COLLEGE OF MEDICINE
DEPT. OF OBSTETRICS AND GYNECOLOGY

Premalignant and Malignant Diseases of the Uterus

Dr.Ayman Hussien Shaamash
MBBCH, MSc., MD. (Egypt)
Professor of OB./Gyn.
Faculty of Medicine.
King khalid University

Contents:

1. Endometrial Hyperplasia
2. Endometrial Carcinoma in situ
3. Invasive Endometrial Carcinoma
4. Other Malignant uterine Tumors

I- Endometrial Hyperplasia

- Excessive proliferation of the endometrial glands & to a lesser extent endometrial stroma
- This results in varying degrees of architectural complexity and cytologic atypia.
- Due to excessive estrogen stimulation
- The clinical significance of this diagnosis is progression to endometrial adenocarcinoma.
- Only 25% of Pt with End Ca have Hx of hyperplasia

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Classification of Endometrial Hyperplasia
WHO classfication

I. Simple hyperplasia - Increased number of glands but regular glandular • architecture
II. Complex hyperplasia - Crowded irregular glands
III. Simple hyperplasia with atypia - Simple hyperplasia with presence of cytologic atypia (prominent nucleoli and nuclear pleomorphism)
IV. Complex hyperplasia with atypia - Complex hyperplasia with cytologic atypia

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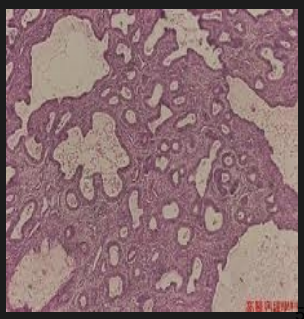
Endometrial Hyperplasia…….Cont.

1-Hyperplasia without atypia (not premalignant)

1-A-Simple

- Microscopically ➡ crowding of the glands in the stroma
- Glands are cystically dilated & "Swiss cheese" appearance
- Commonly asymptomatic
- <1% progress to Ca over 15 Y
- 90% regress



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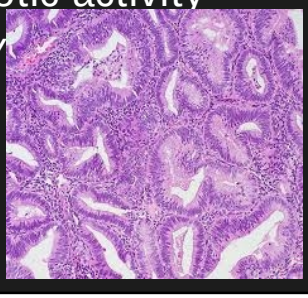
Endometrial Hyperplasia…….Cont.

1-B-Complex hyperplasia without atypia

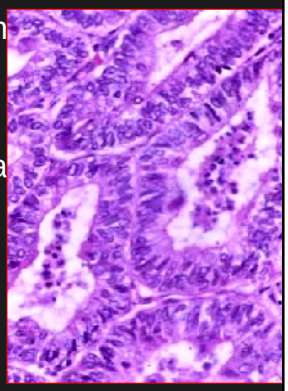
- A complex crowded appearance of the glands with very little stroma
- Epithelial stratification & mitotic activity
- 3% progress to Ca over 13 Y
- 80% regress
- 85% reversal with progestin



Endometrial Hyperplasia…….Cont.

2-Hyperplasia with atypia (premalignant)

- Histologically ➡ endometrial glands are lined by enlarged cells with ↑ nuclear : cytoplasmic ratios
- The nuclei are irregular with coarse chrom & prominent nucleoli
- 50-94% regress with progestin therapy
- A higher rate of relapse after treatment compared to that of lesions without atypia



2-A-Simple

- Progression to carcinoma occur in 8%

2-B- Complex

- Progression to carcinoma occur in 29%

Endometrial Hyperplasia…….Cont.

- Pathophysiology
- Endometrial hyperplasia results from continuous estrogen stimulation that is unopposed by progesterone
- This can be due to endogenous estrogen (Obesity, PCOD, late menopause, tumors).
- or exogenous estrogenic sources (unopposed HRT, tamoxifen)

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Endometrial Hyperplasia……Cont.

- Mortality/Morbidity
- Endometrial hyperplasia is often associated with menorrhagia, metrorrhagia or postmenopausal bleeding.
- Abnormal Pap smear result in atypical glandular or endometrial cells
- Diagnosis is usually made by endometrial biopsy using Pipelle (OPD) or D&C in the operating room.

