlife management and hence, general gynecologists are approached with the common issues related to this age group. It is our aim in this volume to address the most frequently encountered questions and issues plaguing women of this age group.

We have general advice regarding the midlife, midlife health checklists, exercise and activities, fertility concerns, urogynecological issues, abnormal uterine bleeding, metabolic health, osteoporosis, and medicolegal issues which are tackled as a matter of priority. The chapters have been authored by eminent FOGSIans who are authorities in the field and we thank them immensely for their timely contributions. This book is thus the result of the distilling together of several decades of experience in treating patients and we hope it will go a long way to offering practical tips and guidelines in your daily practice.

We wish to thank our FOGSI President Dr Jaideep Malhotra, Secretary General Dr Jaydeep Tank, and the office bearers, without whose blessings and encouragement, this book would not have materialized. We also wish to thank our publishers and the sponsors who will help bring this volume to FOGSIans across the length and breadth of India.

Jayam Kannan
Pratik Tambe

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The editors would like to acknowledge the efforts of all the authors in the preparation of the manuscript. Thanks are also due to Ms Barkha Arora and the team of Jaypee Brothers Medical Publishers (P) Ltd. for their kind cooperation during the layout, design, and printing process. We would also like to place on record our profuse thanks to our education partners for their support and unconditional educational grant which helped this volume see the light of day.

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Midlife Health Checklist

Vaidehi Marathe

INTRODUCTION

Perhaps no other time of life is as plagued with misinformation as middle age. Midlife—the years between 30 and 70, with 40–60 at its core—is the least charted territory in human development. Most researchers focus on childhood, adolescence or old age and the faulty knowledge and unvalidated premises have given people the wrong idea about what really happens in midlife.

While younger adults experience the day-to-day stressors more frequently, midlife adults experience more "overload" stressors—basically juggling too many activities at one time. There are gender differences, however. Midlife women shoulder more "crossover" stressors—simultaneous demands from multiple domains like work and family—than their male counterparts and report higher levels of distress as a result.

Socioeconomic status also makes a difference. Midlife people with lower educational status report the same number of stressors as those with higher educational status, they are more likely to rate stressors as more severe.

KEY ISSUES

The realization that life is progressing rapidly and may be already half gone can feel overwhelming. During midlife, people often consider issues such as life purpose, loss of youth, mortality, their legacy, and their sense of accomplishment and physical adequacy, just to name a few. Women experience anxiety, depression, or feelings of emptiness as a result of midlife transition.

Therefore, a sense of accomplishment can help one smoothly transition into midlife. Making sense of one's life contributions and recognizing individual strengths and accomplishments are considered to be important factors in making peace with the aging process. Of course, it is also possible to retain a youthful spirit, a sense of wonder and possibility, and the desire for adventure, no matter what age an individual attains.

Wellness is a focus that includes a broad range of issues of concern to patients but not necessarily physicians: we as physicians are expert in acute care but not necessarily expert in preventive care. In short, our future success depends on the ability to address wellness issues—such as menopause and midlife health—with our current and prospective patients. Women want to learn about menopause and their health care options but are not receiving the information and consultation they need. Women understand the symptoms of menopause but not its long-term health risks.

CLINICIANS' ROLE

Hence, we should seek to stimulate increased scientific and clinical focus on the midlife and its relevance to health and healthy aging. Over the past two decades, several cohort studies have advanced scientific understanding of the natural history of ovarian aging and begun to elucidate the inter-relationship between ovarian aging and, e.g., bone, cardiovascular, cognitive, and musculoskeletal health. Notably, these studies have also shed light on age-related changes that occur in midlife independent of ovarian aging.

Critical insights include observations that bone loss, osteoarthritis, adverse changes in lipid profiles, diabetes, metabolic syndrome, and sleep disturbances frequently begin and/or accelerate during the midlife period – in some cases accelerated by the endocrine changes associated with the menopause and in others simply coincident with them. It is apparent that healthy behaviors in midlife, such as maintenance of physical activity and healthy body weight may moderate these changes. Furthermore, it is increasingly recognized that healthy lifestyles and control of risk factors in midlife may be beneficial for cognitive health in later years.

While prevention and healthy lifestyles are important at all ages, it is increasingly apparent that health in midlife is an important determinant of a healthy and fully functional life in the following decades and the evidence strongly suggests that the midlife represents a critical window for preventing chronic disease and optimizing health and functioning.

The midlife also warrants attention as a vulnerable window for an important subset of gynecologic and hormone-sensitive conditions.

A healthy lifestyle is the key issue to reduce the burden of illness of these chronic diseases. There is good evidence that a healthy diet, regular physical activity, abstinence from tobacco smoking, at best reduced alcohol consumption and regular screening are essential in this context.

Clinical examination includes a holistic approach to health and we as clinicians play a crucial role.

Assessment

- Detailed history
- Evaluate women's need
- Evaluation of women's individual risk factor
- Assess general condition of patient
- Physical examination:
  - Pulse, blood pressure (BP)
    - Optimal BP (<130/85 mmHg) to be rechecked every 2 years
    - Normal level (<140/90 mmHg) to be checked yearly
    - Greater than 140/90 mmHg, need second measurement to confirm diagnosis of hypertension.
  - Auscultation of the heart and lungs
  - Height, weight, waist circumference, calculate body mass index (BMI)
  - Breast examination
  - Pelvic examination.

This assessment should provide us an opportunity to assess various risk factors.

Risk Factors for Osteoporosis

Major risk factors as defined by WHO are advancing age, prior fragility fracture, low BMI, family history of fracture, smoking and more than three drinks of alcohol per day (grade A).

Environmental factors include nutrition (calcium intake using the quick dietary calculator, protein) physical activity and sunlight exposure, which are important modifiable risk factors in India. Relevance of risk of falling increases with ageing (grade A).

Risk Factors for Coronary Heart Disease

Premature menopause, hypertension, dyslipidemia, homocystenemia, lipoprotein, high-risk C-reactive protein, diabetes mellitus (DM), obesity, sedentary life-style, smoking, and metabolic syndrome.

Risk Factors for Diabetes Mellitus

Advancing age, obesity, family history, hypertension, dyslipidemia, personal history of gestational DM or impaired glucose tolerance, polycystic ovary syndrome, and physical inactivity.

Risk Factors for Deep Vein Thrombosis

- Personal or family history of clots
- Prolonged immobilization surgery or while pregnant or on the oral contraceptive pills.

Risk Factors for Stroke

Hypertension, diabetes, smoking, obesity, atrial fibrillation, asymptomatic carotid stenosis, and hyperlipidemia.

Risk Factors for Alzheimer's Disease

Age, family history, genetic factor apolipoprotein E, mild cognitive impairment, cardiovascular disease (CVD) risk factors, physical inactivity, diabetes, hypertension, dyslipidemia, smoking, obesity, autoimmune diseases, depression and stress, social engagement and diet, head trauma and traumatic brain injury.

CLINICAL EXAMINATION

- General physical examination: Examination of respiratory, cardiovascular system, and bones may detect common age related problems
- Breast examination: This should be carried out regularly due to an increased risk of breast cancer as women get older
- Pelvic examination: This is performed to assess for complications of menopause, such as urogenital atrophy and must include Pap smear.

INVESTIGATIONS

Recommended laboratory tests:

- Complete blood count
- Urine test routine
- Fasting, postprandial glucose level/HbA1c
- Lipid profile
- Serum thyroid-stimulating hormone
- Stool for occult blood
- Pap smear
- Transvaginal ultrasound
- Mammogram/ultrasound
- Eye checkup—intraocular pressures, refractive index, and retina.

COUNSELING

The key to well-being in midlife lies in detail counseling, emphasizing that well-being and quality of life will lower the risk of health problems.

Importance of Healthy Lifestyle

Lifestyle management, balanced diet, adequate physical activity, exposure to sunlight, avoidance of bone depleting

agents such as tobacco, alcohol, mental health and relaxation, immunization and importance of regular screening.

Diet

Well balanced diet helps in weight loss, boosting her self-image. Weight loss of only 5–10% is sufficient to improve many of the abnormalities associated with the insulin resistance syndrome. It will also lower the risk of osteoporosis and heart disease.

Diet rich in calcium keeps the bones strong (Table 1). A well balanced diet should contain plenty of vegetables, fruits and adequate proteins. The ideal protein should be 1.2–1.5 g/kg body weight/day if the woman is exercising regularly. The rest of the calories should be obtained from carbohydrates and fats.

Low sodium intake: Daily salt intake should not exceed 5 g (1 tsp).

Decrease caffeine intake (<3 cups/day), limit alcohol, and avoid use of tobacco (grade B).

Vitamin D: Dietary sources are limited, adequate sunlight exposure has limitations and presently, food fortified with adequate vitamin D is unavailable in India. Urgent and cost-effective measures need to be implemented. Hence, it is recommended to use vitamin D as supplements (grade A).

Exercise

Making exercise a part of life pays in many ways. It helps to lose weight and then maintain it. Aerobic exercise helps in cardiovascular health while weight bearing exercises help in bone health and prevention of osteoporosis. Physical exercise helps to maintain a healthy weight, improves bone density, coordination and balance, muscle strength, joint mobility, and lipid profiles.

Healthy Habits

Quitting smoking, tobacco, and alcohol can reverse the ill effects these habits have on the body.

Immunization

In addition to seasonal flu (influenza) vaccine, the women should be advised about hepatitis B and shingles vaccine, which protects against shingles disease (recommended for healthy adults 50 years and older).

Screening

The most common diseases are those of the vascular system, including heart disease and stroke, and cancer. There is enough data to support how prevention could be advanced if modifiable risk factors are targeted. Prevention strategies will need to focus on improving knowledge about risk factors and changing behavior of women accordingly.

TABLE 1: Calcium content of Indian foods

Dietary product	*Serving*	*Calcium (mg)*
Milk (cows)	1 glass (250 mL)	300
Milk (buffalos)	1 glass (250 mL)	525
Milk low fat	1 glass (250 mL)	300
Curd (cows milk)	1 katori	149
Butter milk	1 glass (250 mL)	75
Channa (cows milk)	25 g	52
Khoa (cows milk)	25 g	239
Cheese slice	20 g	158
Whole milk powder (cows milk)	5 tbsp	300
Chapati	1 (atta 25 g)	12
White bread	1 slice	30
Ragi	25 g	75
Rajma	1 katori (25 g)	65
Soyabean	1 katori (25 g)	60
Kale chane (whole Bengal gram)	1 katori (25 g)	72
Urad dal (black gram dal)	25 g	50
Palak veg	1 katori	73
Beetroot	25 g	50
Methi veg	1 katori	395
Chaulai	1 katori	397
Beans	1 katori	90
Bathua	1 katori	150
Sarso	1 katori	155
Okra (bhindi)	1/2 katori	65
Broccoli	1/2 katori	50
Almonds	1 handful (25 g)	58
Cashew nut	1 handful (25 g)	13
Dried figs	5 whole	95
Gingelly seed (til)	25 g (1 tbsp)	363
Orange	1 medium sized	50
Fish Hilsa	25 g	45
Fish Rohu	25 g	160

OSTEOPOROSIS

Risk of osteoporosis and concomitantly fracture increases with aging and bone loss is associated with menopause. The midlife cohort studies have now documented that bone loss begins prior to the final menstrual period with an accelerated period of loss in bone mineral density (BMD) and bone strength beginning 1–2 years before menopause until 2–5 years into the postmenopause.

As it is estimated that about half of the lifetime loss in BMD occurs during this relatively short period in the midlife, it represents a critical period for interventions to optimize reductions in the loss of bone strength. It is thus appropriate to estimate the future risk of fracture in all women at the age of 50 years or at menopause, whichever occurs first.

Osteoporosis is asymptomatic unless a fracture occurs. Early diagnosis in the asymptomatic period and timely management of osteoporosis will prevent the associated morbidity and mortality. In the absence of a validated population screening tool for postmenopausal osteoporosis in India, a case-finding strategy utilizing clinical risk factors with the addition of dual-energy X-ray absorptiometry (DXA) as needed is suggested (grade C).

Opportunistic screening for women above 40 years is suggested. Risk assessment factors for fractures are derived by history and clinical examination. All women should be screened by DXA at the age of 65 years, if not done before that time (Box 1). At the age of 50, all women should be informed about a bone-friendly lifestyle.

Physical examination should include the height and weight annually, check for balance and gait, get up, and go test by asking the women to get up from the chair without using their arms. Kyphosis and dowager's hump is seen in the late stage of osteoporosis (grade A).

LABORATORY STUDIES (BOX 2)

The fracture risk assessment tool (WHO FRAX): For online use is available for India (http: www.shef.ac.uk/FRAX). Fracture risk assessment tool is a validated and widely accepted tool used worldwide to identify patients in the osteopenia group who are most likely to benefit from treatment. It predicts the 10-year absolute risk for a fracture in an individual and the cost effective analysis determines the interventional threshold above which treatment is cost effective.

Fracture risk assessment tool is country specific and until more Indian data is available on the prevalence of osteoporotic fractures and mortality rates, the usage of FRAX in the Indian context is to be applied cautiously. An enormous advantage of FRAX is that it can be used without BMD, also to identify cases at risk for fractures. In view of the limited availability of DXA machines in India, it will be helpful to use FRAX without BMD in Indian context.

It is suggested to conduct central DXA of spine and hip in all women 5 years beyond the natural age of menopause and in women 5 years since menopause with one high clinical risk or more than two clinical risk factors.

BOX 1 The WHO BMD (T-score) based diagnosis of osteoporosis for postmenopausal women

Normal T-score above (i.e., better than)–1.0

- Osteopenia or low bone mass T-score between –1.0 and –2.5
- Osteoporosis T-score below (i.e., worse than) or equal to –2.5
- Severe osteoporosis T-score below –2.5 with fragility fracture

WHO, World Health Organization; BMD, bone mineral density.

BOX 2 Essential R (grade A)

Tests:

- Complete blood picture,
- ESR random blood sugar
- Serum calcium
- Preferably fasting serum phosphorus serum creatinine
- Serum albumin
- Alkaline phosphatase
- Serum tissue stimulating hormone 25-hydroxy vitamin D
- X-ray of thoracolumbar spine (lateral view)
- PTH (based on clinical judgment)

ESR, erythrocyte sedimentation rate; PTH, parathyroid hormone.

CARDIOVASCULAR RISK

The Women's Health Initiative refocused attention on the midlife as potentially a vulnerable window for interventions to protect heart health with a call for increased research on change in women's cardiovascular risk profile during the menopausal transition. Recent studies support the hypothesis that increase in cardiovascular risk accelerates with ovarian aging.

The Study of Women's Health Across the Nation has documented that levels of total cholesterol, low density lipoprotein and apolipoprotein B, increase significantly in the 2-year window around the menopause. Notably, emerging evidence suggests that the hallmark menopausal symptom, the hot flash, is associated with increased cardiovascular risk profiles.

The incidence of CVD in Indian women has been noted to have significantly risen. The projected deaths from CVDs by 2020 is estimated to be 42% of the total deaths. The prevalence rate of stroke is 45.1/100,000 persons. The case fatality rate is 41% in 30 days. The prevalence of hypertension is 20.4–22% in the urban area and 12–17% in rural area. From the Indian Million Death Study 2009, CVD emerges as the major cause of mortality, 16.8% in the rural and 28.6% in the urban area. Seventy nine percent of sudden cardiac deaths in rural South India occurred at home.

Prevention and Management

- Lifestyle interventions (grade A)
- Encourage optimal BP <120/80 mmHg through lifestyle approaches (grade A)
- Pharmacotherapy if BP ≥140/90 mmHg to avoid end-organ damage, more so in diabetes (grade A)
- Use thiazide diuretics unless there is an absolute contra-indication. Optimal lipid targets (grade A)
- Low-density lipoprotein (LDL) <100 mg/dL, high-density lipoprotein (HDL) >50 mg/dL, triglycerides <l50 mg/dL, non-HDL cholesterol <100 mg/dL (grade A)
- High-risk: Initiate statin if LDL >100 mg/dL (grade A)

- Intermediate-risk: Initiate statin if LDL >130 mg/dL (grade A)
- Lifestyle approaches and pharmacotherapy to achieve near normal HbA1c
- Hemoglobin (<7%) in women with diabetes (grade A)
- Aspirin in high-risk women (75–162 mg/day) (grade A)
- Routine use of aspirin in women <65 years of age is not recommended for myocardial infarction prevention (grade C)
- Hormone therapy (HT) is not indicated solely for primary or secondary cardio protection (grade B).

Obesity

The wide spectrum of morbidities related to excess body mass includes risks for diabetes, hypertension, coronary artery disease, dyslipidemia, malignancy, venous thrombosis, degenerative joint disease, pulmonary compromise, sleep apnea, cholelithiasis, depression, and overall reduced quality of life.

Body Mass Index Category

The various categories of body mass index and respective intervention is shown in box 3.

BREAST CANCER

In India, breast cancer is the second most common cancer with an estimated 115,251 new diagnoses and the second most common cause of cancer related deaths with 53,592 breast cancer deaths in 2008. The age standardized incidence rate for breast cancer in India is 22.9 per 100,000, one-third that of Western countries, and the mortality rates are disproportionately higher.

Non-modifiable risk factors for breast cancer are age, family history, benign breast disease, BRCA – breast cancer) 1 or 2 carriers, early menarche (<12 years), late age at menopause (after age 55), increased breast density, and a chest irradiation between ages 25 and 55 years. Modifiable risk factors are age at first child, breast feeding, parity, obesity, physical activity, and menopausal HT.

BOX 3 Category and intervention

- Underweight (18.5): Encourage balanced diet and exercise
- Healthy (18.5–24.9): Encourage balanced diet and exercise
- Overweight (25–26.9): Lifestyle (diet, exercise, and behavior therapy)
- Overweight (27–29.9): Lifestyle plus drug therapy if comorbidities* exist
- Obese class 1 (30–35): Lifestyle plus drug therapy
- Obese class 2 (35–39.9): Lifestyle plus drug therapy, plus surgery if comorbidities* exist
- Obese class 3 (above 40): Lifestyle, drug therapy, and surgery

*Comorbidities: Hypertension, diabetes, and hyperlipidemias.

Screening Methods

Breast cancer screening includes three methods of early detection (grade C):

- Breast self-examination (BSE): Breast self-examination monthly, starting in the 20s. Clinical breast exams (CBE) every 3 years starting in the 20s till the age of 39, and annually thereafter mammographic screening (annually) starting at the age of 40 years
- Clinical breast exams: For women between 50 and 70 years of age, annual CBE and selective use of mammography, once in 3 years, in high-risk groups, determined by the above mentioned criteria has been found to be equally effective (JNCI, 2011).

  Clinical breast exams involves a systematic examination of the breast skin and tissue for signs and symptoms or any changes including development of a lump or swelling, skin irritation or dimpling, nipple pain or retraction, redness or scaliness of the nipple or breast skin or a discharge other than breast milk. Clinical breast exams should include all the four quadrants of the breast and the central nipple areola complex followed by examination of axilla and supraclavicular fossae (Fig. 1)
- Mammography: An approximate 12–15% reduction in breast cancer mortality is associated with mammography screening for women aged 40–69 years.

  The American Cancer Society recommendation 2018: Women aged 40–44 should have the choice to start annual breast cancer screening with mammograms.

  Women aged 45–54 years should get mammograms every year.

  Women aged 55 years and older should switch to mammograms every 2 years, or can continue yearly screening.

  Screening should continue as long as a woman is in good health and is expected to live 10 more years or longer.
- Magnetic resonance imaging: The MRI screening in combination with mammography is targeted to high-risk patients because of their family history, a genetic tendency, or certain other factors.

CERVICAL CANCER

Cervical cancer is the leading cause of cancer death in women in both rural and urban areas. The Million Death Study 2012 suggests that a 30-year-old Indian woman has about 0.7% risk of dying from cervical cancer before 70 years of age in the absence of other diseases. India contributes to over 25% of the disease burden and more than 26% of the deaths due to cervical cancer worldwide.

Risk Factors

Human papillomavirus (HPV), sexual intercourse at an early age, multiple sexual partners, sexual partners who have had multiple partners, HIV positive status, and smoking.

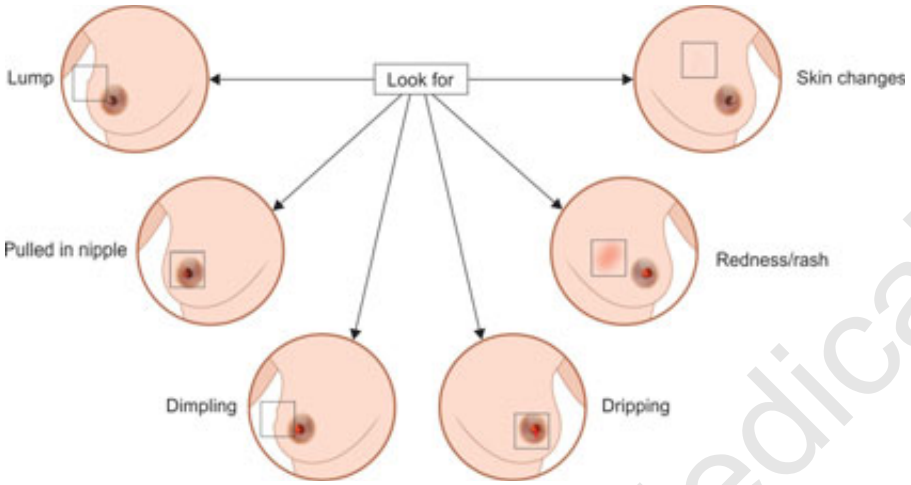

Figure 1: Signs of breast cancer.

TABLE 2: Screening recommendations from different organizations

Screening guidelines		
	ACS/ ASCCP/ ASCP	*USPSTF*
	Recommendations apply to both conventional and liquid based cytology	
When to start	Age 21	Age 21
Intervals	Ages 21–29: Cytology alone every 3 years	Ages 21–29: Cytology alone every 3 years
	Ages 30–65: HPV and cytology "co-testing" every 5 years is preferred or Cytology alone every 3 years is acceptable	Ages 30–65: HPV and cytology "co-testing" every 5 years for women who want to extend their screening interval or Cytology alone every 3 years
When to stop	Women older than age 65 following adequate negative prior screening (women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 years after diagnosis)	Women older than age 65 following adequate negative prior screening (as defined below) and who are not otherwise at high-risk (Adequate negative prior screening is defined as three consecutive negative cytology results or two negative co-tests within 10 years before cessation of screening with the most recent occurring in the past 5 years
Post-total hysterectomy	Women who have had a total hysterectomy (with removal of the cervix) should not be screen unless there is a history of CIN2 or more severe diagnosis in the past 20 years, or a history of cervical cancer ever	Women who have had a total hysterectomy (with removal of the cervix) should not be screen unless there is a history of high grade precancer or cervical cancer

ACS, American Cancer Society; ASCCP, American Society for Colposcopy and Cervical Pathology; ASCP, American Society for Clinical Pathology; HPV, human papillomavirus; USPSTF, US Preventive Services Task Force.

Screening (Table 2)

- Visual inspection
- Visual inspection with acetic acid (VIA)
- Visual inspection with Lugol's iodine
- The Pap smear both conventional and liquid based cytology
- Human papillomavirus DNA testing
- Cervicography
- Papnet
- Polar probe
- The first three are useful at community and low resource setting whereas, the last three are still in the experimental phase.

Primary Level

A single visit approach in the form of "see and treat" which involves VIA followed by cryotherapy. This unique approach is based on the principle that the screening test should provide rapid and accurate results and the treatment modality should be appropriate, adequate, and effective. This approach is useful in primary care level to make the screening program more cost effective.

Secondary and Tertiary Level

The Pap smear and HPV DNA testing are being used commonly.

Colposcopy: For all screen-positive women, for diagnostic confirmation with guided biopsies.

ENDOMETRIAL CANCER

Endometrial cancer (EC) commonly occurs in postmenopausal women. Overall morbidity and mortality of EC is low because most patients present at an early stage because of abnormal bleeding or postmenopausal bleeding. A strong influence of modifiable risk factors such as increasing obesity, life expectancy, and adjuvant tamoxifen use for breast cancer has been attributed. Adenomatous and atypical hyperplasia are the common precursors of endometrial carcinoma.

- Factors that increase the risk of EC are those associated with increase in endogenous estrogens or HT with estrogens.
- Unopposed ET in women with an intact uterus.

Currently, no evidence suggests that transvaginal sonography reduces mortality from endometrial cancer and there is inadequate evidence that endometrial sampling (biopsy) reduces mortality. The early clinical presentation and high early detection rate (85%) make it unlikely that screening will have a successful impact on earlier detection and increased survival rate.

The American Cancer Society (ACS) recommends that at the time of menopause, all women should be made aware of the risks and symptoms of endometrial cancer and strongly encouraged to report any unexpected bleeding or spotting to their physician. For those with increased risk and special situations such as on HT, genetic risk and on tamoxifen therapy should have a complete diagnostic evaluation for abnormal bleeding. Regular screening for high-risk group for endometrial carcinoma has not been fully evaluated.

OVARIAN CANCER

The general or lifetime risk of ovarian cancer is 1.4%. The most common sign of ovarian cancer is enlargement of the abdomen caused by accumulation of fluid or a large ovarian mass. However, many women have bloating or weight gain in the abdominal area, making this sign nonspecific.

Risk Factors

- A first degree relative with ovarian cancer (mother, sister, or daughter)
- Personal history of breast cancer <40 years or age
- Personal history of breast cancer <50 and one or more close relative with breast or ovarian cancer at any age
- Two or more close relatives with breast cancer <50 years of age or ovarian cancer at any age.

Screening

No screening guidelines are available for mass screening for ovarian cancer. Recommendation for screening is dependent on the risk status of women. A heightened awareness of the symptoms of early ovarian cancers on the parts of the patients and practitioners may help to reduce the delay in diagnosis and hopefully result in an improvement in outcome of some progress. For the general population – annual pelvic examination, Pap smear, and transvaginal sonography are recommended as a part of postmenopausal surveillance.

Primary prevention: Limited data are available on the efficacy of prophylactic oophorectomy in decreasing the risk of ovarian cancer in mutation carriers. Still, it is recommended that prophylactic surgery be considered in BRCA mutation carriers who have completed childbearing.

CONCLUSION

The relative lack of attention to midlife health ignores the evidence that critical changes are occurring during this life-stage that warrant changes in lifestyle, behavior, social engagement, and healthcare practices. As suggested by the old saying, "At 40, your eyesight starts to go; at 50 everything else starts to go" the midlife is a period of substantial physiological change that requires adaptive change to optimize health and functioning. Our goal should be to identify the physiological changes of the midlife, the triggers and nature of the aging- and ovarian-aging related processes that are initiated during this life-stage, and the critical factors, particularly modifiable ones, that influence the risk of healthy versus unhealthy aging so that midlife should be a healthy happy life changing experience.

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2

CHAPTER

Metabolic Health in Midlife

Charmila Ayyavoo

INTRODUCTION

Metabolism is defined as the breakdown of food and the transformation to energy. Alteration in metabolism is common in midlife and results in various metabolic disorders such as obesity, type 2 diabetes mellitus (T2DM), systemic hypertension, dyslipidemia, and cardiovascular disease (CVD). The US Census defines middle life as ages 45–64 years.

Metabolic diseases are currently the greatest threat to global human health and welfare. The metabolic syndrome is a combination of several of these disorders. The five measurable parameters for the metabolic syndrome include elevated blood pressure and triglycerides, central obesity, reduced high-density lipoprotein (HDL) cholesterol and elevated fasting plasma glucose. These increase the risk for atherosclerotic heart disease and T2DM.

Women are as susceptible as men to metabolic disorders, more so in midlife. The prevalence of metabolic ill-health increases with age. Obesity, lack of exercise and smoking contributes to the severity of metabolic issues. The rising trend has been attributed to greater industrialization and urbanization.

OBESITY IN MIDLIFE

Obesity is a major health concern in the world. Women in midlife tend to gain weight at the rate of 0.5 kg/year. The fat deposition in women in their midlife is central in distribution. It is deposited in viscera rather than in the subcutaneous tissues as the women age. This makes the female figure change from a "pear" to an "apple". Abdominal obesity is double that of general obesity in 73.8% women aged 60 years. Women are stratified into three categories based on waist circumference (WC). These are low-risk group with a WC of <80 cm, intermediate with a WC of 80–89 cm and high risk with a WC of >90 cm. These correspond to body mass index (BMI) ranges of 25 kg/m^2, 25–29.9 kg/m^{2,} and >30 kg/m^2. This increase in abdominal fat is associated with an increased risk of CVDs and non-insulin dependent diabetes mellitus. Visceral abdominal fat plays a far more important role than subcutaneous fat in altered metabolism. Increase in WC is an indirect evidence and easily measurable parameter of central obesity.

Obesity also contributes to menstrual irregularities and an increased risk of uterine prolapse. It is a risk factor for endometrial and breast cancer. Women with obesity have a poor body image and are prone to depression.

THE EFFECT OF OBESITY ON METABOLISM

Fat is an endocrine organ which produces various adipokines such as leptin, adiponectin, resistin and inflammatory factors–plasminogen activator inhibitor-1, interleukin-6, and tumor necrosis factor. The above factors from the abdominal fat leads to elevated triglyceride concentration, increased insulin resistance, and disrupt the metabolism. This leads on to metabolic syndrome, T2DM and CVDs. With increasing age, the reduction in estrogen and imbalance in estrogen: androgen ratio contributes to an increased risk of CVDs in menopausal women.

THE EFFECT OF OBESITY ON MENSTRUAL CYCLES

Anovulation in the perimenopausal period causes menstrual irregularities. It may be associated with polycystic ovarian syndrome (PCOS), hyperinsulinemia and insulin resistance. PCOS women with obesity may have worsening of symptoms. Even in the absence of PCOS, women with raised BMI may develop amenorrhea, oligomenorrhea, and dysmenorrhea.

THE ASSOCIATION OF OBESITY WITH FIBROIDS

Women with increased BMI are more likely to develop fibroids. There is a 21% increase with every 10 kg increase in weight.

THE ASSOCIATION OF OBESITY WITH CANCER

Women with obesity have high levels of estrogen and hyperandrogenism. This increases the risk of endometrial and breast cancers. When there is increased fat, there is increased insulin level due to insulin resistance. This raised insulin reduces the hepatic production of sex hormone binding globulin. There is an increased peripheral aromatization of androgens. Free sex hormone levels are increased and they contribute to an increased cancer risk in midlife.

MANAGEMENT

Weight loss is the corner stone of treatment of obesity in midlife. A weight reducing diet and increased exercise improves the quality of life. Weight loss improves the metabolic profile and insulin sensitivity.

DIABETES MELLITUS

The incidence of diabetes mellitus has increased over the years and now is considered as an epidemic. The increase is attributed to lifestyle changes. These changes have caused increase in overweight individuals, obesity and reduced physical activity. These changes in the environment when superimposed on genetic predisposition cause an increase in insulin resistance. This works in tandem with progressive β-cell failure in the pancreas. Blood sugar levels rise which are first in the nondiabetic range. A further reduction in the secretion of insulin as the individual ages causes increasing glycemia. In addition to diabetes, the insulin resistance and impaired insulin secretion predispose to the development of major cardiovascular risk factors which include hypertension and dyslipidemia. Diabetes development will further predispose to the development of microvascular and cardiovascular complications.

The risk factors that predispose to the development of type 2 diabetes are women above the age of 45 years, a BMI >25 kg/m^2, family history of diabetes mellitus in a first-degree relative, a sedentary lifestyle, gestational diabetes, hypertension, and dyslipidemia.

Interventions are suggested to prevent the progression of the disease. The interventions are lifestyle modification and the usage of drugs. In a study by Knowler et al., they randomly assigned 3,234 nondiabetic women with elevated fasting and post-load plasma glucose concentrations to placebo, metformin 850 mg twice daily or a lifestyle modification program which had a goal of 7% weight loss and 150 minutes of physical activity per week. The mean age of the participants was 51 years, the mean BMI was 34.0; 68% were women, and 45% were members of minority groups. The lifestyle intervention reduced the incidence by 58% (95% confidence interval, 48–66%) and metformin by 31% (95% confidence interval, 17–43%), as compared with placebo. The lifestyle intervention was significantly more effective than the usage of metformin.

The transition from the early metabolic abnormalities that happen before the development of diabetes like impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) to diabetes takes many years. Once diabetes sets in, there is a greatly increased risk for CVDs as well as long-term complications affecting the eyes, kidneys, and nervous system. The major morbidity and mortality due to diabetes are due to the duration of the disease, the levels of glycemia and the development of other risk factors.

There have been major trials to examine whether interventions can prevent or delay the development of diabetes in individuals with IFG or IGT. The screening tests for IFG/IGT are same as for diabetes. A fasting plasma glucose and 2-hour oral glucose tolerance test (OGTT) are the tests of choice for screening for all states of hyperglycemia. A 2-hour OGTT is essential to identify women with IGT which needs initiation of treatment with metformin. If women are started treatment with metformin, routine monitoring of the disease is with HbA1C once in 6 months. If the individual is not on drug therapy, she can undergo an annual visit.

Diabetes is known to cause depression and has an adverse impact on employment, absenteeism and work productivity. An analysis done by Tuncell et al. provides evidence that diabetes affects patients, employers, and society by causing work loss and health-related limitations for those who remain in employment. This study has been done to longitudinally examine the effects of diabetes on labor market outcomes. Women with diabetes had two more work-loss days compared with women without diabetes. When compared with individuals without diabetes, men and women with diabetes were 5.4% and 6% points respectively, more likely to have work limitations.

COMORBID CONDITIONS

Women with T2DM are also at risk for obesity, hypertension and dyslipidemia. They are also prone to develop hearing impairment, sleep apnea, nonalcoholic fatty liver disease, periodontal disease, cognitive impairment, depression, and fractures. Annual examination is mandatory by a dentist. Cancers of liver, pancreas, endometrium, colon/rectum, breast, and bladder have been found to increase in diabetic patients in some studies. This may be related to the associated obesity. Women in midlife should undergo specific cancer screening.

GOALS OF MANAGEMENT IN MIDLIFE

- Diabetes is associated with morbidity because of the end-organ damage it causes. Interventions at the appropriate time will limit this damage. Women should undergo ongoing evaluation as they age for diabetes related complications
- Glycemic control has been proved to minimize the risks for retinopathy, nephropathy and neuropathy. An HbA1C target of less than 7% should be the goal of any therapy. For older patients and for women with other comorbidities, a higher target can be set

- Prevention of cardiovascular morbidity should also be a target. This can be achieved with aggressive management of hypertension, reduction of cholesterol, and use of aspirin if there is a high-risk
- Smoking women should be asked to stop smoking
- Systems of care should be in place to maximize level of care
- Intensive insulin therapy when needed should necessitate a referral to an endocrinologist for optimum management. Primary level care should be enough in milder cases.

Vaccination in Diabetes

Women with diabetes should receive influenza vaccination yearly. Pneumococcal vaccination should be given after age 65 years if the initial vaccination was before the age of 65 years. Hepatitis B vaccine should be administered to unvaccinated adults with diabetes. Tetanus and diphtheria vaccinations should also be updated.

Cardiovascular Disease in Women

Cardiovascular disease is the leading cause of death in women. The mortality due to CVD in women has declined in the past 40 years. The Nurses Health Study was conducted in 85,941 women and they were followed up for 14 years. The incidence of coronary heart disease (CHD) was compared between 2 time periods. Coronary heart disease decreased by 31% in the years 1992–1994 compared to the years 1980–1982. In this period, smoking had decreased by 41% but overweight women had increased by 38%. The conclusion of the study was that reduced smoking habits caused a 16% decline and improvement in diet had caused a 16% decline. On the contrary, the increase in body weight accounted for a 8% increase in CHD.

The primary cardiovascular risk factors are the following in women:

- Personal history of CHD or other atherosclerotic vascular disease (peripheral arterial, cerebrovascular, and aortic disease)
- Age over 55
- Family history of premature CHD (first-degree male relative under age 50 or a female under age 60)
- Hypertension
- Dyslipidemia—high low-density lipoprotein (LDL) and/or low HDL
- Diabetes mellitus
- Metabolic syndrome
- Chronic kidney disease (CKD)
- Smoking
- Postmenopausal status
- Psychological stress (e.g., depression, posttraumatic stress disorder)
- Inflammatory/rheumatic diseases
- Pregnancy-related complications (e.g., eclampsia, pre-eclampsia, gestational hypertension, gestational diabetes).

There are certain risk factors for CVD which are unique to women and some risk factors which are common to both genders.

RISK FACTORS WHICH ARE UNIQUE TO WOMEN

Age at Menarche

Early age at menarche is associated with future risk of CHD and CVD. In a study of 1.2 million women with a mean age of 56 years with CVD (no known CVD at baseline), 25% reported that the age at menarche was below 13 years and 4% reported menarche at 10 years or younger. A similar result was obtained in a 2014 meta-analysis of six smaller cohorts in 150,000 women. The study concluded that each one year increase in age at menarche was associated with a 3% reduction in total mortality due to CVD.

Menopause

Cardiovascular disease is not common in premenopausal women in the absence of risk factors. The American College of Cardiology and American Heart Association have issued guidelines that state that the postmenopausal state is a risk factor for CHD with the same weight as the male sex. Early natural menopause at <44 years is associated with an increase in risk of CVD. The results on assessment of whether CVD risk is more in natural menopause or in surgical menopause is conflicting. In the Nurses Health Study, bilateral oophorectomy and not natural menopause was associated with an increased risk.

In another study, increased carotid artery intima media thickness which is a marker of subclinical atherosclerosis was not different in women with natural or surgical menopause. The risk for CVD correlated to the years since menopause. Menopause is not directly responsible for increase in CVD. The Women Health Initiative proved that hormone replacement therapy (HRT) has no role to play in the primary prevention of CVD. The HERS study proved that there is no benefit of HRT in secondary prevention of CHD.

Hysterectomy

Hysterectomy is not associated with an increase in CVD risk.

Premenstrual Syndrome

In the second Nurses' Health Study, women with premenstrual syndrome showed a higher risk of developing hypertension.

Pregnancy Complications

Certain pregnancy associated complications like pre-eclampsia, gestational hypertension, and gestational diabetes mellitus have been associated with increased CVD in midlife.

A history of a spontaneous pregnancy loss and preterm birth is also associated with an increased risk of myocardial infarction in later life.

A dropping hemoglobin in the second and third trimesters was found to be associated with a greater risk of CVD death.

Risk Factors Common with Men

The risk factors which both men and women share are age, family history of hypertension, dyslipidemia, diabetes mellitus, CKD, and metabolic syndrome.

Lifestyle Factors

Lifestyle factors which have an impact on developing CVD are smoking, dietary habits, obesity, excess alcohol, sedentary life style, and psychosocial factors. The American Heart Association recommends a target BMI of less than 25 kg/m^2 and a WC of less than 35 inches to reduce the risk of developing CVD. Depression is also associated with an increased CVD. A study was conducted among women in Stockholm on the psychosocial factors contributing to CVD events. They reported that marital stress more than work stress or living alone contributed to a three-fold increase in CVD events.

Depression was an independent risk factor for death in the Nurses' Health Study.

Women in midlife with no history of CVD should undergo cardiovascular assessment once in 3–5 years. This will identify CVD risk factors and serve as a guide for appropriate management. The treatment needs individualization. A healthy diet and an exercise regime are mandatory at this age in life.

CONCLUSION

Midlife is a transient phase in the lifecycle of women. She needs to prepare for old age and look forward in terms of the years to live. Metabolic health is very important in midlife. Parameters of metabolic health like waist circumference, blood pressure, blood glucose and lipid profile need to be evaluated. Even if one component of the metabolic syndrome is present, there should be an evaluation of the other factors. Clustering of risk factors for diabetes and cardiovascular disease are common. Individual risk factors are to be treated when present. Therapeutic changes in life style are made and obese women in midlife with multiple risk factors are advised to undergo weight management. Optimum management of metabolic health in midlife will lead to a healthy and happy old age.

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3

CHAPTER

Ultrasound of Menopausal Pelvis

Narendra Malhotra, Jaideep Malhotra, Neharika Malhotra, Rishabh Bora

INTRODUCTION

With the increase in life expectancy, the menopausal population is on the rise, and this has confronted the gynecologist with a host of new gynecological pelvic pathologies.

The ultrasound technology, which is presently available, offers a unique insight into the anatomical, physiological, and pathological states of the women in the menopausal age group.

The images offered by modern day transabdominal and transvaginal ultrasound transducers with facilities for high frequency, color-flow mapping, duplex Doppler studies, and three-dimensional (3D) reconstruction have revolutionized the approach to the clinical problems of a woman beyond her reproductive years.

NORMAL ENDOMETRIUM IN MENOPAUSE

The atrophic endometrium appears on ultrasound as a "pencil-line" echogenicity (Fig. 1), which represents the thickness of tissues between two sides of the atrophic basal endometrium. The measurement on an ultrasound scan should definitely include the maximum anteroposterior thickness in the sagittal long-axis view (Box 1). Whenever a fluid collection is present in the endometrium, the depth of the collection should be excluded from the total thickness. The correlation of thickness measurements, altered echotexture and sensitivity and specificity considerations has been discussed in the section on postmenopausal bleeding of this chapter.

Hormone replacement therapy tends to increase the endometrial thickness to about 1–1.5 mm for continuous estrogen or estrogen/progesterone therapy and to about 3 mm for sequential therapy regime. Women on sequential therapy have more variations in thickness in each month at different duration, with the thinnest endometrium following progesterone withdrawal.

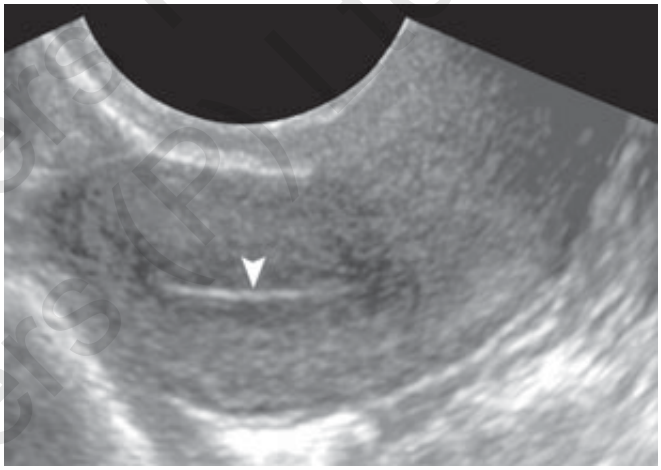

Figure 1: Endometrial atrophy. Transvaginal sonogram in longitudinal plane reveals a very thin endometrium (arrowhead) measuring 2 mm.

BOX 1 Points to remember

- The endometrium to be measured should include the maximum anteroposterior thickness in the sagittal long-axis view
- If a fluid collection is present in the endometrium, the depth should be excluded from the total thickness

The cut off level of the endometrial thickness for detection of endometrial disease should also be based on the length of time since menopause. A 3 mm cut off limit after 5 years or more since menopause greatly improves the specificity and also the false-positive rate.