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Role of TVS and Hysteroscopy

- Endovaginal US has a sensitivity of 96% for ruling out endometrial carcinoma if endometrial echo complex is less than 5 mm.
- Persistent bleeding, despite a thin stripe still warrants tissue biopsy because of the risk of type 2 cancer that is not associated with endometrial hyperplasia
- If hyperplasia is diagnosed by office biopsy, one should consider D&C +hysteroscopy to rule out atypia or cancer prior to medical management

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Endometrial Hyperplasia…….Cont.

- Progestins can effectively treat hyperplasia , control bleeding and prevent cancer.
- Hyperplasia without atypia responds well (98%) in 3-9 monts ,But response is 90 % with atypia.
- definitive treatment with hysterectomy , due to the high rate of endometrial cancer with atypia.
- D&C and Pipelle biopsy only sample 50% of endometrium, focal carcinoma may be missed.
- Continued surveillance after regression of the lesion every 6-12 months if risk factors persist

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Regimens of Progestin therapy

- Medroxyprogesterone acetate, 10-20 mg continuous, or cyclic14 days per month
- Micronized vaginal progesterone, 100-200 mg continuous or cyclic14 days per month
- Levonorgestrel-containing IUD (Mirena), continuous for1-5 years
- Megestrol acetate , 40-200 mg per day, usually reserved for atypical hyperplasia

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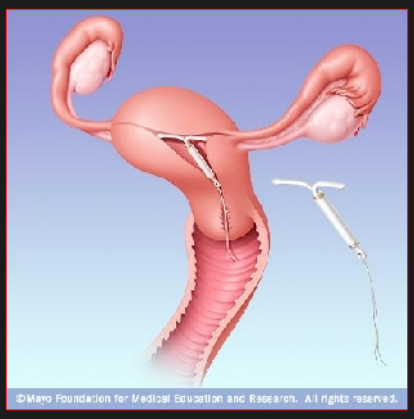
LNG- IUD (Mirena) and Endometrial Hyperplasia



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II- CARCINOMA IN SITU (Stage 0)

- Histologically differentiated from carcinoma by

1- Presence of intervening stroma between abnormal (atypical) glands

2-There is no evidence of invasion of glandular basement membrane

3-Severe cases is difficult to differentiate from Carcinoma so should managed as Carcinoma

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III- Endometrial Cancer

Epidemiology

- The most common GYN malignancy in the U.S.(23:100 000), 4th most common in women
- 2-3% of women develop in lifetime
- Mean age is 60 years
- Majority are diagnosed early due to bleeding
- >90% 5-year survival for stage I disease
- Overall 5-year survival for all stages is 60-

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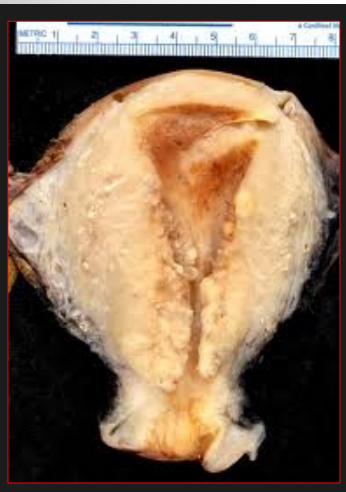
Risk factors for Endometrial Cancer

- Increased estrogen
  - Hormone therapy
  - Obesity
  - Anovulation/PCOS
  - Estrogen secreting tumors
  - Older age
  - Infertility
  - Early menarche
  - Late menopause
- Genetics
  - HNPCC
  - Caucasian



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Endometrial Cancer……..cont.