Endometrial thickness is usually greater in asymptomatic, hypertensive postmenopausal women receiving antihypertensive drugs than in untreated hypertensive and normo-

BOX 2 Parameters to evaluate the endometrium

- Thickness
- Echo pattern
- Time since menopause
- Any hormone replacement therapy
- Any antihypertensive drugs
- Sonohysterography for focal lesions as screening test

tensive patients: 6.2 mm compared to 4.3 mm and 3.6 mm, respectively.

Transvaginal sonohysterography after a saline infusion improves the detection rate of focal abnormalities. Similar improvement of results has been reported with 3D ultrasound studies (Box 2).

Postmenopausal Bleeding

Atrophic endometrium (estrogen deficient), as it is prone to superficial ulceration, is the most common cause of postmenopausal bleeding. Approximately 80% of endometrial cancers occur in postmenopausal women, and because these patients commonly present with vaginal bleeding, it has been a dilemma in gynecologic practice to sample such an endometrium.

Endometrial measurements by transvaginal scanning in women with postmenopausal bleeding can be used to differentiate between a pathological and a normal endometrium.

Karlsson et al. evaluated 1,168 postmenopausal patients with bleeding by transvaginal ultrasonography and curettage. They confirmed the cut off value of 5 mm, below which the risk of endometrial abnormality is low (5.5%). They also suggested refraining from curettage when the endometrial thickness measurement was less than 5 mm.

Sheikh et al. in their study found that focal increased echogenicity, diffuse increased echogenicity and diffuse inhomogeneity definitely increase the predictability of pathologic findings. In addition, these findings, even in an endometrium which is thinner than the cut off values of normal postmenopausal endometrium, are indicators for inclusion in the group for invasive endometrial sampling (Fig. 2).

This study added the dimension of abnormal echogenicity of the endometrium to the currently followed criterion of endometrial thickness with a view to enhance accuracy, both for a better prediction of atrophy and a higher prediction for endometrial cancer. Expectant management can be offered to patients with a homogeneous endometrium, which is 6 mm thick or less. Aggressive evaluation for a malignancy must be made if there is a focal increased echogenicity or a diffuse inhomogeneity even in a thin endometrium.

Recent studies have concurred with these conclusions made at the end of the last century and have highlighted the utility of saline infusion sonohysterography, color Doppler and 3D techniques in further enhancing ultrasound-histopathology correlation and differentiate more reliably between

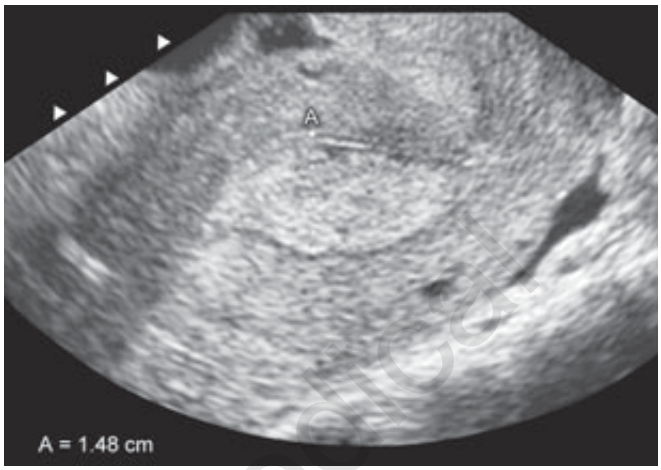

Figure 2: Transvaginal ultrasound of a postmenopausal woman with vaginal bleeding shows an abnormally thickened endometrium. Endometrial biopsy revealed atrophic endometrium.

patients who need an endometrial sampling and those who could be offered prudent expectant management.

ENDOMETRIAL FLUID COLLECTIONS

Fluid collections in the endometrium in many postmenopausal women mostly represent transudates associated with cervical stenosis. One needs to check the endometrial layer peripheral to the fluid collection. If it is 3 mm or less, the endometrium is usually inactive. If the peripheral endometrium is 4 mm or thicker, sampling is essential (Fig. 3).

MYOMETRIUM IN MENOPAUSE

The myometrium also atrophies during and after menopause resulting in a reduction of uterine size, but no appreciable change in echo pattern. Arcuate arteries may calcify (Fig. 4), particularly in the diabetic patient and show as a speckled

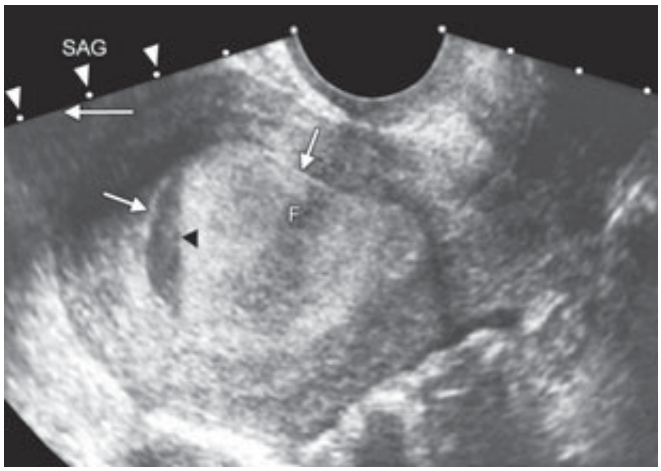

Figure 3: Endometrial atrophy and cervical stenosis. Echogenic fluid (F) fills and distends the uterine cavity and shows a fluid-fluid level (black arrowhead).

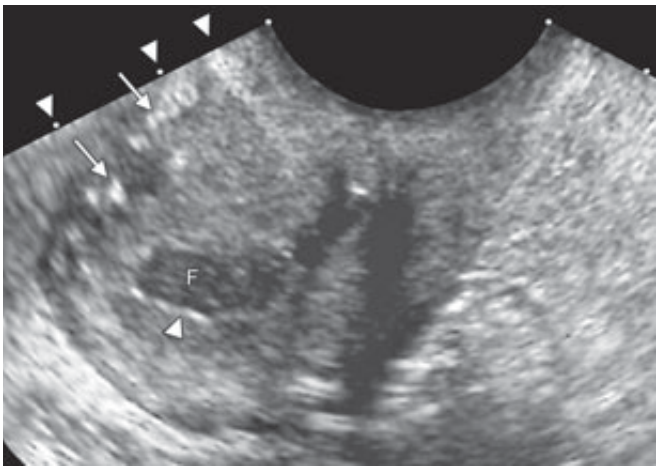

Figure 4: Transvaginal image of the uterus of an 85-year-old woman reveals calcification in the arcuate arteries (arrows).

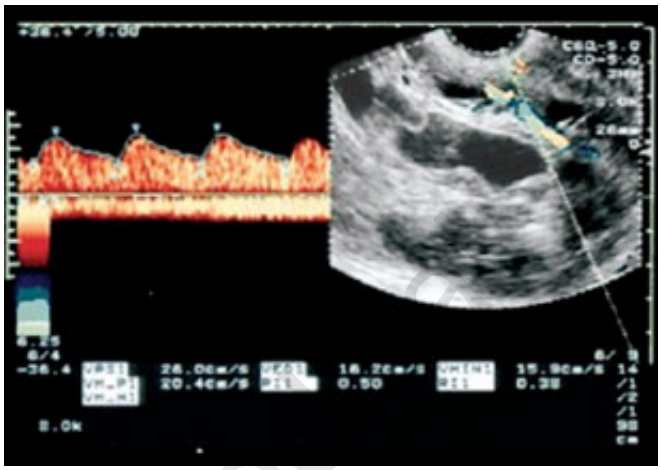

Figure 5: Increased ovarian blood flow on color Doppler ultrasound examination.

pattern in a small uterus. Fibroids undergo a reduction in size after menopause and variably shrink and calcify.

NORMAL ATROPHIC OVARY

The ovary lacks follicles after menopause and therefore looks like an area of nonspecific solid echoes making it more difficult to identify on ultrasound scans. More so the problem is compounded by the presence of overlapping bowel segments and the relatively increased distance of the shrunken ovary from the iliac vessels, which we use as landmarks in a menstruating female. Almost every ovary can however be visualized depending on the equipment resolution and experience of the observer. What one needs to remember is that nonvisualization of the ovary is never an indication that the ovary is normal. Ovarian volume shows a progressive decrease from 8.6 ± 2.3 mL in the first menopausal year to 2.2 ± 1.4 mL after more than 15 years after menopause.

OVARY AND OVARIAN CANCER SCREENING

More than two thirds of the cases of ovarian cancer are diagnosed when they reach stage III or IV. Women in stage I have a 3 in 4 five-year survival, whereas advanced disease shows a 9–28% survival only. Eighty percent of ovarian cancers occur in women 50 years or older. The need to evaluate the menopausal woman for cancer is therefore obvious. Even though screen positives are high and the cost-effectiveness and cost efficiency are poor, the dramatically better quality of life after an early versus a late diagnosis in a single patient justifies this so-called inefficient screening.

An annual pelvic examination, tumor marker levels, and grayscale ultrasonography with color Doppler and 3D reconstruction of tumor vascularity have emerged as a reliable ovarian cancer screen when used together (Fig. 5).

The criteria for diagnosis remain the same as in the premenopausal age group. These include grayscale observations of a solid mass, a cystic mass with solid areas, focal or diffusely thick walls or septations, mural nodules and heterogeneous internal echoes. Pelvic and para-aortic lymph node enlargement, ascites, suprarenal and liver metastases and pleural effusions can be elucidated by transabdominal ultrasound. Color flow and 3D vascular reconstruction criteria include abnormal calibration of vessels, dichotomous branches, elongation, coiling, aneurysms, vascular lakes, arteriovenous anastomoses and venovenous anastomoses. Low resistive and pulsatility indices are inadequately wide range to be reliable. These criteria and conclusions of other workers suggest that a cystic structure less than 30 mm in size, unilateral, unilocular and with no internal echoes, solid areas or nodules, which is avascular on color flow mapping may be re-evaluated 6 and 12 weeks later and then annually if it does not increase or change in morphology or vascularity. Any mass with abnormal vascularity and all masses greater than 50 mm in size warrant surgical evaluation. Aspirates obtained even under ultrasound guidance do not contain an adequate representation of cells from the tissue of origin to justify the technique. All masses associated with a rising CA 125 level warrant surgical evaluation. It must be remembered that not all adnexal cysts are ovarian in origin and that the demonstration of an atrophied ovary separate from the cyst should bring into consideration the possibilities of peritoneal inclusion cysts, residual postinflammatory cysts, tubal lesions, and postendometriosis residual fluid loculi. All these lesions are avascular on color flow mapping and may be seen in up to a fifth of postmenopausal women.

CONCLUSION

High technology implementations both in their cheaper and expensive top of the line avatars improve disease detection in the postmenopausal women. Awareness of the imaging armamentarium and appropriate referrals in the context of time, place, and expertise will continue to enhance the quality of life in this group of patients. It is suggested for efficient screening of ovarian and endometrial disease

in the perimenopausal and menopausal age groups, a routine transvaginal scan with color flow mapping should be done along with a Pap smear examination every year. This will ensure an effective screening and early detection of malignancies and improve the health of menopausal age group women.

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4

CHAPTER

Exercise in Midlife

Sasi B Avirneni, Sajana Gogineni

Physical activity is something you do, physical fitness is something you acquire

INTRODUCTION

Fitness is important at all ages, more so for women beyond 40 because the reproductive hormones start waning, resulting in huge bodily changes. Muscles start to age and that is why most women feel lethargic and easily fatigued nearing menopause.

The lean muscle mass is the most metabolically active tissue in the body and when the muscle mass is lost body metabolic rate comes down and fat starts accumulating around the trunk, which can contribute to weight gain. If we don't put sufficient stress on muscles, as weeks pass by slowly we will grow weaker, which can make everyday activities difficult to perform.

It is important to start with a strength training workout because at this age, women are at a higher risk of losing lean muscle mass. The increasing morbidities due to coronary artery disease, diabetes mellitus, metabolic syndrome, and fractures (especially neck of femur), are all because of the sedentary lifestyle, poor exercise and bad eating habits.

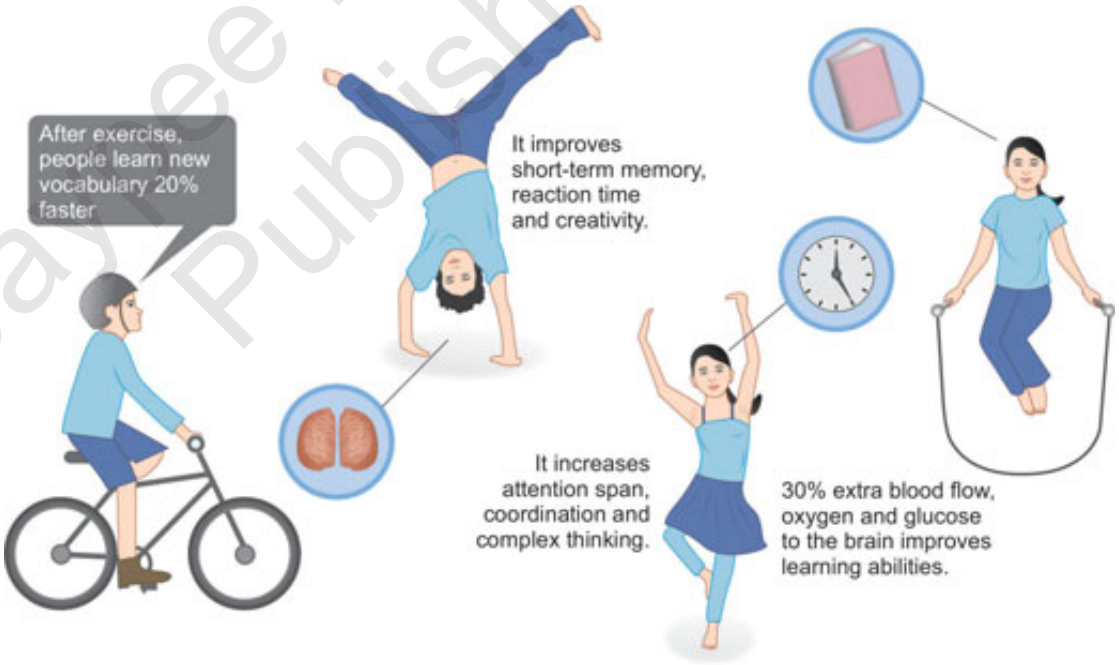


Figure 1: Benefits of exercise.

THIS IS EXACTLY HOW MUCH **YOU HAVE TO WALK** TO START **LOSING WEIGHT**

Week	Warm-up	Walk for	Cool down	Total time	Sessions/ week
1	5 min	10 min	5 min	20 min	3
2	5 min	15 min	5 min	25 min	4
3	5 min	20 min	5 min	30 min	4
4	5 min	20 min	5 min	30 min	5
5	5 min	25 min	5 min	35 min	4
6	5 min	30 min	5 min	40 min	4
7	5 min	30 min	5 min	40 min	5
8	5 min	35 min	5 min	45 min	4

Figure 2: Walking as a means of losing weight.

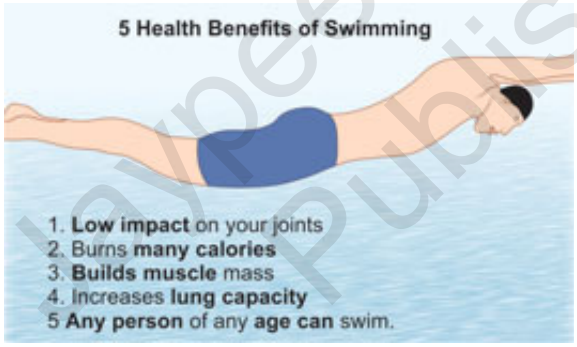


Figure 3: Health benefits of swimming.

EXERCISE AND ENDORPHINS

Exercise and physical activity both have impact on menopause related symptoms, by producing hypothalamic and peripheral β-endorphins.

- Exercise helps to lose weight
- Relieves vasomotor symptoms, fatigue, and depression
- Improves cognitive function, sleep pattern and bone mineral density
- Helps maintain normal lipid levels and reduces cholesterol plaques that can lead to stroke and myocardial infarction
- Helps build and maintain healthy bones, muscles and joints
- Reduces risk of developing colon cancer, by releasing antioxidants and removing free radicals
- Helps prevent obesity, a major risk factor for many diseases and cancers
- Activates antioxidant enzymes that protect cells from free radical damage
- Increases insulin sensitivity, control blood glucose and thereby control weight
- Boosts alertness, possibly by triggering the release of epinephrine and norepinephrine
- Improves memory and intellectual function.

PRECAUTIONS

Exercise has been shown to slow and even reverse age-related decline in mental function and loss of short-term memory. Once the mind is set on picking up exercise as a daily routine

Figure 4: Simple exercises at the gym.

the next most important question is what kind of exercise to and how to start? It is worthwhile to begin under supervision of a trainer for all beyond 40.

It is important to have a routine health check before starting an exercise program including blood pressure, blood sugars and inform your trainer about pre-existing health issues.

COMPONENTS OF AN EXERCISE PROGRAM

- Aerobic activity
- Strength training
- Flexibility training.

The use of an exercise log will help to plan and keep track of the exercise program.

Aerobic Activity

It is continuous movement that uses big muscle groups and is performed at an intensity that causes the heart, lungs, and vascular system to work harder than at rest. Cardiorespiratory fitness is built through aerobics. Aerobic exercise conditions and strengthens the heart, respiratory system, muscles, and immune system. Aerobic activities can be both outdoor and indoor.

Outdoor Activities

Walking, jogging/running, cycling, swimming, basketball, soccer, jumping rope.

Indoor Activities

Treadmill, stair climbing machine, stationary bike, elliptical trainer, rowing machine, aerobics, boxing, etc.

Strength Training

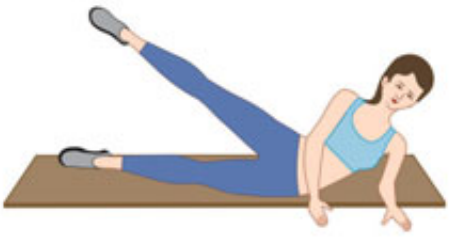
Free weights: Use of dumbbells and/or bars with weights on the ends, involves balance and coordination, useful for enhancing function in daily activities and recreational sports.

The most convenient form of resistance exercise are pushups, pull-ups, lunges, squats.

Flexibility Training

Flexibility gets restricted with disuse and ageing. Benefits of doing flexibility exercise are:

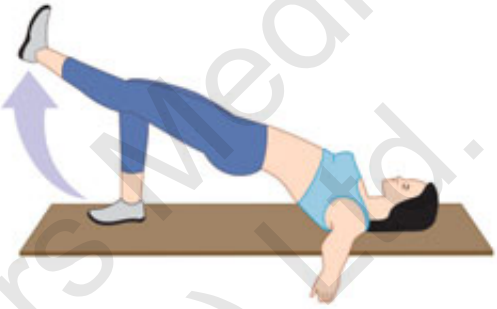
- Decreased chance of muscular injury, soreness, and pain
- Helps prevent and reduce lower back pain
- Improves joint health (tight muscles stress our joints)
- Activities include stretching, yoga, pilates, tai chi.



1. Side saddle leg lifts

2. Bent-knee reverse hip raise

3. Step-ups



4. Single-leg hip raise

5. Plank booty leg lifts

6. Squat step with resistance band

7. Side-lying leg raises

8. Squat with kick

Figure 5: No equipment bodyweight workout.

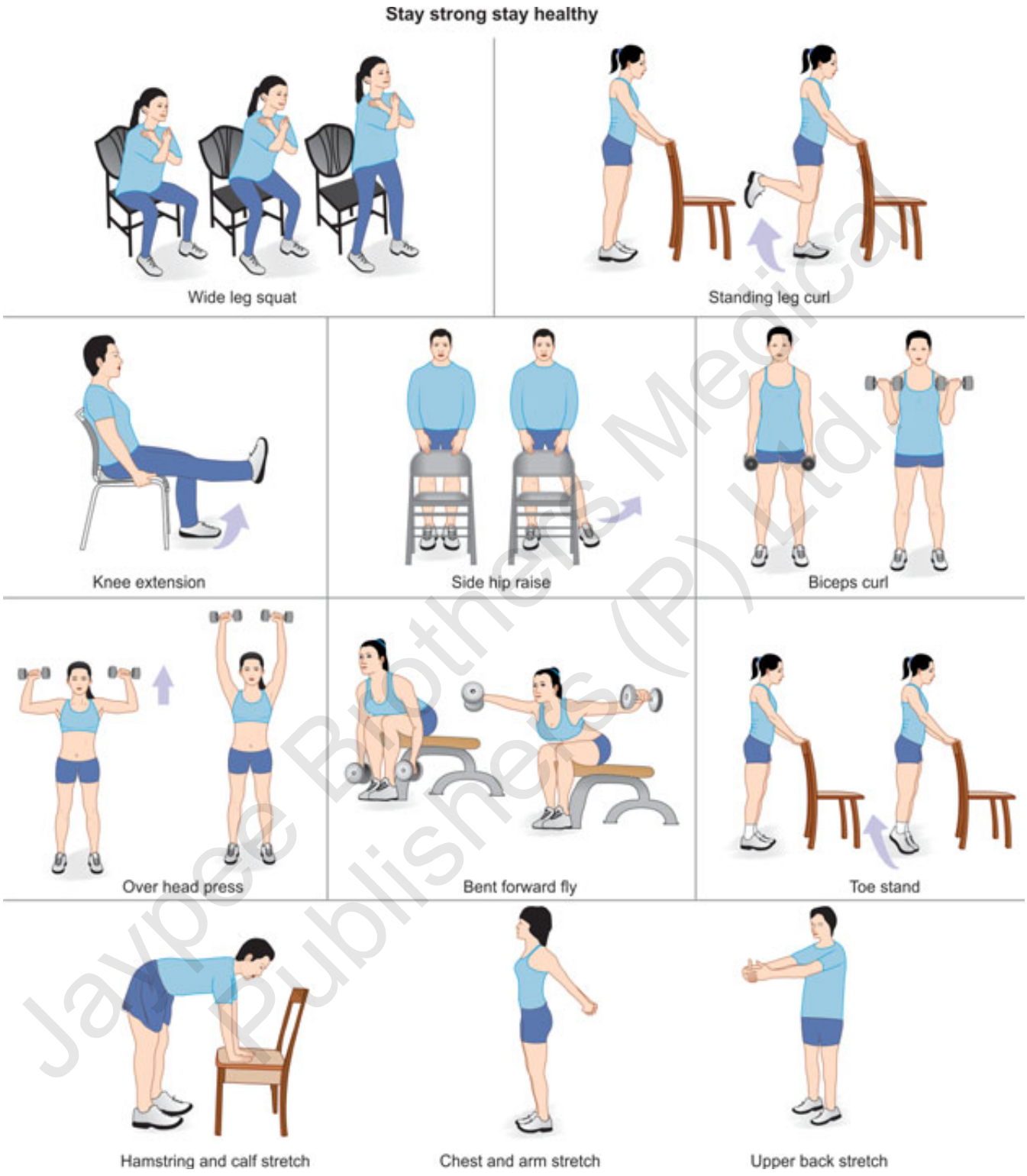


Figure 6: Simple exercise routine for those with a sedentary lifestyle.