- Symptoms & Signs:
  - Postmenopausal bleeding (90%)
  - Postmenopausal offensive discharge (pyometra)
  - Perimenopausal with irregular heavy menses, increasingly heavy menses
  - Abnormal Endometrial cells on Pap smears
  - Late stage ….symptoms of Local pelvic spread

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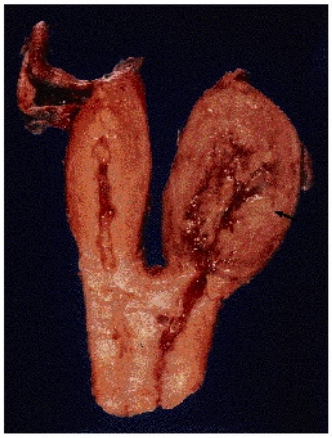
Preoperative Work-up

- Endometrial biopsy
- Transvaginal Ultrasound
- For suspected advanced stage :
  - Cystoscopy
  - Sigmoidoscopy
  - CT of abdomen/pelvis, chest
- Labs
  - CBC
  - Chem
  - Liver function tests
  - EKG, CXR



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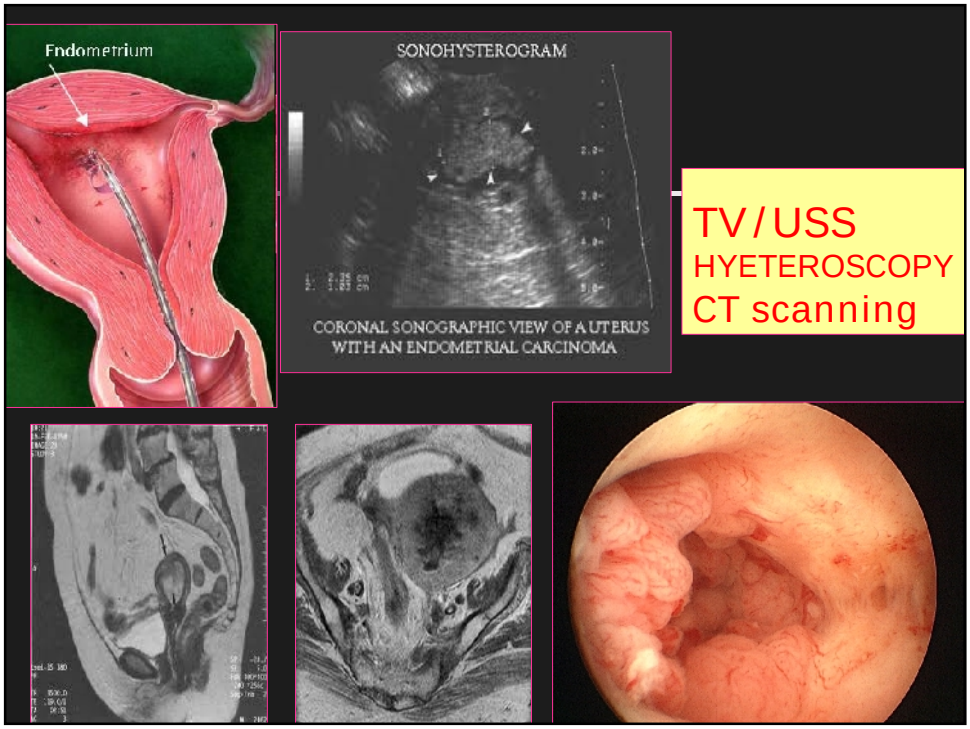


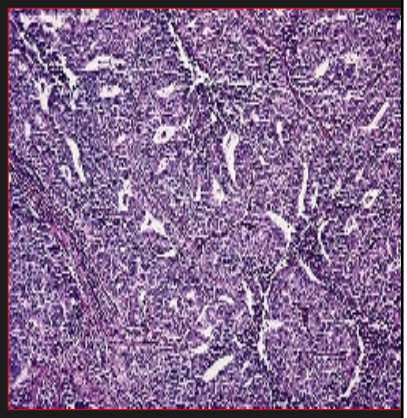
Histopathology

Estrogen dependent

- Adenocarcinoma, the most common, is usually preceded by adenomatous hyperplasia with atypia (80%)

NON Estrogen dependent

- adenosquamous carcinoma (15%) Tamoxife nuse
- Papillary serous adenocarcinoma (3-4%)
- Clear cell
- Undifferentiated