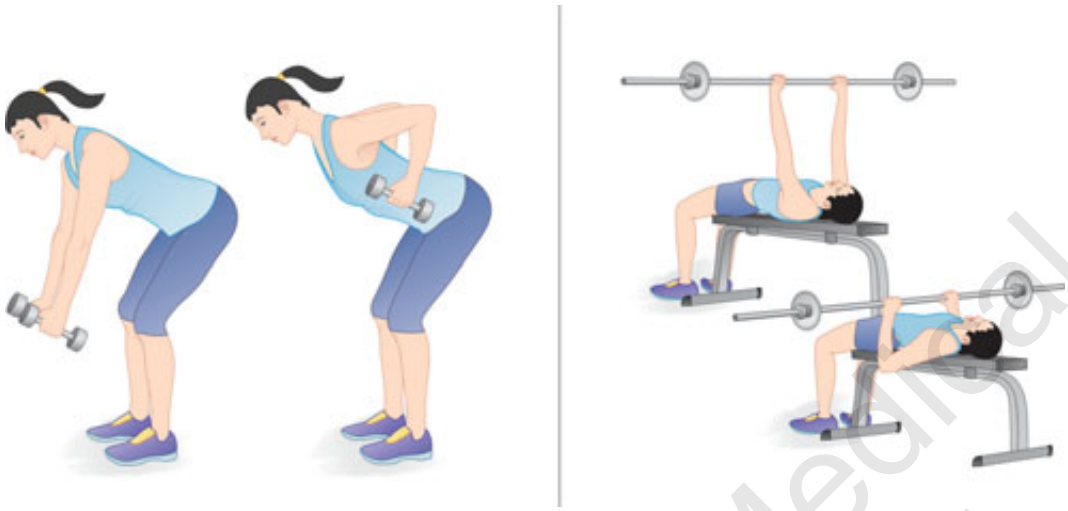


Figure 7: Resistance training.

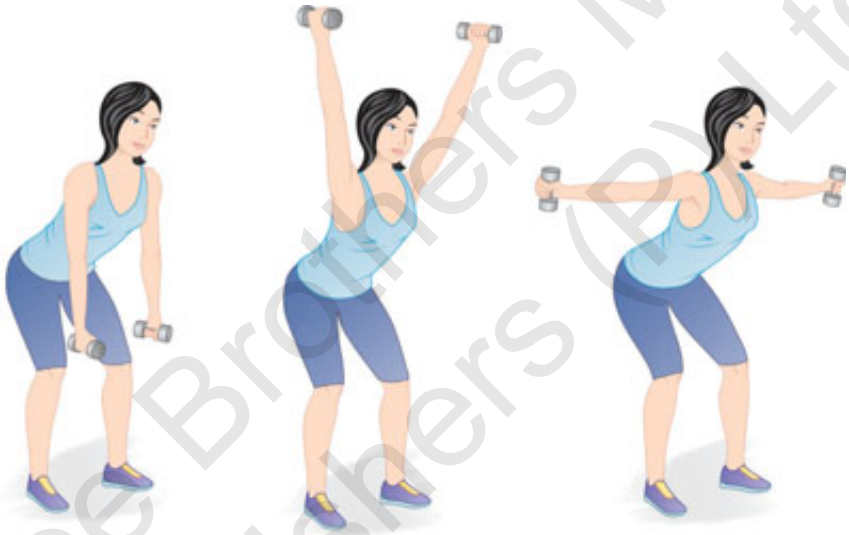


Figure 8: Resistance training.

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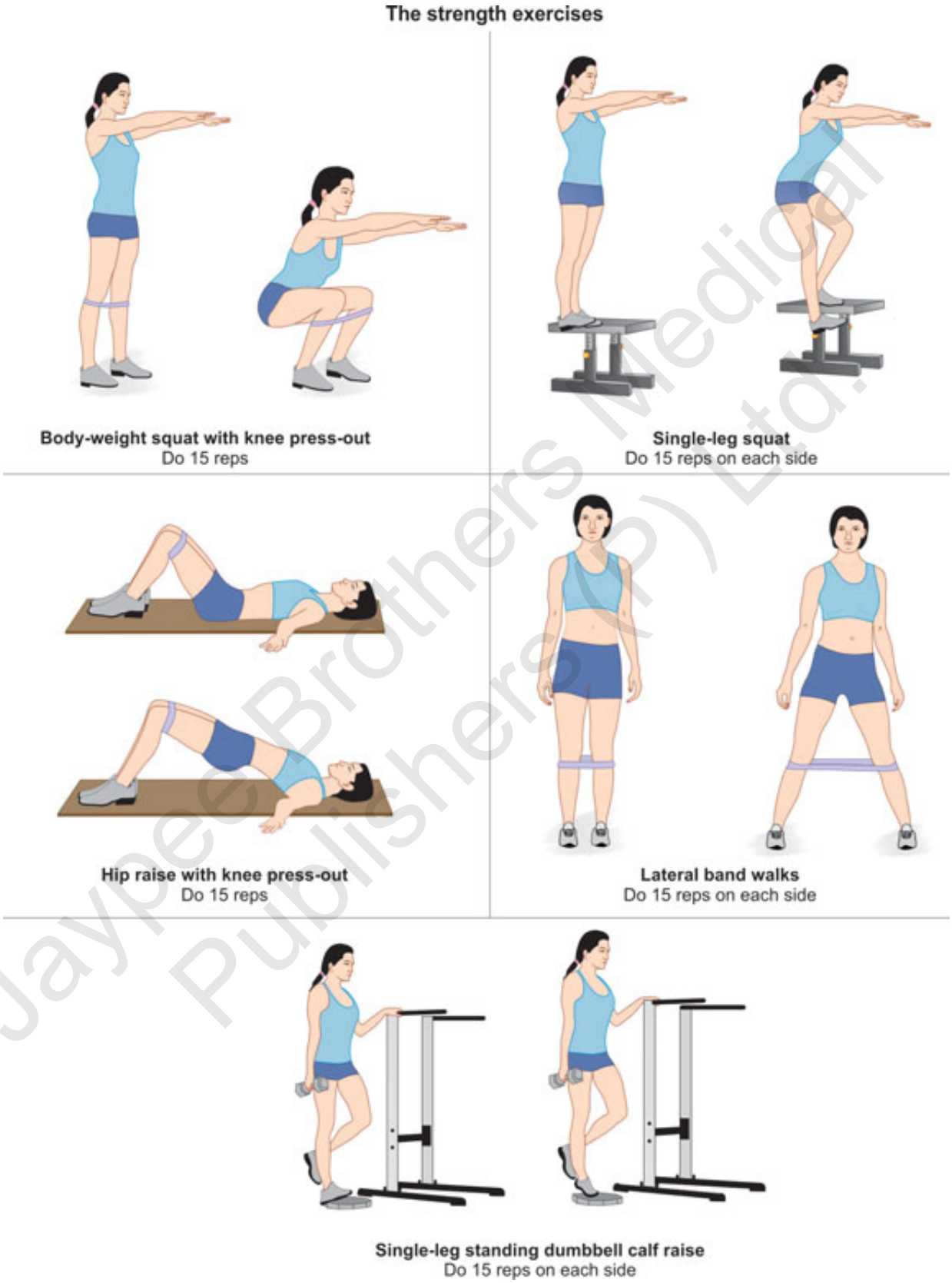

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Figure 9: Correct posture is important.

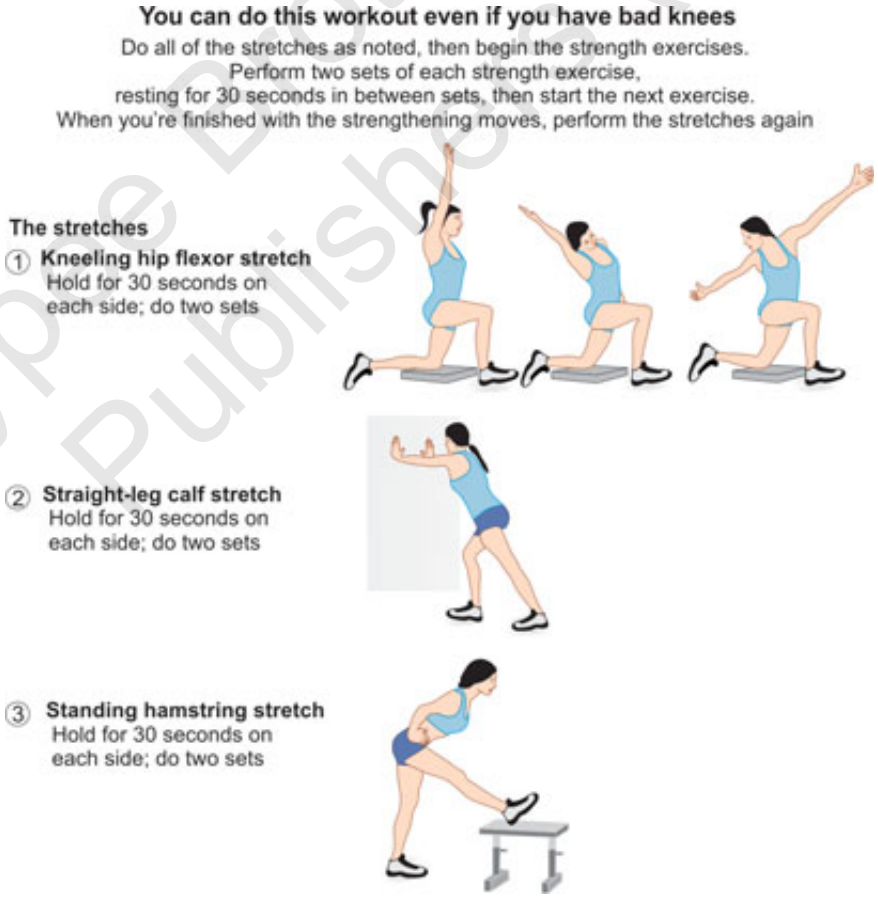


Figure 10: Stretches are important to prevent injury.

Figure 11: Everyday yoga.

Figure 12: Excuses for failing to work out.

Once the importance of exercise is understood, types of exercise it is equally important to understand the time to be spent on each kind of exercise:

Frequency: 3–5 days per week

Aerobic exercise: A minimum of 3 days a week are necessary to reach most exercise goals and minimize health risks

- Strength training: A minimum of 2 days per week
- Flexibility training: A minimum of 3-5 days per week
- Duration:
  - Aerobic: 20–60 minutes of continuous aerobic activity
  - Strength: 1–3 sets of 8–12 repetitions
  - Stretching: Stretch all muscle groups and hold positions for 10–30 seconds.

Common barriers for women to exercise:

- Lack of time
- Lack of motivation
- Parenting demands
- Lack of energy
- Health conditions
- Lack of money.

FEW TIPS TO OVERCOME THE BARRIERS

- Lack of time: Many women juggle child-rearing, household duties and paid work, and don't find time for themselves. Try to exercise whenever possible. Three 10-minute bouts of physical activity over the day have the same health benefits as a continuous 30 minute session
- Lack of motivation: Some women don't feel motivated without a training partner. Remedy would be to find a training partner, join a local walking group. Need not be gyms and jogging. Better alternate would be dancing, roller skating which suits to individual physique and would be fun as well
- Parenting demands: Try to share child rearing and household chores with partner, friends, and family. Or paid childcare is an option. Include physical activity in caring

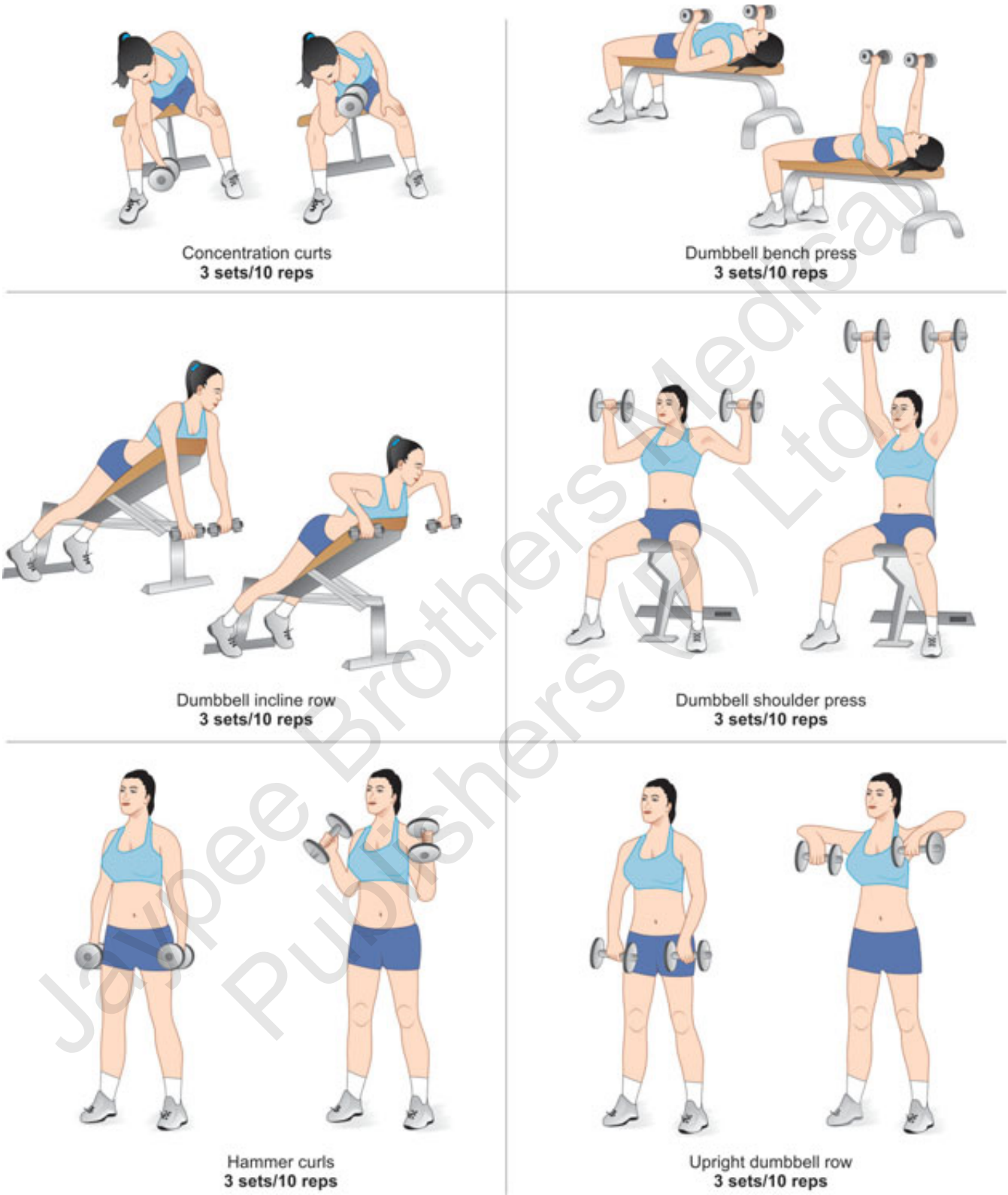
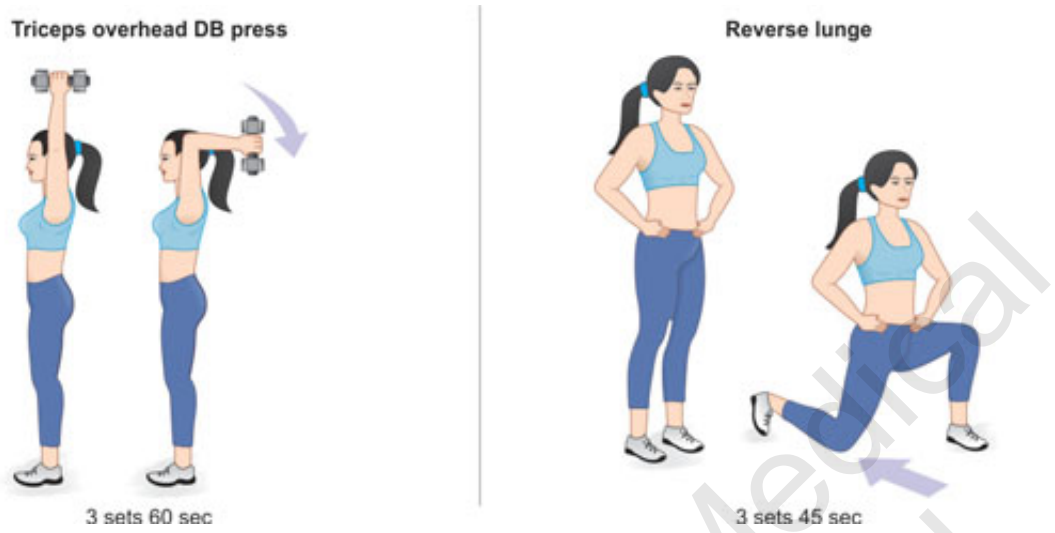


Figure 13: Sample dumbbell workout.

DB, dumbbells.

Figure 14: Dumbbell workout.



DB, dumbbells.

Figure 15: Dumbbell workout.

- Lack of energy: Regular exercise give the energy to better cope with the demands of daily life to overcome the fatigue which is a by-product of a busy lifestyle
- Health problems: Older women are more likely to have a chronic health condition (e.g., arthritis) that limits their participation in some forms of exercise. Talk to your doctor about appropriate forms of exercise. In most cases, physical limitations don't rule out all activities. For example, exercise in water (such as aquarobics) is an enjoyable option for many people with arthritis
- Lack of money: Exercise doesn't require expensive clothes or a gym membership. One of the most beneficial forms of exercise is free – brisk walking. Some of the community centers offer a range of physical activity classes and childcare at modest prices.

SOME TIPS TO STAY SAFE AND INJURY FREE EXERCISE

- Equipment: Fitness equipment/safety
- Buy appropriate shoes
- Wear comfortable clothing
- Not too hot! Not too cold!
- Run and walk with a friend
- More fun, safer, with a physical and mental support system
- Night time: Stay to the well-lit areas
- Select activities that are fun to you!
- Be aware of the body. Think about how the particular exercise feels like. If something doesn't feel right, stop immediately and seek medical advice
- Warm up and cool down. Try slow stretches initially. Cool down with slow stretching
- Pace oneself. Having at least one recovery day each week to rest. If pain is experienced, advised to rest until the pain subsides
- Mix it up. Try other sports and exercises to reduce the risk of overtraining
- Strap or tape. If a joint is prone to injury, strap or tape it before exercising. Consulting a physiologist or physiotherapist to obtain a program, to strengthen the injured area and to get an advice on proper taping techniques
- Stay hydrated, as one to one and a half liters of fluid is lost for every hour of exercise. So drink water before, during and after a session
- Clothing should be according to the weather
- Do the exercise in the right way, to use the muscles correctly
- Check your equipment periodically for safety
- The moderate-intensity activity, allows to talk but not to sing
- Vigorous activity results in an inability to say more than a few words without pausing for a breath.

EXAMPLES OF MODERATE INTENSITY EXERCISE INCLUDE

- Brisk walking (100 steps/min)
- Dancing
- Swimming or aqua aerobics
- Gentle cycling (5–9 mph)
- Badminton or doubles tennis
- Volleyball.

Figure 16: Upper body workout.

EXAMPLES OF VIGOROUS INTENSITY EXERCISE INCLUDE

- Running
- Power walking at 5 mph or more, or walking uphill briskly
- Cycling faster than 10 mph
- Aerobics
- Martial arts
- Competitive sports (football, basketball, rugby etc.)
- Skipping/jump rope
- Rowing.

FREQUENTLY ASKED QUESTIONS

What Time of Day Is Best?

- Choose the most convenient time for your schedule
- Choose a regular time—the same time every day
- Timing may depend on the activity you choose.

Can I Eat Before Exercise?

- It is best not to eat a meal for 2 hours beforehand
- Be sure to drink plenty of water before and during exercise.