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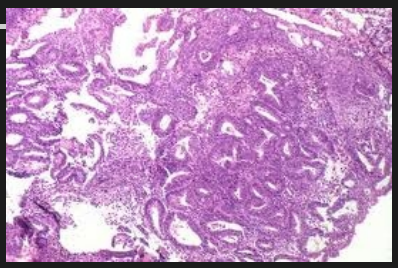
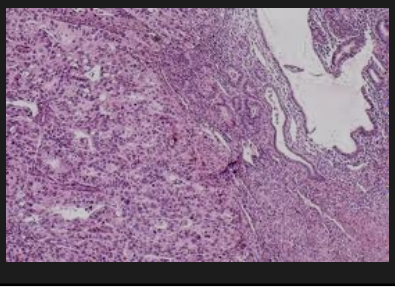
Grading of Endometrial Cancer

- FIGO G1:<5% solid/non glandular areas
- FIGO G2 6-50% of solid/non-glandular areas
- FIGO G3 >50% of solid/non glandular areas





Spread of the tumor

1. Direct/l ocal spread accounts for most local extension beyond the uterus.
2. Lymphatic spread accounts for spread to pelvic, para-aortic, and, rarely, inguinal lymph nodes.
3. Hematologic spread to the lungs, liver, bone, and brain
4. Peritoneal/transtubal spread results in intraperitoneal implants, with papillary serous carcinoma , similar to ovarian cancer.

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Staging of Endometrial Cancer

I: Confined to uterine corpus

0 atypical adenomatous hyperplasia
IA Limited to the endometrium
IB invades < ½ of myometrium
IC invades > ½ of myometrium

II: invades cervix,not beyond uterus

II-A endocervical glandular involvement only

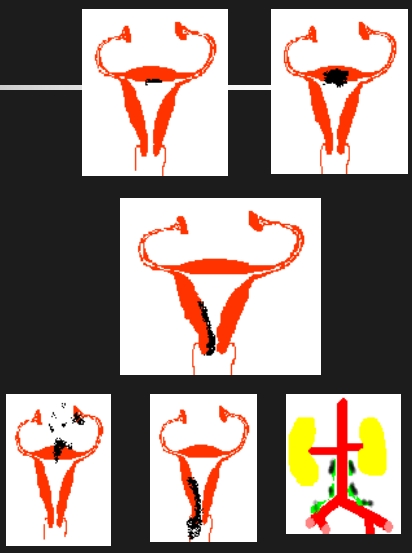
II B cervical stromal invasion

III: local and/or regional spread

IIIA: invades serosa/adnexa
IIIB: vaginal or parametrial involvement
IIIC: metastasis to pelvic or para-aortic LN

VI: Spread out side tue pelvis

IVA: invades bladder/bowel mucosa
IVB: distant metastasis



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Treatment of Endometrial Carcinoma

- Based on tumour grade and depth of myometrial invasion
- Primarly Surgical: TAH/BSO and pelvic washings ± pelvic and periaortic node dissection general trend (controversial)
- Stage I - TAH/BSO and washings
- Stages II and III- TAH/BSO and washings and LN dissection
- Stage VI - NO surgical option
- Adjuvant radiotherapy: based on depth of myometrial invasion,tumour grade, and/or lymph node involvement
- Hormonal therapy - progestins for distant or recurrent disease
- Adjuvant chemotherapy – Cisplatin, if disease progresses

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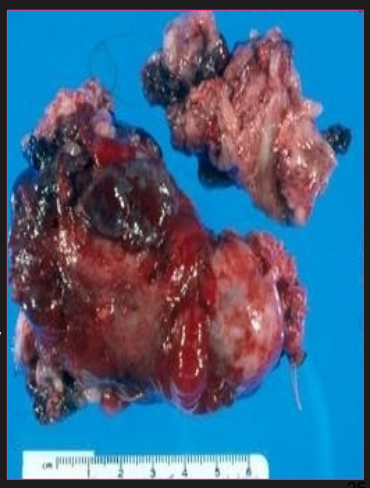
VI- UTERINE SARCOMA

- Rare - 2-6% of all uterine malignancies
- Arise from stromal components (endometrial stroma, mesenchymal or myometrial tissues)
- Greater tendency to disseminate hematogenously
- 5-year survival - 35%



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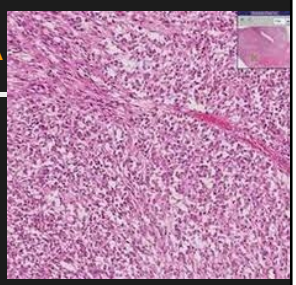
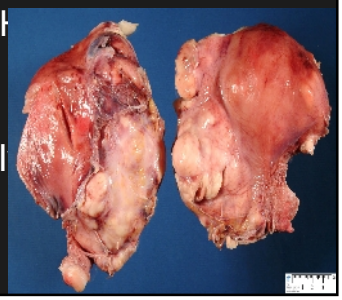
LEIOMYOSARCOMA



- May be associated with leiomyoma
- with rapid growth+bleeding
- Average age of is 55 years
- Histologic distinction (from leiomyoma)
  - Dx: mitotic count (~10 mitosis/l0 H
  - tumour necrosis
  - cellular atypia
- Most are diagnosed postoperativel after uterus removed for fibroids



Clinical Features & TREATMENT

- Rapidly enlarging fibroid in a post-menopausal woman
- Treatment
- TAH/BSO
- NO adjuvant therapy given if disease confined to uterus and low malignant potential (mitotic index is low)
- Radiation if high mitotic index
- Chemotherapy (-25% response rate) if tumour spread beyond uterus

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ENDOMETRIAL STROMAL SARCOMA

- Presents mainly in perimenopausal women (45-50 years)as abnormal uterine bleeding
- Diagnosed by histology of endometrial biopsy or D&C
- Treatment
- TAH/BSO, ALWAYS remove ovaries
- Hormonal therapy (progestins) in low grade sarcoma ONLY

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MIXED MULLERIAN SARCOMA

- 40% of all uterine sarcomas, poorest overall survival (like high grade leiomyosarcomas)
- Clinical Presentation
- post-menopausal bleeding 90% of cases • lesions are soft to palpation
- 1/3 have polypoid tumour protruding through CX.
- Treatment is the same as leiomyosarcoma, radiation often used

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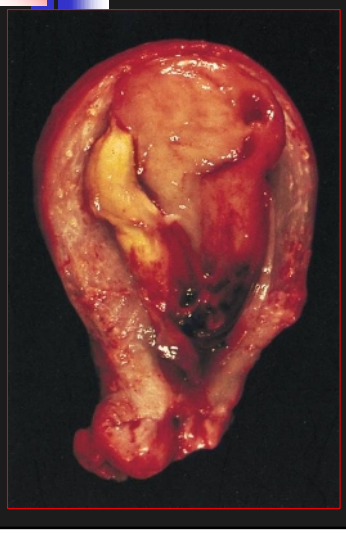