Should I Exercise When I'm Sick?

- No, especially if you have a fever.

WARNING SIGNS

- Stop exercising when you feel dizzy, nauseated, chest pain, chest tightness, excess sweating, or tingling in ears, and consult your doctor
- Always remember crash dieting and crash exercising is not recommended; that would be more hazardous than beneficial
- Schedule an exercise program which you can enjoy and workout.

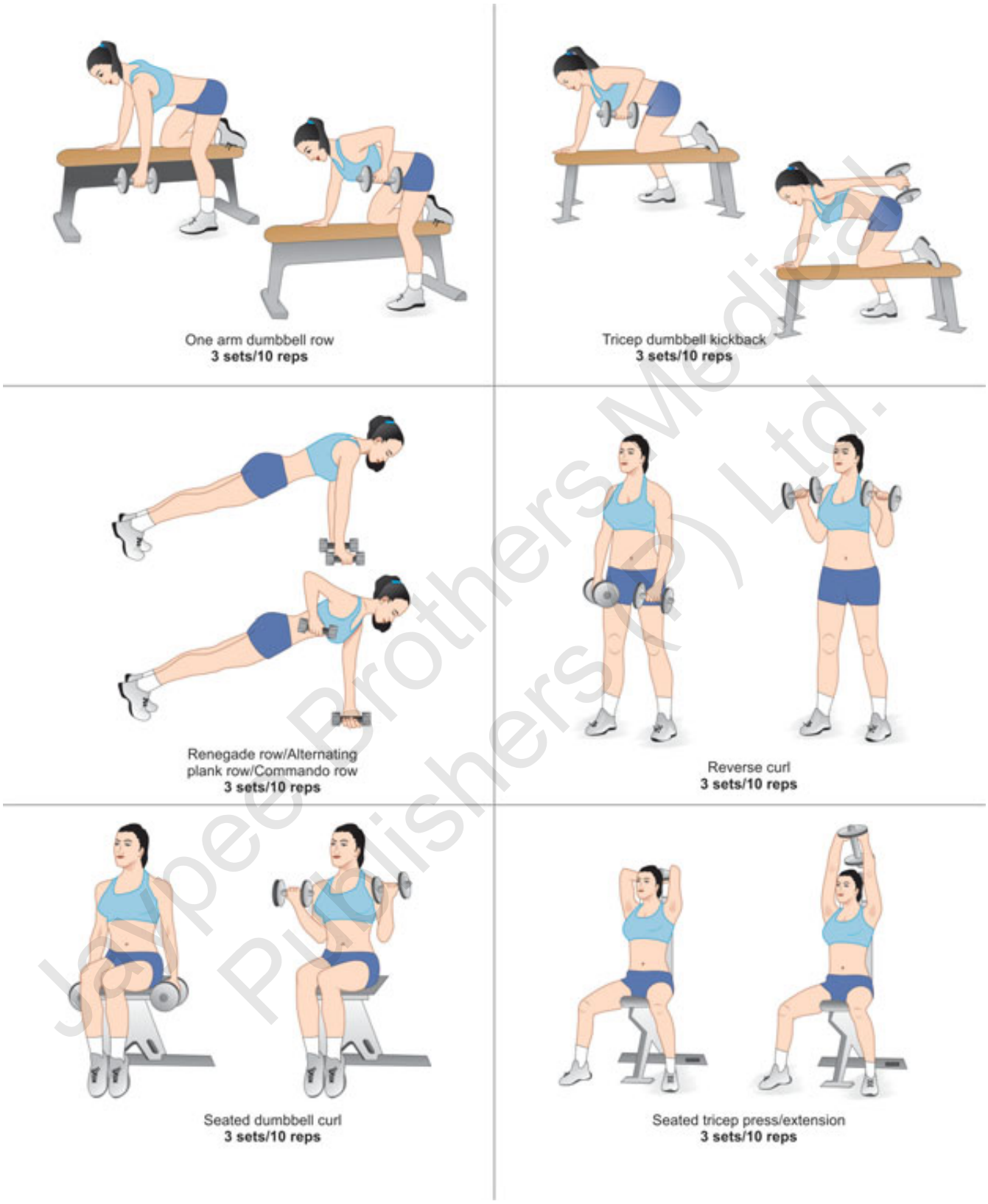


Figure 17: Advanced dumbbell workout.

"The first wealth is health."

Happy exercising and experience the change in the body and mind.

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5

CHAPTER

Urogynecological Issues in the Midlife

Rajendra Nagarkatti, Pratik Tambe

INTRODUCTION

The midlife is a special period of adult life. The aging process affects each individual differently. Of the many factors responsible for the process of aging, sex is one factor. Women usually exhibit major signs when affected by the menopause.

Urogynecological disorders are one of the chief group of disorders which are encountered with greater frequency in this age group. Others include systemic disorders like diabetes, hypertension, heart disease, osteoporosis and orthopedic issues. We focus on urogynecological conditions, their diagnosis and tools to correctly identify and treat these problems in the midlife population.

DIAGNOSTIC CHALLENGES

Most women in India often do not seek help for their health issues until later stages of disease. This is especially the case in urogynecological disease as women are often embarrassed to admit such problems and to express themselves to their healthcare providers. In standardized questionnaires, often these issues are not inquired for and this delays their diagnosis even further.

PRESENTING COMPLAINTS

When patients do present, it is most commonly with symptoms suggestive of urinary tract infections (UTIs) (frequency, urgency, and fever), urinary incontinence (urge, stress, or mixed), vaginal prolapse and rarely, urinary retention. Often, there is a cluster of symptoms interspersed with systemic complaints and arriving at a complete diagnosis requires patient history taking and a focused clinical examination.

HISTORY TAKING, PHYSICAL EXAMINATION, AND BASIC INVESTIGATIONS

A complete history with origin, duration, progress, aggravating, and relieving factors is of benefit. An obstetric history, past history of similar complaints, surgical history, per speculum examination and per vaginal examination is mandatory. In women who are able to understand the instructions, a voiding diary and dietary chart is of immense value in arriving at a specific diagnosis. Age, parity, mode of delivery, menopausal status, sexual activity, comorbidity, and previous pelvic surgery are some of the important points in the history.

Pad testing has been described in various textbooks as an efficient means of identifying the presence and site of various urogenital fistulae, but in practice the results may not always be clear cut. An ultrasound of the pelvis with measurement of postvoid volume, intravenous urogram and cystourethrography are some of the noninvasive methods employed to arrive at a diagnosis.

URINARY TRACT INFECTION

Owing to loss of protective estrogen and thinning of the vaginal mucosa and supporting fascia, UTIs are more common in the midlife. A small proportion of these patients may present with recurrent infections, necessitating the ruling out of diabetes mellitus and a culture for isolating the responsible organism with antibiotic sensitivity testing. Ultrasound imaging of the pelvis to rule out rare bladder stones and an interval cystoscopy may be indicated in certain patients.

In recent years, there has been an upsurge in the usage of single dose fosfomycin, nitrofurantoin, cranberry extract, and d-mannose for uncomplicated UTI and prophylaxis respectively. Local estrogen creams and occasionally horm-

onal hormone replacement therapy may be of benefit in patients with atrophic vaginitis and recurrent local and ascending infections.

VOIDING DYSFUNCTION

Normal voiding is achieved by a voluntarily initiated continuous detrusor contraction that leads to complete bladder emptying within a normal time span and in the absence of obstruction. Female voiding dysfunction (VD) is a complex disorder, lacks definition, and is poorly understood and difficult to manage.

Voiding dysfunction is a diagnosis by symptoms and urodynamic investigations and is defined by the International Continence Society/International Urogynecological Association (ICS/IUGA) as abnormally slow and/or incomplete micturition. Abnormal slow urine flow rates and abnormally high post void residuals, the basis of this diagnosis. This diagnosis should be based on a repeated measurement to confirm abnormality. On urodynamics, these measures are peak flow rates of <15 mL/second and/or 200 mL or more of residual urine. The true estimate of this condition may be between 4.2 and 46.4% of the population.

URINARY INCONTINENCE

A common presenting complaint in the midlife age group, urinary incontinence can be of various types typically described as stress, urge, overflow, or mixed. These are further described and classified by the ICS. It has been said that the best anti-incontinence procedure as far as success is concerned is the correct evaluation.

URODYNAMIC STUDIES

Urodynamic studies are a combination of tests that involve simultaneous measurement of various physiological parameters of urethral and bladder function during bladder filling and emptying. Urodynamic studies include cystometry, urethral pressure measurements, uroflowmetry, pressure flow studies, surface electromyography, video urodynamics and ambulatory urodynamic monitoring.

Unfortunately, these tests are not widely available, may not be cost effective, require specialised equipment and are therefore, inaccessible to many patients. While there is no widespread consensus regarding their utility, they are mainly used in a tertiary care setting for the diagnosis and prognostication of the various types of urinary incontinence.

Pandey D et al. attempted to evaluate the role of urodynamic studies over 6 months in a specialized urogynecological unit. They particularly studied cystometry and urethral pressure measurements in detail as these are the most frequently used in clinical practice involving women.

Cystometry is the continuous measurement of the pressure/volume relationship of the bladder to assess sensations, detrusor activity, bladder capacity, and bladder compliance. Urethral pressure is an important determinant of urinary continence. The urethral closure pressure represents the difference between the urethral pressure and the simultaneously recorded intravesical pressure and it represents the ability of the urethra to prevent urinary leakage.

Out of 550 women whom they studied, the mean age of the population was 62.71 ± 10.92 years. Total 84.16% (170 women) were postmenopausal. More than a third (36.22%) of the menopausal women had surgical menopause, of which in two of these women ovaries were removed. The mean menopausal years at the time of presentation were 15.00 ± 11.33 years. Mean parity was 2.24 ± 1.26 with a predominance of vaginal deliveries. Nineteen (9.41%) women were nulliparous. Only one woman in the study group had a ventouse delivery while two had forceps delivery. Twelve women in the group underwent Caesarean delivery and three out of these never experienced a vaginal birth. More than half (59.90%) women were sexually active.

There was a history of one or more major gynecological pelvic surgeries in 88 women which included hysterectomy (abdominal, vaginal, or laparoscopic), conventional repair of vaginal prolapse (without mesh) and mesh repairs (abdominal sacrocolpopexy or vaginal sacrospinous fixations). Total 28.21% had some surgery for rectification of pelvic floor relaxation such as colporrhaphies, mesh fixations (abdominal or vaginal), and sling operations. Two women had undergone Wertheim's operation for early stage cervical carcinoma. Overall, around half (43.56%) had some kind of gynecological pelvic surgery.

Women with stress incontinence were younger (59.84 ± 10.52 years) as compared to urge incontinence (65.33 ± 9.95 years), mixed incontinence (64.30 ± 11.01 years) and unspecified urinary incontinence (65.44 ± 13.77 years). Less women in this group had attained menopause (71.88% as compared to 88–100% in other groups) and more were sexually active (70.31% as compared to 40–69% in other groups). Around half of women with stress urinary incontinence had tried pelvic floor muscle training before presenting. This was followed by 44.44% in urge incontinence and 38.81% in mixed incontinence. A high proportion of women (66.67%) who had undergone vaginal hysterectomy were noticed in the group of unspecified urinary incontinence.

TREATMENT OPTIONS FOR URINARY INCONTINENCE

Pelvic floor muscle training (PFMT) is the first-line conservative therapy for urinary incontinence in women. Other active treatments include: physical therapies (e.g., vaginal cones), behavioral therapies (e.g., bladder training), electrical or magnetic stimulation, mechanical devices (e.g., continence pessaries), drug therapies (solifenacin, oxybutynin, and duloxetine), and surgical interventions including sling procedures and colposuspension.

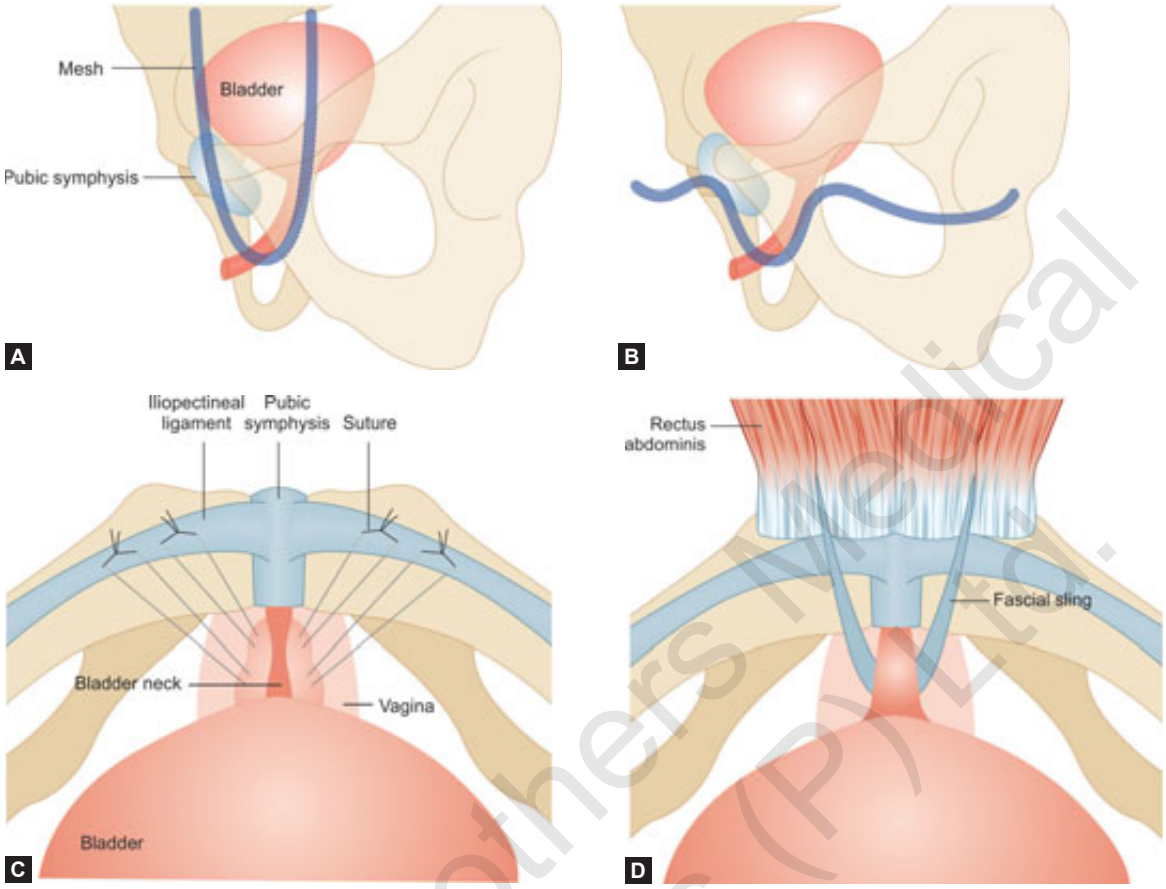

Figure 1: Surgical perspectives in urinary incontinence correction.

PELVIC FLOOR MUSCLE TRAINING VS OTHER THERAPIES

A Cochrane systematic review evaluated the effects of adding PFMT to any other active treatment for urinary incontinence in women.

Thirteen trials met their inclusion criteria, comprising women with stress urinary incontinence (SUI), urgency urinary incontinence (UUI) or mixed urinary incontinence (MUI); they compared PFMT added to another active treatment (585 women) with the same active treatment alone (579 women). The majority of the trials did not report the primary outcomes such as cure or improvement, quality of life (QoL) or measured the outcomes in different ways. The quality of evidence was either low or very low.

More women reported cure or improvement of incontinence in two trials comparing PFMT added to electrical stimulation to electrical stimulation alone, in women with SUI, but this was not statistically significant [9/26 (35%) versus 5/30 (17%); risk ratio (RR) 2.06, 95% confidence interval (CI) 0.79–5.38]. More women reported cure or improvement of incontinence in another trial comparing PFMT added to vaginal cones to vaginal cones alone, but this was not statistically significant [14/15 (93%) versus 14/19 (75%); RR 1.27, 95% CI 0.94–1.71].

With regard to condition-specific QoL, there were no statistically significant differences between women (with SUI, UUI, or MUI) who received PFMT added to bladder training and those who received bladder training alone at 3 months after treatment, on either the Incontinence Impact Questionnaire-Revised scale [mean difference (MD) -5.90, 95% CI -35.53–23.73] or on the Urogenital Distress Inventory scale (MD -18.90, 95% CI -37.92–0.12).

A similar pattern of results was observed between women with SUI who received PFMT plus either a continence pessary or duloxetine and those who received the continence pessary or duloxetine alone.

RETROPUBIC COLPOSUSPENSION

A meta-analysis of 46 trials involving 4,738 women revealed a significant incidence of cure rates with retropubic colposuspension procedures (Fig. 1). Overall cure rates were 68.9–88.0% for open retropubic colposuspension. Two small studies suggest lower failure rates after open retropubic colposuspension compared with conservative treatment. One trial suggests lower failure rates after open retropubic colposuspension compared to anticholinergic treatment.

Evidence from six trials showed a lower failure rate for subjective cure after open retropubic colposuspension than

after anterior colporrhaphy. Such benefit was maintained over time (RR of failure 0.51; 95% CI 0.34–0.76 before the 1st year, RR 0.43; 95% CI 0.32–0.57 at 1–5 years, and RR 0.49; 95% CI 0.32–0.75 in periods beyond 5 years). In comparison with needle suspensions there was a lower failure rate after colposuspension in the 1st year after surgery (RR 0.66; 95% CI 0.42–1.03), after the 1st year (RR 0.48; 95% CI 0.33–0.71), and beyond 5 years (RR 0.32; 95% CI 15–0.71).

Evidence from 12 trials in comparison with suburethral slings found no significant difference in failure rates in all time periods assessed. Patient-reported failure rates in short, medium, and long-term follow-up showed no significant difference between open and laparoscopic retropubic colposuspension, but with wide CI. In two trials, failure was less common after Burch (RR 0.38 95% CI 0.18–0.76) than after the Marshall-Marchetti-Krantz procedure at 1–5-year follow-up. The evidence does not show a higher morbidity or complication rate with open retropubic colposuspension, compared to the other open surgical techniques, although pelvic organ prolapse is more common than after anterior colporrhaphy and sling procedures.

VAGINAL TAPE AND MESH PROCEDURES

Women with mixed incontinence are ideal candidates for surgery but are also likely to need adjunctive treatment for their urgency incontinence. Synthetic midurethral sling placement is currently the first-line surgical procedure, with a cure rate of >80% and low morbidity rate as reported by the most recent Cochrane meta-analysis.

Both the retropubic and transobturator techniques are based on a strip of polypropylene mesh. Unfortunately, in recent years the complications of vaginal mesh surgery have become a common cause of litigation and this is in spite of the risk of complications being lower for midurethral slings than for mesh for prolapse. Hence, these procedures need meticulous documentation of the consent process. For women who seek nonmesh-based procedures, a fascial sling or retropubic urethropexy are viable options as described above, with similar overall efficacy and similar complication rates.

Persistent stress urinary incontinence after an initial surgery should prompt an updated diagnostic evaluation; subsequent stress incontinence surgery is a possibility for women whose initial surgery was not successful and whose diagnosis remains stress urinary incontinence but are generally less successful than the primary procedure.

CONCLUSION

In the midlife population, incontinence symptoms are widely prevalent, have a substantial impact on the QoL and are associated with have immense ramifications vis-à-vis personal and healthcare provider expenditure. All types of incontinence are more common with age and obesity and hence the public health burden of these conditions is increasing.

Typically, presentation is late, clouded by other symptoms and signs, concurrent medical disorders and presents a diagnostic challenge. Besides the basic tenets of a careful history and clinical examination, it is essential to subject this population to urodynamic studies where these are available. A proper diagnosis is the most important step in offering appropriate therapy.

A wide variety of drug treatments in combination with pelvic floor exercises have been shown to be effective. In patients with mixed incontinence, surgery remains the best option with a 5-year cure rate of between 70 and 95%.

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6

CHAPTER

Management of Acute Abnormal Uterine Bleeding

Hephziabh K Navamani

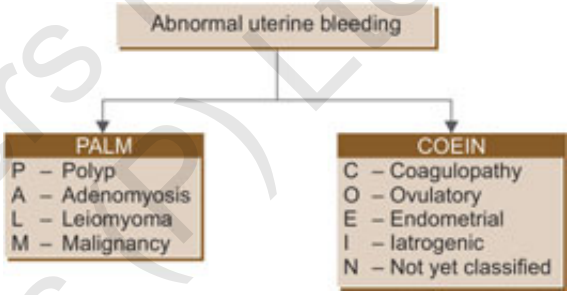
INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as any bleeding from genital tract which is a deviation from normal in frequency, cyclicity, or quantity. Abnormal uterine bleeding is the common gynaec disorder accounting to 30% of outpatient clinic. Etiologies can be multifactorial or similar to chronic AUB. Abnormal uterine bleeding can occur at any age. It is usually seen in extremes of age, following pregnancy and lactation. In India, incidence of AUB is 17. 9% (Alka Kriplani et al.). Abnormal uterine bleeding is a common and debilitating condition with high direct and indirect costs (Whitaker et al.). A total of 55.7% of adolescents have abnormal uterine bleeding in the first year of menarche due to immaturity of hypothalamic–pituitary–ovarian axis leading to anovulation. Similarly, AUB can occur in perimenopause women due to anovulation. In perimenopause age group, it is mandatory to rule out malignancy. Abnormal uterine bleeding directly affects the quality of women's life and it causes significant impact on women's health and their family.