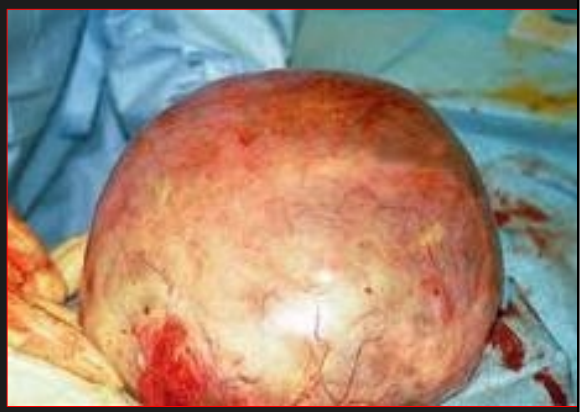

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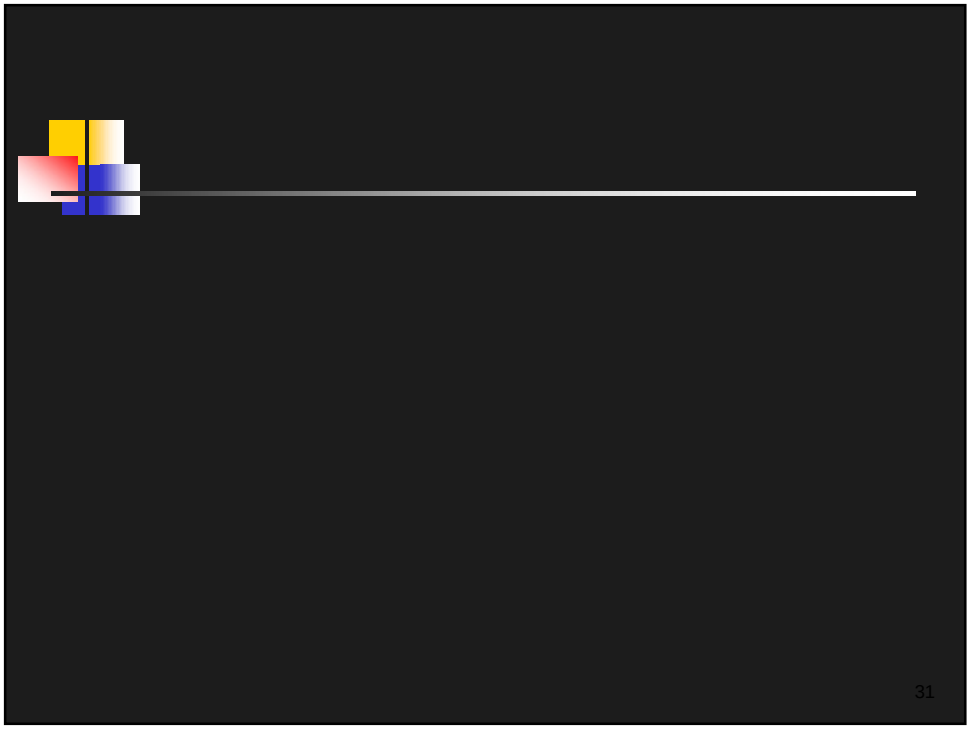

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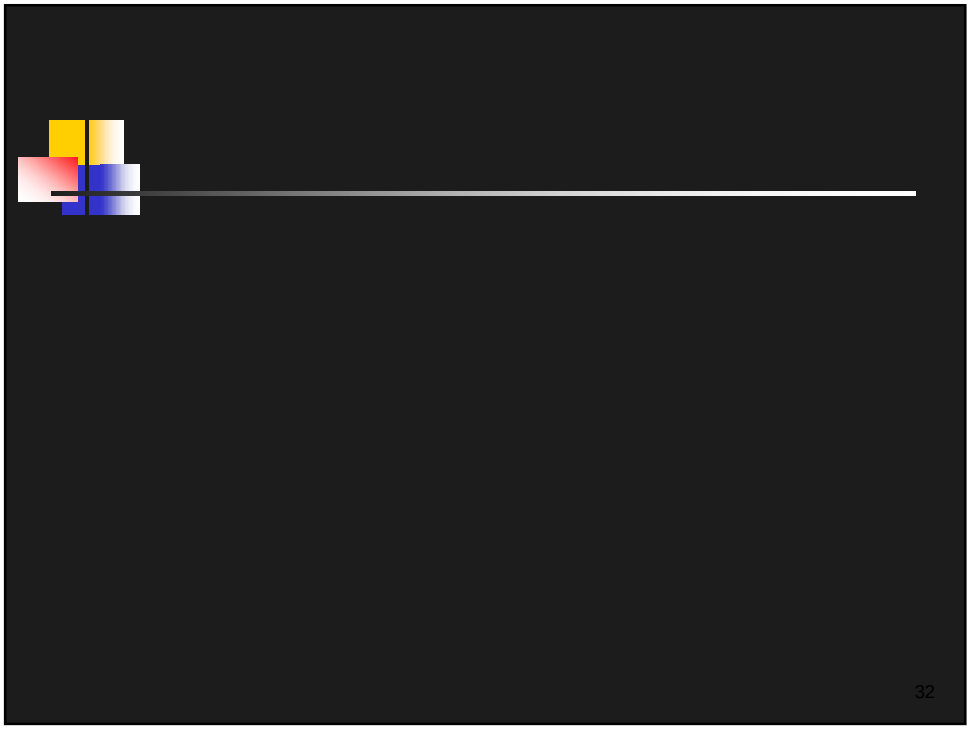

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