NOMENCLATURE OF ABNORMAL UTERINE BLEEDING

In order to standardize definitions, nomenclature and the underlying categories of etiology AUB were redefined by Federation of International Gynaecology and obstetrics (FIGO) in 2009 (Fraser et al.) by the FIGO Menstrual Disorders Group (FMDG) (Munro et al.). This new system is known by acronym—PALM-COEIN. This system is based on etiopathology and facilitates investigation and comparison of similar patient populations and thereby aid research and improve evidence-based care. The "PALM" denotes structural and can be assessed visually (imaging and histopathology) and the "COEIN" denotes nonstructural (Flowchart 1).

With regard to volume, however, both the Royal College of Obstetricians and Gynaecologist (RCOG) and American College of Obstetricians and Gynecologists (ACOG) prefer the patient-centered definition of heavy menstrual bleeding, "excessive menstrual blood loss which interferes with a woman's physical, social, emotional, and/or material quality of life" as an indication for investigation and treatment options(NICE).[5]

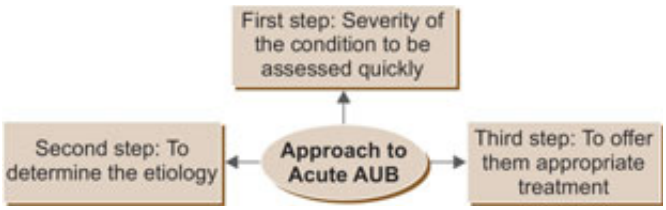


Flowchart 1: Etiology of abnormal uterine bleeding.

In acute AUB women will have heavy bleeding episode sufficient enough to require immediate intervention. It can occur spontaneously or on superimposed chronic AUB.

There are three steps to approach acute AUB:

- First step is to take quick history regarding menstrual history, similar past history and history suggestive of bleeding diathesis like bleeding associated with dental work, epistaxis, frequent gum bleeding, family history, and medical disorders
- Second Step is physical examination done to assess signs of hypovolemia and hemodynamic instability. Speculum examination to rule out bleeding from vagina or cervix. Pelvic examination will identify structural cause for AUB
- Third step is if patient is aerodynamically unstable, she should be resuscitated with two wide bore needle and blood transfusion and clotting factor replacement should be initiated. Laboratory tests, imaging investigation to be undertaken based on clinical diagnosis (Flowchart 2).



AUB, abnormal uterine bleeding.

Flowchart 2: There are three steps to approach acute abnormal uterine bleeding.

TABLE 1: Investigations for abnormal uterine bleeding

Nonstructural	*Structural*
• Complete blood count • Coagulatory profile—aPTT, PT, platelet count • Von Willebrand antigen, factor VIII, • Ristocetin cofactor assay • Thyroid function test—T3, T4, TS • Liver function test	• Transvaginal sonography (TVS) and color Doppler: Endometrial thickness <4 mm—atrophic, >12 mm, hyperechoic and regular outline, angiogenesis, and neovascular signal-indicates endometrial hyperplasia • Fibroid, adenomyosis, endometrial polyp, adnexal pathology can be ruled out • Saline infusion sonography—superior to TVS in diagnosing endometrial polyp and submucous fibroid

PTT, partial thromboplastin time; aPTT, activated partial thromboplastin time.

INVESTIGATIONS

Based on the etiopathological causes, AUB is classified as structural or nonstructural (Table 1).

According ACOG guidelines, endometrial sampling should be done after 35 years either by Pipelle curette or hysteroscopic directed biopsy.

By doing endometrial sampling, we can exclude, retained products of conception, can determine the functional state of the endometrium, can rule out endometrial carcinoma, and can have incidental therapeutic advantage when curettage is done.

Hysteroscopy can be done as outpatient procedure and has replaced dilatation and curettage. This has the advantage of direct visualization of the endometrial lesion, intrauterine pathology like endometrial polyp, and submucous fibroid and biopsy can be taken under direct vision. Hysteroscopy directed biopsy is the best method and gold standard method to evaluate the endometrial pathology

Endometrial sampling: Pipelle sampler is a blind procedure can be done as outpatient procedure without anesthesia and easy to use.

MANAGEMENT

Main aim in the management of acute AUB is (Flowchart 3):

- First to control heavy bleeding
- Later to reduce bleeding and regularize the subsequent cycles
- Once acute episode is managed, it should be managed with long-term therapy.

Acute AUB management depends on the following factors:

- Age
- Hemodynamic condition
- Etiology
- Underlying medical condition
- Desire for fertility.

Hemodynamic condition unstable: Women should be admitted to hospital and should be stabilized with packed cell transfusion or clotting factor.

First line of treatment is hormonal medical therapy, in the absence of underlying bleeding disorder. After stabilizing the patient, bleeding is controlled by intravenous conjugated equine estrogen 25 mg intravenously 4-6 hours up to 3 doses stops bleeding within 8 hours in 72% of patients. Conjugated equine estrogen is more effective in obtaining hemostatsis (Food and Drug Administration) for acute AUB.

Combined Oral Contraceptive

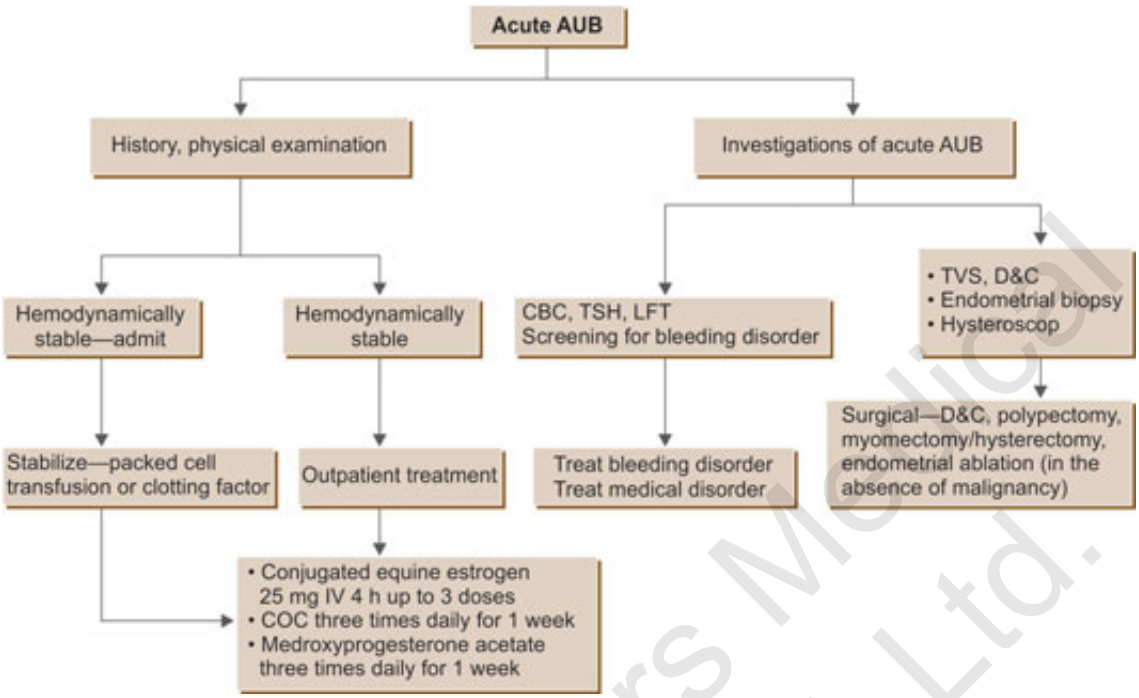
Three times daily for 1 week stopped bleeding in 88% women and medroxyprogesterone acetate three times daily for one week stopped bleeding in 76% within 3 days (Munro et al.). Combined oral contraceptive causes endometrial atrophy and it suppress the hypothalamo-pituitary axis more effectively. Combined oral contraceptives containing 30–35 µg ethinylestradiol regulate bleeding pattern significantly and result in reduction in menstrual blood loss (MBL) of up to 43% (Dijkhuizen et al.). Although less effective at reducing blood flow than the levonorgestrel-releasing intrauterine system (LNG-IUS) in patients with heavy menstrual bleeding (Endrikat et al.). Combined oral contraceptives are easily-administered, and preparations may be changed in these event of side-effects. When withdrawal bleeds are unacceptably heavy, running pill packets back-to back for 3–6 months is advisable. Absolute and relative contraindications to oral contraceptive to be considered.

Medroxyprogesterone Acetate

10 mg three times daily for 1 week. Orally active potent progestins, practically replaced the use of estrogen and has become mainstay in the management of AUB. Progestins therapy is effective in anovular AUB. It stimulates 17 ß-hydroxy steroid dehydrogenase, inhibits induction of estrogen receptor, and has antimitotic effect on the endometrium

Antifibrinolytic Agent-tranexamic Acid

This medication inhibits dissolution of the naturally occurring microthrombi in small endometrial vessels during menstruation. It has been shown to reduce MBL by around 50%, though antifibrinolytic agent reduces bleeding only by30–55% (Lethaby et al.). It can be used either orally or intravenously in acute AUB; 10 mg/kg intravenous maximum



AUB, abnormal uterine bleeding; CBC, compelte blood count; TSH, thyroid stimulating hormone; LFT, liver function test; TVS, transvaginal sonography; D&C, dilatation and curettage; IV, intravenous; COC, combined oral contraceptive.

Flowchart 3: Algorithm for acute abnormal uterine bleeding.

600 mg/dose, 1.3 g orally three times per day every 8 hours for 5 days. It is highly acceptable to patients having a low side-effect profile, but is contraindicated in patients with a personal history or strong family history of thrombosis due to its thrombogenic nature.

The use of nonsteroidal anti-inflammatory drugs (NSAID) alone or in combination with tranexamic acid may be continued for as long as it is beneficial to the patient. NSAIDs have been shown to reduce MBL by 20–45%. Mefenamic acid (500 mg up to TDS) is the most commonly-used NSAID for heavy menstrual bleeding but other NSAIDs such as ibuprofen or naproxen may also be used.
The usual NSAID contraindications apply to agents.

Desmopressin

Analog of arginine can be given intranasal, intravenous, or subcutaneously—1.5 mg/mL—total 150–300 mg in 30 mL diluted in von Willebrand syndrome and recombinant factor VIII and von Willebrand factor also are available and may be required to control severe hemorrhage in von Willebrand disease. Desmopressin must be used with caution because of the risk of fluid overload. Deficiency due to other factors require factor-specific replacement. Patient with bleeding disorders or platelet function abnormalities should avoid nonsteroidal anti-inflammatory drugs to avoid drug interaction and to prevent platelet aggregation and to avoid liver dysfunction which will subsequently affect clotting factors. Prudent to take hematologist opinion for bleeding disorders

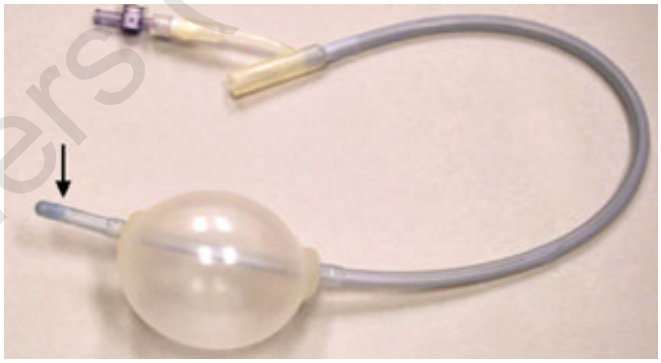


Figure 1: Intrauterine tamponade with Foley catheter.

Mechanical Method

Intrauterine tamponade with 26F Foley catheter inflated with 30 mL of saline can control bleeding (Fig. 1).

Surgical Methods

Indicated when patient does not respond to medical treatment or when medical treatment is contraindicated.
Surgical management depends (Table 2):

- On the severity of bleeding
- Stability of the patient
- Woman's desire for future fertility
- Structural cause.

TABLE 2: Surgical management in abnormal uterine bleeding

Abnormal uterine bleeding	*Surgical treatment*
Uterine disorders	Dilatation and curettage/hysteroscopic directed biopsy
Endometrial polyp, submucous fibroid	Hysteroscopic polypectomy/ myomectomy
Adenomyosis	Hysterectomy, adenomyomectomy (not frequently performed)
Abnormal uterine bleeding women who do not wish to preserve menstrual or reproductive function and malignancy should be ruled out	Endometrial ablation
Huge fibroid with abnormal uterine bleeding in younger age	Myomectomy
In abnormal uterine bleeding when medical management fails in older women	Hysterectomy

Dilatation and Curettage

When done alone without hysteroscopy is an inadequate tool for evaluation of uterine disorders and may provide only temporary reduction in bleeding. Ideal is dilatation and curettage with concomitant hysteroscopy when intrauterine pathology is suspected or a tissue sample is required.

Polypectectomy

Hysteroscopic surgical removal (polypectectomy) should be used for endometrial polyp and sub mucous fibroid. Multiple polyps or polypoidal endometrium and fertility is not desired—LNG-IUS can be combined with surgical removal.

Endometrial Ablation

Endometrial ablation should be considered for failed medical treatment, women who do not wish to preserve menstrual or reproductive function, uterus normal size or not bigger than 10 weeks pregnancy size, women who want to avoid longer surgery, and women who prefers to preserve her uterus.

Various procedures of endometrial ablation are first generation where it requires hysteroscopic endometrial ablation by resectoscope, loop, roller ball coagulation, and laser transcervical endometrial resection. This is appropriate if hysteroscopic myomectomy is to be included in the procedure.

Second generation should be used when there is no structural or histological abnormality or malignancy. They are radiofrequency induced thermal ablation, cavaterm balloon therapy, microwave endometrial ablation and laser therapy.

Myomectomy

Women with huge fibroid with AUB having a severe impact on women's quality of life require myomectomy.

Hysterectomy

The definitive treatment for controlling heavy bleeding. It is indicated in complex atypical hyperplasia in older women, failed medical therapy in perimenopausal women, failed endometrial ablation, and other pelvic pathology that needs concomitant surgery.

Uterine Artery Embolization

This procedure is successful in controlling acute AUB. Case report are available.

CONCLUSION

The PALM-COEIN classification facilitates accurate diagnosis and appropriate treatment. Hysteroscopy directed biopsy and imaging will assist in diagnosing the underlying cause. When woman is hemodynamically unstable, stabilize her with packed cell and clotting factor. Initial management will be medical and decision should be taken based on their medical history and contraindication for it. Surgical treatment is offered when medical therapy fails, when bleeding is severe and when patient is stable. Treatment should be individualized based on the severity, desire for retention of fertility, contraceptive needs, and to achieve improved quality of life.

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7

CHAPTER

Osteoporosis: Silent Thief and Killer

Maninder Ahuja

INTRODUCTION

Osteoporosis is a systemic skeletal disease characterized by low bone mass, deterioration of bone tissue, disruption of bone architecture, compromised bone strength, and leading onto increased susceptibility to fractures.

These fractures can cause lots of mortality because of hip fractures and morbidity hip and wrist fractures and deformity and functional impairment like in kyphosis.

Bone strength reflects the integration of three main features:

- Bone density
- Bone structure
- Bone mineral density (BMD) bone quality.

Structural information can be there by noninvasive and nondestructive techniques as, computed tomography (CT), particularly volumetric quantitative CT, high-resolution CT (hrCT), micro-CT, high-resolution magnetic resonance imaging (hrMRI), and micro-MRI. Volumetric quantitative CT, hrCT, and hrMRI are generally applicable *in vivo*, while micro-CT and micro-MRI are principally used *in vitro*.

It is a silent disease until it is complicated by fractures that can occur following minimal trauma that is why it is called "silent thief and killer" and osteoporosis fractures steal one's quality of life.

Aim of osteoporois management is to early diagnose and prevent first fracture to prevent morbidity and mortality because of hip and various other fractures (WHO Consensus Development Conference 1991).

EPIDEMIOLOGY

Overall survival is increasing, average of women in India is now approximately 69 years and many surviving up to 80 years and beyond. So more women are surviving in midlife beyond the years of 50 years and suffering from osteoporosis. One out of three females in India suffers from osteoporosis. It is reported that osteoporotic fractures occur 10–20 years earlier in Indians compared to Caucasians. High prevalence of postmenopausal osteoporosis in Indian women may be due to inadequate nutrition including wide prevalence of vitamin D deficiency, sedentary lifestyle, and early menopause.

The Delhi Vertebral Osteoporosis Study reported a prevalence of 17.1% of vertebral fractures among the 415 female subjects (age >50 years).

In a similar study in Rohtak, incidence of low trauma or fragility fractures of hip, spine and wrist was reported to be 34.3/100,000 women over the age of 50.

The fact is that a woman's risk of developing an osteoporosis-related hip fracture is equal to her combined risk of developing breast, uterine, and ovarian cancer. However, we still do not have any concentrated efforts to look at burden of disease. In women fracture occur much earlier than their men counterparts.

Increasing longevity and a greater proportion of the Indian population over the age of 50 years are likely to result in an increased number of people affected by osteoporosis. In 2013, estimates suggested that approximately 50 million people in India had T-scores of <–1.3. In industrialized Western countries, more than one-third of women older than 65 years suffer from symptoms of osteopenia/osteoporosis, a disorder characterized by low bone mass (Table 1).

Following issues would be discussed:

- Risk factors for osteoporosis

TABLE 1: Prevalence of osteoporosis and osteopenia (low bone mass)

Women	*Year*		
	2002	*2010*	*2020*
Osteoporosis	7,800,000	9,100,000	10,500,000
Low bone mass	21,800,000	26,000,000	30,400,000

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- Prevention
- Diagnosis physical signs
- Investigations
- Management nonmedical
- Medical
- Follow up.

Risk factors can be modifiable and nonmodifiable.

Nonmodifiable risk factors:

- Low bone mass
- Aging
- Rheumatoid arthritis
- Menopause.

Modifiable risk factors:

- Nutrition
- Exercise
- Menstrual function
- Body mass index <19 kg/m^2
- Low bone mass
- History of fragility fractures in self or family
- Poor nutrition (with deficient calcium and vitamin D intake)
- Smoking (active or passive)
- Excessive alcohol use >3 drinks/day
- Sedentary lifestyle
- Pregnancy, lactation, and menopause.

Determinants of Bone Mass

- Genetic factors
- Nutrition
- Exercise
- Menstrual function.

Determinants of Bone Loss

- Bone remodeling
- Hormone status
- Calcium Intake
- Vitamin D
- Alcohol intake
- Smoking
- Other dietary factors
- Physical activity
- Chronic diseases and medications like glucocorticoids, aromatase inhibitors.

PEAK BONE MASS DENSITY

Peak bone mass is the mass attained till the age of 19–21 years in females and males respectively, this is followed by a plateau till 30–35 years and them BMD starts falling with age and other risk factors.

The saying goes osteoporosis is a disease of adolescence which presented in midlife:

- The percentage of patients with osteoporosis increases progressively with age
- Bone mass is an important determinant of fracture risk. Low bone mass is noted in more than 40% women >40 years and increases to 62% by age 60 and 80% by the age of 65 years
- For every 10% decline in bone mass there is an approximate doubling of fracture risk in the population
- At any age among adults, the amount of bone tissue that is present in the skeleton is the algebraic sum of skeletal mass accumulated during growth and consolidation (peak bone mass) and the subsequent loss of bone tissue that occurs with aging.

Peak bone mass (PBM) depends on attainment of height, weight, and muscular mass in adolescents, hence exercise—high impact aerobics, calcium, vitamin D, and proper nutrition are main stay. If we cannot attain this PBM then it reflects in middle age as osteopenia and osteoporosis.

Prevention of osteoporosis:

- Achieving PBM density
- Prevention of falls and fractures
- Prevention by life style factors
- Prevention and decrease in resorption by medications
- Treatment of fractures.

In India, there is low calcium intake starting from toddlers, adolescent, pregnancy, lactation, and menopause even vitamin D levels are low in our population. This results in failure to achieve PBD in our adolescents. In women, peak bone mass is achieved by the second decade and begins to decrease thereafter after 35 years of age.

RISK FACTOR ASSESSMENT

The most important risk factors for osteoporosis-related fractures are:

- Prior fracture(s) with trivial trauma as an adult, which strongly predicts the potential for future fractures and
- Low BMD in patients with or without fracture
- Advancing age
- Family history of osteoporosis, fractures in first-degree relatives
- Loss of more than 1.5 inch height loss
- Vitamin D deficiency (very common in India)
- Low calcium intake (<300 mg/day)
- Tobacco use
- Alcohol intake more than 7 oz per week
- Weight loss and low body weight
- Any condition that increases the risk of falling
- Other secondary causes of bone loss (which may be present in up to one-third of women)
- Activity level, and lifestyle
- Extremely important is the total amount of bone a woman has at the time of menopause.

BONE REMODELING

The process of bone remodeling that maintains a healthy skeleton may be considered a preventive maintenance program, continually removing older bone and replacing it with new bone. Bone loss occurs when this balance is altered, resulting in greater bone removal than replacement.

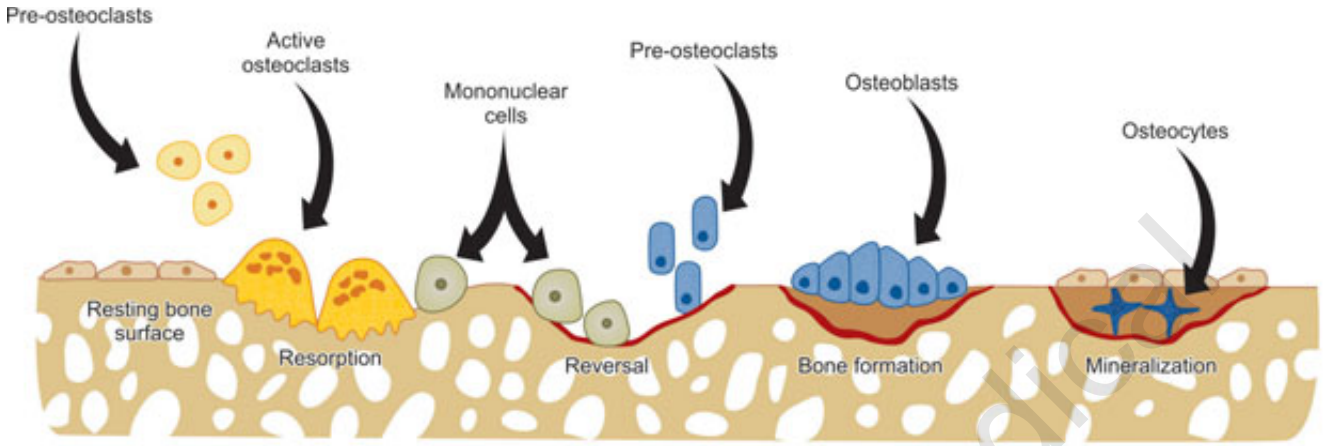

Figure 1: Bone remodelling.

The imbalance occurs with menopause and advancing age. With the onset of menopause, the rate of bone remodeling increases, magnifying the impact of the remodeling imbalance. The loss of bone tissue leads to disordered skeletal architecture and an increase in fracture risk.

Figure 1 shows the changes within cancellous bone as a consequence of bone loss. Individual trabecular plates of bone are lost, leaving an architecturally weakened structure with significantly reduced mass. Increasing evidence suggests that rapid bone remodeling (as measured by biochemical markers of bone resorption or formation) increases bone fragility and fracture risk.

Bone is continually remodeled throughout our lives in response to microtrauma. Bone remodeling occurs at discrete sites within the skeleton and proceeds in an orderly fashion, and bone resorption is always followed by bone formation, a phenomenon referred to as coupling.

Dense cortical bone and spongy trabecular or cancellous bone differ in their architecture but are similar in molecular composition. Both types of bone have an extracellular matrix with mineralized and nonmineralized components. The composition and architecture of the extracellular matrix is what imparts mechanical properties to bone.

Bone strength is determined by collagenous proteins (tensile strength) and mineralized osteoid (compressive strength). The greater the concentration of calcium, the greater the compressive strength.

In adults, approximately 25% of trabecular bone is resorbed and replaced each year, compared with only 3% of cortical bone.

Osteoclasts, derived from hematopoietic precursors, are responsible for bone resorption, whereas osteoblasts, from mesenchymal cells, are responsible for bone formation. The two types of cells are dependent on each other for production and linked in the process of bone remodeling. Osteoblasts not only secrete and mineralize osteoid but also appear to control the bone resorption carried out by osteoclasts.

Osteocytes, which are terminally differentiated osteoblasts embedded in mineralized bone, direct the timing, and location of bone remodeling. In osteoporosis, the coupling mechanism between osteoclasts and osteoblasts is thought to be unable to keep up with the constant microtrauma to trabecular bone. Osteoclasts require weeks to resorb bone, whereas osteoblasts need months to produce new bone. Therefore, any process that increases the rate of bone remodeling results in net bone loss over time.

During the resting stage of remodeling, the bone surface is inactive and is covered by bone-lining cells. The activation phase occurs next and is thought to be induced by structural or biomechanical requirements of the skeleton. During this phase, the mineralized bone surface is exposed and pre-osteoclasts are recruited to the resorption site. Once osteoclasts come in contact with the bone surface, they become active and begin the resorption phase of the cycle.

Once resorption is complete, there is a 1–2 week period before formation commences. This period is termed reversal. The formation stage then occurs in two stages: the synthesis of bone matrix by osteoblasts and the subsequent mineralization of the matrix as mentioned previously (Cowin, 2001).

According to the World Health Organization, osteoporosis is defined based on the following bone density levels:

- Bone mineral density is compared to two norms—healthy young adults (T-score) and age-matched
- Age matched (Z-score) (Fig. 2)
- A T-score within 1 SD (+1 or –1) of the young adult mean indicates normal bone density
- A T-score of 1–2.5 SD below the young adult mean (–1 to 2.5 SD) indicates low bone mass
- A T-score of 2.5 SD or more below the young adult mean (> –2.5 SD) indicates the presence of osteoporosis.

Estrogen deficiency is a dominant pathogenic factor in bone loss. This can be noted for the first time during perimenopause. From 1.5 years before menopause to 1.5 years after menopause, spine BMD decreases by 2.5% per year, compared with a premenopausal loss rate of 0.13% per year.

At menopause, an accelerated loss of bone occurs, which results in a 2.5–3% reduction in bone mass per year for the first 5 years; thereafter, the rate of loss of bone ranges from 1 to 2% per year. Dramatic changes in bone architecture

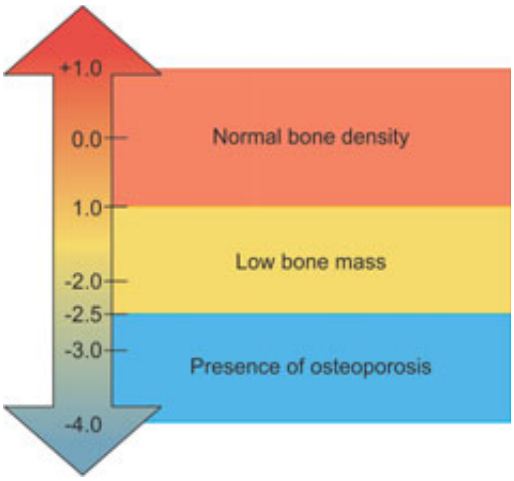

Figure 2: Bone mineral density and osteoporosis.

accompany this loss in bone, greatly increasing the risk of fracture. Every standard deviation of reduction in bone mass results in a 1.5–2-fold or greater risk of fracture**.**

ROLE OF OESTROGEN IN OSTEOPOROSIS

- Estrogen action on bone is mediated by direct effects on bone through the estrogen receptor and by effects on collagen. The accelerated decline in bone mass that occurs with estrogen deficiency is mediated by a variety of mechanisms, but the primary event is increased resorption (osteoclastic activity), which becomes uncoupled from bone formation (osteoblastic activity)
- There are also indirect effects mediated by parathyroid hormone and cytokines, which oppose the resorptive effects. Osteoprotegerin (OPG), for example, a member of the TNF-receptor (tumor necrosis factor receptor) family, is a soluble protein that inhibits osteoclastic bone resorption. Osteoprotegerin is secreted by osteoblasts and binds to OPG ligand, a factor necessary for osteoclastogenesis. Serum levels of OPG appear to be significantly elevated in postmenopausal women with osteoporosis. In addition, estrogen enhances OPG secretion by osteoblasts *in vitro*, suggesting that OPG may have an important role in the antiresorptive action of estrogen on bone
- In postmenopause, the positive effects of estrogen on growth factors, calcitonin, vitamin D metabolism and calcium absorption are also diminished.

BIOCHEMICAL MARKERS OF BONE TURNOVER

Biochemical markers of bone turnover could reflect primarily formation and are tested in serum:

- Osteocalcin
- Bone specific alkaline phosphatase
- Amino-terminal type 1 collagen
- Carboxy terminal type 1 collagen
- Increase when response to anabolic agents.

Resorption markers are urinary C- or N-telopeptide collagen breakdown products:

- Pyridinoline
- Deoxypyridinoline
- Aminoterminaltelopeptide
- Carboxyterminal telopeptide.

Decrease when response to antiresorptive agents.

These biochemical markers are not useful in the diagnosis of postmenopausal osteoporosis because the values in normal and osteoporosis show a substantial overlap. However, they may be useful in the following situations:

- Assessing response to antiresorptive therapy and anabolic therapy
- Assessing compliance to medications.

Three main sites of increased risk of fracture in postmenopause women are (Figs 3 and 4):

1. Wrist fractures are first to occur
2. Hip fractures cause most mortality and morbidity. About 25% of fracture hip cases die within 6 months and those who survive had morbidity
3. Spine and 30% of spine fractures go unnoticed and are most common of fragility fractures.

Spinal Complications of Osteoporosis

- Kyphosis
- Vertebral wedging
- Compression fractures.

These lead to development of kyphosis or Dowager hump in women which leads onto problems of mobility, digestion and respirations. The most common fractures due to osteoporosis are vertebral fractures, and yet less than a third of all vertebral fractures are clinically diagnosed (Fig. 5).

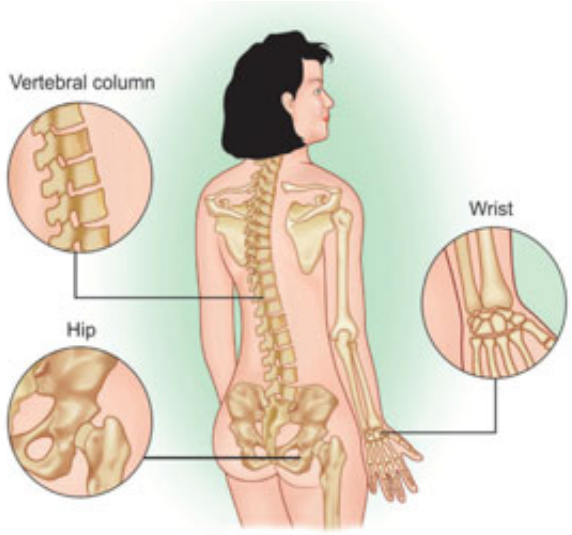

Figure 3: Fracture hip.

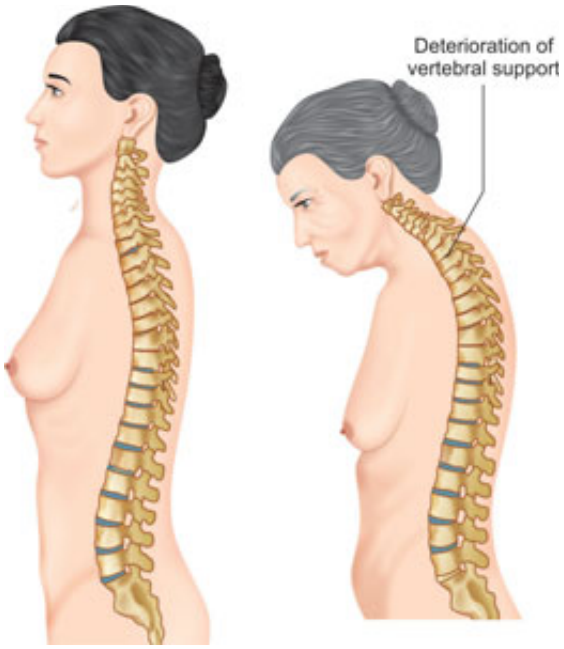

Figure 4: Fracture spine.

Figure 5: Kyphosis.

DIAGNOSIS OF OSTEOPOROSIS

Gold standard for diagnosis of osteoporosis by BMD is by dual-energy X-ray absorptiometry (DEXA) scan as low BMD is a risk factor for fractures. Peripheral DEXA scan on calcaneus and other sites are not specific so should not be used for starting treatment but can be used for sensitization and screening purposes.

Fracture risk calculations tools are available which can calculate fracture risk by clinical signs and symptoms. They are sensitive but not specific.

Indications of DEXA scan:

- All women 5 years beyond the age of natural menopause
- Women less than 5 years since Menopause with a particular risk factor
- Women with fragility fractures
- Women in menopause transition with secondary causes
- Radiological evidence of osteopenia and presence of vertebral compression fractures
- Before initiating pharmacotherapy for osteoporosis.

The interval testing should be based on calculated individual risk, mostly be scheduled between 1 and 5

PREVENTION AND MANAGEMENT OF OSTEOPOROSIS

A management strategy focused on lifestyle approaches may be all that is needed for women who are at low risk for osteoporotic fracture.

These lifestyle modifications are:

- No smoking
- Calcium 1,200–1,500 mg/day
- Vitamin D 800–1,000 IU per day
- Exercise.

There is evidence that vitamin D supplementation is associated with increases in bone mineral density and reductions in fractures, particularly when combined with adequate calcium intake. Raising serum 25(OH)D from 50 to approximately 80 nmol/L improves calcium absorption, raises BMD, and reduces both fall and fracture risk.

A recent review and guideline statement from Osteoporosis Canada recommends increased vitamin D supplementation for low-risk adults (without osteoporosis or conditions affecting vitamin D absorption) from 10 μg (400 IU) daily to 10–25 μg (400–1,000 IU) daily. In those at high risk for adverse outcomes from vitamin D insufficiency (e.g., recurrent fractures or osteoporosis and comorbid conditions that affect vitamin D absorption), recommendations have been increased from 20 μg (800 IU)/day to 20–50 μg (800–2000 IU) daily; some of these patients need doses higher than 50 μg (2,000 IU) daily, and monitoring of the serum 25(OH)D response is appropriate. The optimal level of serum 25(OH)D for musculoskeletal benefits is estimated to be at least 75 nmol/L.

Recommendations by Indian Menopause Society are:

- Calcium 800 mg/day in postmenopausal women. Recommended dose does not cause renal calculi
- Vitamin D3 (cholecalciferol) 60,000 IU/week for 8 weeks or 60,000 IU/day for 10 days followed by 60,000 IU once or twice a month
- Sunlight exposure of 20% body surface area without sunscreen for 30 minutes between 10:00 AM and 3:00 PM
- Vitamin D should be taken with milk.

However, mainstay is exercise as sarcopenia and osteoporosis go hand in hand and we need weight bearing and resistance exercises, to build up muscles and BMD also and especially for back muscles to prevent kyphosis (Fig. 6), wrist muscles, to prevent fractures of wrist, to strengthen thigh and buttock muscles to prevent fractures of hip bone. Quadriceps muscles weakness causes buckling of knees in old women so these muscles have to be strengthened. These exercises and

Figure 6: Wide grip pulley press.

Figure 7: Seated rowing.

proper calcium and nutrition should be started at adolescent level itself so that they do not have a negative BMD at midlife. Exercise specially weight bearing and resistance exercise have no age bar and can be started at any age even 80–90 years and they do increase functional independence and increase in strength and increase in bone density.

Back Exercises for Kyphosis

The thoracic kyphosis of estrogen-deficient women has been found to be directly correlated with weakness of the back extensor muscles, and increasing the back extensor strength has been shown to decrease the kyphosis. In this instance, when the torso is carried flexed forward, the patient will need to retrain the extensor muscles of the spine with isotonic resistance exercises. This is most effective when done in an upright, weight-bearing position. So from 35 years onwards all women should do resistance exercises to strengthen back muscles (Fig. 7).

Prevention of Falls

Other nonpharmacological strategies are prevention of fall so leading onto reduction in fractures. These consist of fall prevention in the houses by removing obstacles in the walking path by not having loose rugs or wires, in the bathrooms rails to assist in balance, lighting and no slippery surfaces.

Recommendations for Pharmacological Treatment

- All postmenopausal women with total hip or spine T scores worse than –2.5
- All postmenopausal women with total hip or spine T scores from –2.0 to –2.5 and at least one additional risk factor for fracture
- All postmenopausal women with an osteoporotic, vertebral fracture (no bone mineral density is needed).

In premature menopause: Hormone therapy is recommended for prevention of osteoporosis till the time of her natural menopause and then it can be substituted by other pharmacological agents along with lifestyle modifications and exercise. Evidence supporting recommendations for duration of treatment is limited. Individuals at high risk for fracture should continue osteoporosis therapy without a drug holiday.

Data for the above recommendation come from the FLEX study (long-term alendronate treatment) and the risendronate discontinuation study.

- Several other agents are as effective as hormone therapy in preventing fracture due to osteoporosis:
- Bisphosphonates: Alendronate, risedronate, and ibandronate are commonly used for both prevention and treatment of osteoporosis. For prevention alendronate is available as a daily tablet of 5 mg and a weekly tablet of 35 mg. For treatment of postmenopausal osteoporosis, the doses available are 10 mg tablets daily and 70 mg tablets weekly. For maximal gastrointestinal absorption and to reduce the incidence of esophageal irritation, alendronate must be taken in the morning on an empty stomach (1/2 hour before breakfast) with about 240 mL of plain water and the patient must remain upright for half hour after ingestion
- Bisphosphonates in combination with estrogen are more effective than either agent alone
- Selective estrogen receptor modulators: Selective estrogen receptor modulators (e.g., raloxifene) are indicated for the prevention and treatment of osteoporosis. They are not indicated for the treatment of menopausal symptoms and may even aggravate hot flashes in some women. They also do not help vaginal atrophy. As with estrogen, a past history of venous thrombosis is a contraindication to their use. Current venous thrombosis is an absolute contraindication. They have a favorable effect on lipid profile and are cardioprotective. Available as 60 mg tab/day for prevention as well as treatment.

Several other agents are as effective as hormone therapy in preventing fracture due to osteoporosis:

- Zoledronic acid is a new bisphophosphonate approved by Food and Drug Administration (FDA). A single intravenous infusion of zoledronic acid 5 mg over 15 minute period once in a year decreases bone turnover and improves bone density and is effective in reducing hip, vertebral, and other fractures
- Calcitonin: The nasal spray used for osteoporosis treatment that inhibits bone resorption and reduces fracture rates. Nasal irritation and cost limit its use. Calcitonin is available as a subcutaneous injection (about 100 IU per day) and as a nasal spray (about 200 IU per day) for treatment of postmenopausal osteoporosis
- Parathyroid hormone (e.g., teriparatide): Daily subcutaneous injections are used for osteoporosis treatment. Parathyroid hormone is FDA approved but carries a black box warning about possible risk for osteosarcoma based on rat studies
- Tibolone is a synthetic steroid with oestrogenic, progestational and androgenic properties. It is metabolized by local tissue enzymes and, therefore, provides a unique "tissue specific approach" to menopause. It treats climacteric symptoms and does not increase mammographic breast densities (although data on breast cancer occurrence are not yet available). Tibolone seems to exert osteoprotective effects similar to estrogen, as judged by bone density and bone markers, but data on fracture prevention are awaited. The recommended dose is 2.5 mg daily. It increases libido, reduces hot flushes, and so can be prescribed for that effect along with to prevent osteoporosis
- Osteoprotegerin: This is a new drug and it is a naturally occurring protein and is a negative regulator of osteoclast formation that has shown promise as a potential treatment for osteoporosis.

CONCLUSION: THE WAY FORWARD

Very essential to create awareness and have impact to prevent osteoporosis by working at prevention at family level, schools, society, and organizational levels by proper vitamin D, calcium, exercise, and attainment of peak bone density at adolescent levels and prevention of loss at later ages.

"Keep them fit at forty, strong at sixty, and independent at eighty."

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8

CHAPTER

Fertility in the Midlife

Pratik Tambe

INTRODUCTION

As societies and cultures advance, with increasing levels of education, urbanization and women empowerment, a unique set of problems present themselves. For the practicing gynecologist, one of these is the issue of fertility in the midlife. With a higher proportion of women working shoulder-to-shoulder with men, education and career being prioritized over marriage and child-bearing, increasing numbers of women are leaving it late to find a partner and have a baby.

In large swathes of the developed world and also in the urban heavily populated metros of India, pollution, industrialization, environmental toxins and other unknown agents have indirectly influenced fertility among modern women. Intracellular stress and reactive oxygen species have also been proven to have a role in influencing oocyte quality and endometrial dysfunction, thus affecting blastocyst implantation.

Hence, for many women the fear is that they may have missed the bus and lost sight of the important objective of having a family in their quest for a stable and productive career. The "biological clock" is ticking and in recent years with the advent of modern methods of diagnosis, larger proportions of women are being diagnosed with premature ovarian insufficiency, poor ovarian reserve, and aging oocytes which lead to infertility and first trimester losses consequent to aneuploidies.

OVARIAN PHYSIOLOGY FROM FETAL TO ADULT LIFE

As we are aware, the primordial germ cells which are concentrated in the ovaries and which give rise to the mature oocyte during every menstrual cycle in the reproductive career of a woman are at maximal numbers during fetal/intrauterine life. In fact, at 20 weeks of intrauterine life, there are approximately 6–7 million oocytes which steadily decline as a woman's age advances. At birth this falls to 1–2 million; at puberty to 3–500,000; 25,000 at age 37 years and 1,000 at the age of menopause.

Typically, fecundity (the ability to have a live birth in contradistinction to fertility) decreases gradually over age in parallel with declining oocyte populations; however, this falls rapidly after the age of 37 years in Caucasian women and may occur up to 5–6 years earlier in Indian women. This is in parallel with a decrease in oocyte quality as evidenced by microscopic appearances of oocytes and their consequent embryos, rising levels of serum follicle stimulating hormone (FSH) and decline in plasma concentrations of anti-Mullerian hormone (AMH) and inhibin B.

AGE-RELATED DECLINE IN FERTILITY

Since with advancing age, sexual activity also declines, it is difficult to pin fertility decline on aging oocytes alone (Fig. 1 and table 1). However, in clinical trials on women undergoing

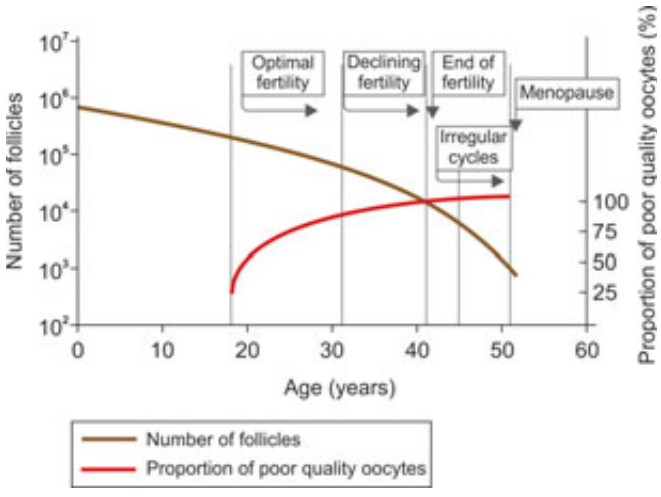


Figure 1: Age related fall in oocyte numbers and declining oocyte quality.

TABLE 1: Age-specific live birth rates per started cycle

Age (Years)	*Live birth rate (per started cycle)*
<35	41.5%
35–37	31.9%
38–40	22.1%
41–42	12.4%
43–44	5%
>44	1%

donor insemination, success rates over 12 cycles fell from 74% in women <31 years of age to 54% for women >35 years.

Experience from *In vitro* Fertilization/ Intracytoplasmic Sperm Injection

The success rates of *in vitro* fertilization and embryo transfer (IVF/ET) programs in the US reflects a similar age-related decline. The age of the spouse/female partner is one of the most important determinants of the success rate of an IVF cycle. This is a key concept in counselling couples prior to starting a treatment cycle.

While most couples receive counselling prior to their treatment, it is important to convey an age-specific, couple-specific success rate which takes into account various factors including the background etiology, age, and multiplicity of factors responsible for infertility in each individual couple.

OTHER FACTORS

With advancing age, other conditions are also encountered with increasing frequency, e.g., fibroids, tubal disease, and endometriosis. These further compound the issue of fertility treatment and appropriate counseling and treatment is essential.

Poor Ovarian Reserve

The concept of women's ovaries not responding to stimulation has been extensively studied over the past two decades. Many women in the "midlife" period will probably fall into this group which exhibits declining/poor ovarian reserve.

The ESHRE (European Society for Human Reproduction and Embryology) Working Group on Poor Ovarian Response Definition published the Bologna criteria for defining poor ovarian response in 2011, which was a landmark event. Prior to this, researchers used different methodologies to measure and study poor responders and comparing studies was not possible owing to differences in the definitions and study methods utilized.

Bologna Criteria

At least two of the following three features must be present:

(Two episodes of poor ovarian response (POR) after maximal stimulation are sufficient to define a patient as poor responder in the absence of advanced maternal age or abnormal ovarian reserve test)

1. Advanced maternal age (≥40 years) or any other risk factor for POR
2. A previous POR (≤3 oocytes with a conventional stimulation protocol)
3. An abnormal ovarian reserve test [i.e., antral follicle count (AFC) <5–7 follicles or AMH <0.5–1.1 ng/mL].

Ovarian Reserve Testing

One of the key set of investigations performed before offering treatment for the subfertile couple with advancing years is those for determining the ovarian reserve. These are indirect determinants of fertility and fecundity. With widespread availability, these are now performed quite easily with reproducibility in most metros in India.

The set of tests commonly ordered include basal serum FSH, serum inhibin B, ovarian volume on transvaginal ultrasound and more recently, the antral follicle count (AFC) and serum AMH.

Antral Follicle Count

The AFC is one of the easiest tests to perform. With the wide availability of high resolution ultrasound machines in the consulting rooms of fertility physicians, a simple transvaginal scan on day 2 or 3 of the cycle is performed to locate and identify the number of follicles between 2 and 9 mm size in both ovaries. An antral follicular count of less than 5 is generally considered to be indicative of a poor response.

While a small proportion of women may be reluctant to be examined during the menstrual period, with good counseling and physician interaction, most will agree and this goes a long way toward individualizing the patient's treatment regimen and the starting dose of gonadotropins during the cycle.

Anti-Mullerian Hormone

The AMH is produced by small antral and preantral follicles up to 7–8 mm in size. It has a variety of actions in embryonic and fetal life and in adult life it inhibits FSH mediated granulosa cell proliferation, follicular growth and aromatase activity.

The level of AMH in plasma provides an indirect quantitative measure of the number of follicles in the ovaries. It is an excellent predictor of ovarian reserve. While the ideal test is the response of the ovaries to stimulation, AMH is a good surrogate marker (Table 2).

The choice of stimulation protocol, type of gonadotropin preferred, advantages of using recombinant preparations, individualizing drug dosages, counseling regarding self-administration of medication are factors important to the success rate of the treatment offered, but sadly beyond the scope of this discussion.

TABLE 2: Comparison of most commonly used markers of ovarian reserve

Characteristic	*Age*	*AMH*	*FSH*	*AFC*
Prediction of poor response	+	+++	++	+++
Prediction of hyper-response	+	+++	–	++
Low intercycle variability	+++	++	–	++
Low intracycle variability	+++	++	–	++
Blinded to operator	+++	+++	+++	–
Applicable to all patients	+++	+++	+	+
Cost effectiveness	+++	–	–	–

AMH, anti-Mullerian hormone; FSH, follicle stimulating hormone; AFC, antral follicle count.

WHICH IS THE BEST PREDICTOR OF OVARIAN RESERVE?

While this continues to be a matter of debate in both ART and non-ART settings, AFC and AMH have by and large proven repeatedly to be of immense benefit especially for counselling patients before IVF cycles.

The AMH and AFC exhibit equivalent performance characteristics. Large scale multicenter RCTs with centralized assay performance have demonstrated that AMH is substantially the more accurate and robust biomarker, probably reflecting difficulties with standardization of AFC determination.

The AFC retains some advantages: Particularly immediacy and accessibility; however, international standardization of AMH combined with a stable automated assay is likely to enhance its performance as the biomarker of choice in predicting the ovarian response in assisted conception.

The latest data from various studies now support the notion that chronological age and genetic markers' inclusion may increase the reliability of AFC and AMH.

IMPROVING OOCYTE QUALITY, YIELD AND ENHANCING TREATMENT SUCCESS

While many strategies have been tried for improving the oocyte quality and yield in these patients, the success rates are variable. Some trials show encouraging results while others show no benefit as compared to placebo. The availability of a standardized definition to provide a level playing field in the shape of the Bologna criteria has helped matters tremendously.

Adjuvant therapy with growth hormone and androgens is backed by good quality evidence which shows consistent results from many trials. Cost-effectiveness, availability, affordability, and patient compliance are key issues which determine the uptake and continued usage of these adjuvant therapies.

HUMAN GROWTH HORMONE

Human growth hormone modulates the action of FSH on granulosa cells. It upregulates the local synthesis of insulin-like growth factor 1 (IGF-1). The IGF-1 amplifies the action of FSH on both theca and granulosa cells. Recent meta-analysis of several trials has shown a conclusive benefit with human growth hormone administration. However, the costs associated are a key issue and in a country like India where all treatment is privately funded, it is often out of the reach of many women.

EXOGENOUS ANDROGENS

In vivo, androgens are produced by the theca cells and promote the initiation of growth of the primordial follicles (Fig. 2). Androgens also increase the growing preantral and antral follicles. Based on this rationale, exogenous administration of androgens like testosterone and dehydroepiandrosterone (DHEA) has been attempted to improve oocyte quality and yield in these patients.

It is however; important to note that any such administration has to take place at least 2–3 cycles prior to the treatment cycle to be of any significant benefit to the patient. Typically, the follicles that grow in the index or treatment cycle are recruited 90–120 days prior to the beginning of stimulation, as can be seen in figure 3.

The most recent Cochrane meta-analysis on androgens for women undergoing assisted reproduction included 17 trials and concluded that DHEA and testosterone supplementation may be associated with increase in live birth rates in this group of patients.

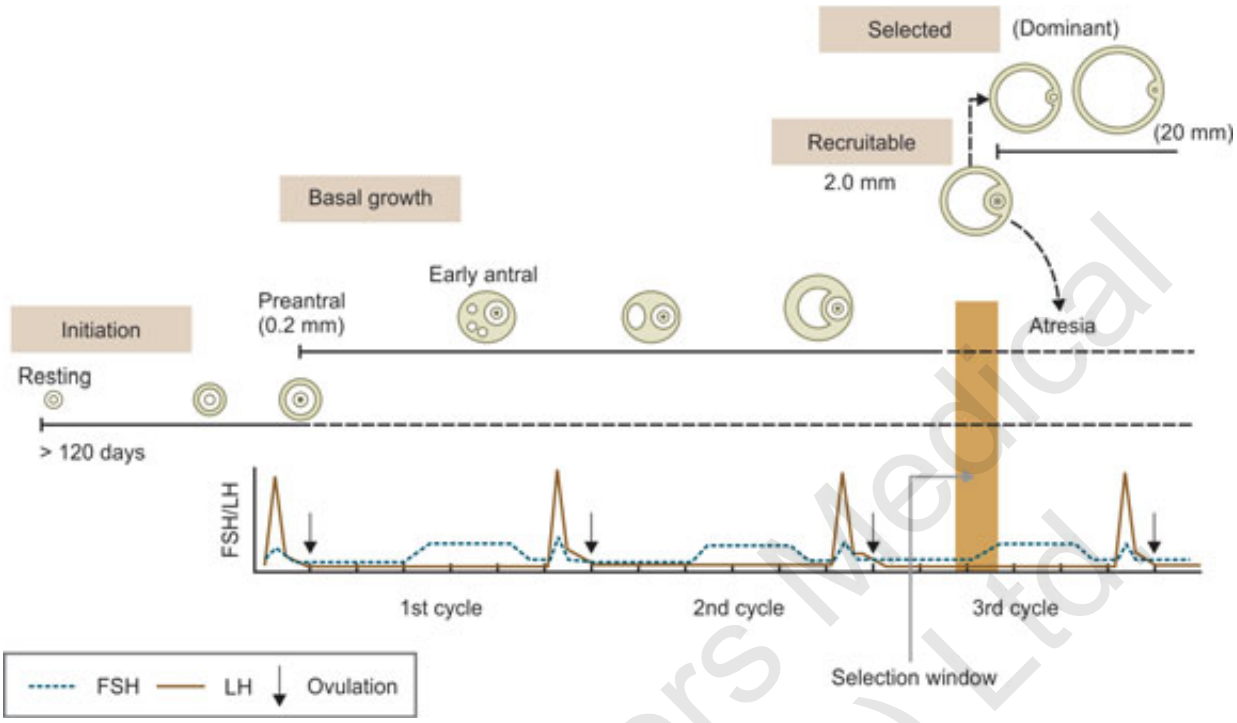
MISCARRIAGE RATES

Irrespective of treatment modality, women of advanced age have a propensity to aneuploidy including trisomies 21, 13, and 18 with attendant increase in first trimester miscarriage rates (Table 3). Autosomal trisomies are related to changes in the meiotic spindle that predisposes to nondisjunction. In IVF cycles where morphologically normal and well progressing embryos are selected for transfer, the aneuploidy rates and miscarriage rates are high.

OOCYTE DONATION

This avenue of treatment is often unavailable for legal or religious reasons in many countries of the world. In India, we are fortunate that it is still available and falls under the purview of the Indian Council of Medical Research guidelines and the draft Assisted Reproductive Technology Bill. Irrespective of the recipient's age, the live birth rates per started treatment cycle are as high as 51% with oocyte donation as reported by Centers for Disease Control Atlanta.

The characteristics of an ideal oocyte donor include: Age less than 30 years, should have at least one child previously which is genetically normal with no inherited diseases,



FSH, follicle stimulating hormone; LH, Luteinizing hormone.

Figure 2: Follicular recruitment, pre-antral and antral phases.

TABLE 3: Fetal loss risks by maternal age

Age (Years)	*Spontaneous miscarriage rate*
<33	9.9 %
33–34	11.4 %
35–37	13.7 %
38–40	19.8 %
41–42	29.9 %
>42	36.6 %

donor free from communicable diseases, no significant past or family history of medical disorders, tested negative for thalassaemia, normal intelligence quotient and should undergo human immunodeficiency virus testing every 3 months.

SOCIAL FREEZING AND OOCYTE CRYOPRESERVATION

Increasing numbers of women in the developed world are now choosing to freeze their eggs at a young age to be utilized later when they have found a partner and are ready to start a family. It is also worthwhile to understand that this would not have been possible without advancements in vitrification and cryopreservation technology.

This is an excellent alternative which can be offered to women in India who choose to spend time building a career before embarking on creating a family. Public awareness and social media campaigns to educate and extol the virtues of oocyte vitrification programs are the need of the hour.

RECOMMENDATIONS AND CONCLUSIONS

The fecundity of women decreases during the reproductive years primarily because of continuous physiological oocyte atresia which begins prior to birth and becomes accelerated beyond 35 years of age. It is significantly compromised before the onset of perimenopausal menstrual irregularity, with no external distinguishing symptoms and signs.

The American College of Obstetricians and Gynecologists and American Society for Reproductive Medicine recommend that education, awareness and counseling regarding the impact of age on fertility is essential. Women older than 35 years should receive expedited evaluation and treatment after 6 months of failure to conceive after trying. In women >40 years of age, immediate evaluation and treatment are indicated.

Ovarian reserve testing is indicated prior to initiation of treatment. Individualization of treatment with tailor-made protocols is of paramount importance. Adjuvants like exogenous androgens and human growth hormone are of proven benefit where the patient can afford them and continue therapy for an adequate period of time prior to the actual treatment cycle.

For women who wish to pause the biological clock, oocyte vitrification and egg banking programs are now widely available. For those who show a persistent poor response by the Bologna criteria, oocyte donation may be a worthwhile avenue to pursue.

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9

CHAPTER

Medicolegal Issues

MC Patel

HYSTERECTOMY IN MIDLIFE

Consent: Does It Concern?

As soon as any patient enters in consulting room of doctor and if he accept her to treat, it becomes contract or implied contract between patient and treating doctor. Doctor offers his expert medical services and patient pays or promises to pay for the same.

WHAT IS CONTRACT?

Every promise and promises, forming the consideration for each other is agreement. When agreement is enforceable by law, it becomes contract.

To become valid and legally enforceable contract it should fulfil following criteria:

- Parties involved should be major and with sound mind
- It should be free without any coercion
- It should be for lawful consideration and lawful object.

According to section 13 of Indian Contract Act 1872: "PARTIES AD IDEM", "two or more persons are said to consent, when they agree upon the same thing in same sense."

WHAT IS CONSENT IN MEDICAL PROFESSION?

It is willingness or permission by patient or his/her representative for examination, treatment, any procedure, or any surgery.

Criteria for Valid Consent

- Competency to give consent.
  Who can give consent?
  - Major (more than 18 years) with sound mind
  - Legal guardian for minor or mentally challenged
  - In unconscious and/or emergency patient guardian can give consent
  - In absence of guardian, teacher or principal of the school for school student.
- Not under influence of any drugs, intoxicated substance or anesthesia
- No fraud, no coercion
- No undue influence
- No misrepresentation
- No mistake of fact and/or of law
- It should be informed consent. Element of adequate information is very important criteria to become valid contract
- Patient and relatives should have been explained about alternative modalities of treatment with side and after effects, with probability of success/failure
- It should be written as oral consent is difficult to prove, if patient becomes hostile.

In consumer complaint no. 54/2013, in a case of Mr C Jaypal Reddy versus Dr Yashodhara Group of Hospital, Dr Padmini Valluri and others Hon'ble Justice JM Malik in NCDR has categorically said that, "consent is not mere a piece of paper on which patient and his relative sign but consent should be considered as a document of proof of communication and counseling done to the patient and his relative".

In short, "consent is a documentation of communication between doctor and patient and his representative".

Hysterectomy is very common operation in day to day practice of any gynecologist. It could be abdominal, vaginal including non-descent vaginal, total laparoscopic with or without unilateral or bilateral salpingo-oophorectomy, with or without anterior colporrhaphy and or posterior colpoperineorrhaphy.

Consent will defer little in each type with common element remaining same. Route and type of operation should also be explained.

Common Format of Consent

Hysterectomy with/without salpingo-oophrectomy

Registration/Indoor no. : .....

Name of Patient: ..... Age: ..... years

Address: .....

.....

Provisional Diagnosis: .....

Permanent Diagnosis: .....

Type of operation: .....

(Operation title)

I,.....undersigned give my valid consent for (name of operation)..... of my own/my wife/daughter/mother and/or medication /investigation /anesthesia /therapy/procedure etc.

(There should be separate consent for surgery, anesthesia, and blood transfusion)

to Dr.....

I have been explained as follows.

The following operation will be performed:

Removal of uterus (womb) will be performed from explained route (abdominal/vaginal/laparoscopic) with/without removal of unilateral/bilateral fallopian tube/s and/or removal of unilateral/bilateral ovary/ies (sometimes decision to remove ovary/ies is taken during surgery. It should be explained prior and specific consent should be taken respectively).

I have been explained about expected out come and likelihood of success to be Good/Fair/Poor.

I had been explained about following (but not limited to the following) risk and complications of the procedure/operation

- In spite of all care and caution there is possibility of injury/damage to urinary bladder, ureter, and bowel
- In case of injury to bowel, help of general or gastrointestinal surgeon may be required
- In case of injury/damage to bowel in few cases colostomy may be required which may be closed by further surgery few weeks later
- In case of injury /damage to ureter/urinary bladder help of urologist may be required and further surgery related to that may be required and it would be done by urologist at the same time or later on as the case may be
- Injury to near bye blood vessels may occur which may lead to bleeding and which may require blood/blood products transfusion and/or further surgery. Risk involved in this type of situation is also explained to us
- Decision to remove ovary/ies might have to be taken at the time of operation in few cases, if not planned originally
- It may lead to adhesions(bands of scarred tissues) in future which may lead to bowel obstruction in some cases. It could be short-term or long-term complication, which may require further surgery
- Vault prolapse(vagina coming out of introitus)
- Pain during sexual intercourse or altered sexual function after colporrhaphy
- Incontinence or retention of urine
- Fistula (path) (connection) may develop between bladder and vagina, ureter and vagina, bowel, and vagina or peritoneum
- Difficulty in passing urine immediately following operation which could be temporary may require catheterization simple or continuous till patient passes urine by her own without any difficulty
- Stress urinary incontinence of urine may occur where urine leaks on coughing, sneezing or perform activity involving abdominal straining. It is likely that it may be noticed after operation only which was not before operation, which could be due to unknown weakness of bladder muscle or sphincter
- Bowel obstruction after operation
- Bleeding after few days of operation may occur in few cases (secondary hemorrhage)
- Infection requiring antibiotics for longer period and further treatment
- Poor wound healing
- Incisional hernia
- Formation of granulation tissues at vaginal vault leading to prolonged white discharge including blood stained discharge in some cases
- Wound scar may develop keloid formation, i.e., skin may be thickened, red and may lead to pain and itching
- Allergic reaction of drug or by blood transfusion
- In very rare situation partial lung collapse increasing chest infection requiring antibiotics and physiotherapy

- Vasovagal shock, stroke, or in rare case heart attack may occur due to strain on the heart
- Blood clotting in leg (deep vein thrombosis) causing pain and swelling. Clot may break and embolus may cause damage to vital organs, i.e., heart, lung, brain, kidney, liver, etc.
- Loss of function of any limb or organ or paresis/paraplegia/quadriplegia
- Cardiac arrest and death may occur in very rare cases as a result of operation.

In case of oophorectomy (removal of ovaries):

- Feeling of depression and anxiety
- On set of menopause and menopausal syndrome in premenopausal women if both ovaries are removed
- Alternative modalities of treatment with other procedures and supporting information regarding the same is explained to us
- Ill effects of refusal of treatment/operation/procedure including effects on the prognosis and substantial risk of no treatment is also explained.
- It was discussed in detail about situation if procedure turns out to be harmful or unsuccessful and explained by Dr.....

I admit and acknowledge that doctor has explained about:

- My medical condition and proposed operation, including additional treatment required, if doctor thinks it necessary for me in unexpected situation, the risks including specific risk to me
- The anesthesia risk with anesthetic risk required for this operation in general and specific to me
- Tissue and blood removed could be used for diagnosis and further treatment plan
- Any change of anesthesia, operative procedure, removal of any organ as deemed necessary at the time of medication, investigation or operation
- I have been explained that after the above operation instead of desired benefit some complication may occur and to avoid the same necessary care will be taken by Dr (Surgeon).....and Dr (Anesthesiologist).....or any other doctor suggested by them
- I had been explained everything in language which we understood
- I had been encouraged to ask any question related to this operation and had been answered well all the questions asked, way in which we could understood
- I am free to change my mind at any time before operation preferably following discussion with my doctor/s
- I understand that image/s and video footage may be recorded as a part of and during operation
- I accept that medicine is not exact science and I also understand limitation of it and no guaranty can be given about result or outcome of operation.

I have read and understood the above writing.
Above writing has been read out to me and explained everything to me in the ……language by (interpreter) (in case of patient not understanding language of consent printed in) which I understand (in case of patient giving thumb impression).

I have understood the aforesaid and I am giving my free consent willingly with sound mind, without any undue influence, coercion, fraud, misrepresentation or mistake of facts.

I request Dr ..... to perform upon me the above mentioned operation

Doctor

Sign: …….
Name: ……..
Address: ……. …….
……. …….
Date: ……. Age: ……..

Patient/Guardian

Sign/thumb impression: …….
Name: ……
Address: ……. …….
……. …….
Date: ……. Age: ……..

Witness

Sign: …….
Name: ……
Relation with patient: …….
Address: ……..…….
……..…….
Date: ……. Age: ……..
Time…….

Witness

Sign: …….
Name: ……
Relation with patient: …….
Address: ……..…….
……..…….
Date:……. Age:……..
Time…….

Reference: A case of Samira Kohli versus Dr Prabha Manchanda. Criteria are taken from this case which were discussed in Supreme Court in 2008.