

# PATHOLOGY DIAGNOSIS OF CANCER

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DIAN YULIARTHA LESTARI

A solid orange horizontal bar at the bottom of the slide.

# HISTOLOGIC METHODS

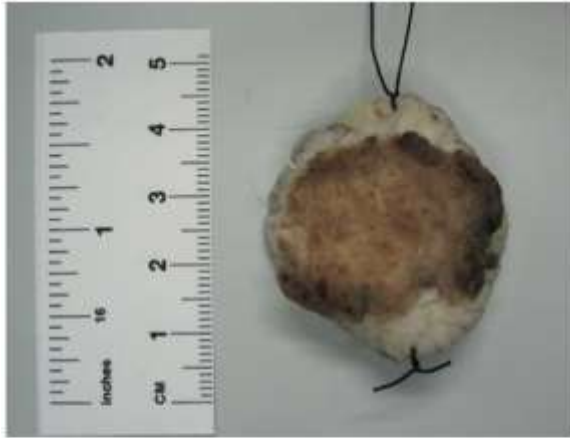
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## PARAFFIN EMBEDDING TECHNIQUE

- Hasil operasi → diagnosis final
- Biopsi → diagnosis pre-operatif; diagnosis final
- Tahapan :
  - Makroskopik → cut section
  - Mikroskopik : Prosesing → embedding → potong dan pewarnaan H&E

## FROZEN SECTION

- Penderita masih berada dalam ruang operasi (durante operasi)
- Dilakukan pengambilan sedikit jaringan (biopsi)
- Tanpa Fixasi
- Hasil dilaporkan dalam 5-15 menit
  - → Representatif / tidak
  - → JINAK / GANAS



**Figure 5.4** A medium-sized skin sample is seen with a central lesion. This could be described as 'A skin ellipse x by y by z mm depth is seen with an orientation suture, designated 12 o'clock. The sample shows a central yellow-brown nodule z mm that is k mm clear of the closest margin'. It is sectioned into parallel slices and then placed into a cassette (see Fig. 5.3).



**Figure 5.3** Tissue blocks are placed into the cassette. Note they should not fill the cassette, and must permit room for processing fluid circulation. The orientation of the blocks is enhanced by a sponge securing the specimens in sequential position and a colored agar marker allows designation of the order of slices taken. The samples have been marked with different colored inks to permit designation of the sidedness of the samples and the resection margins.

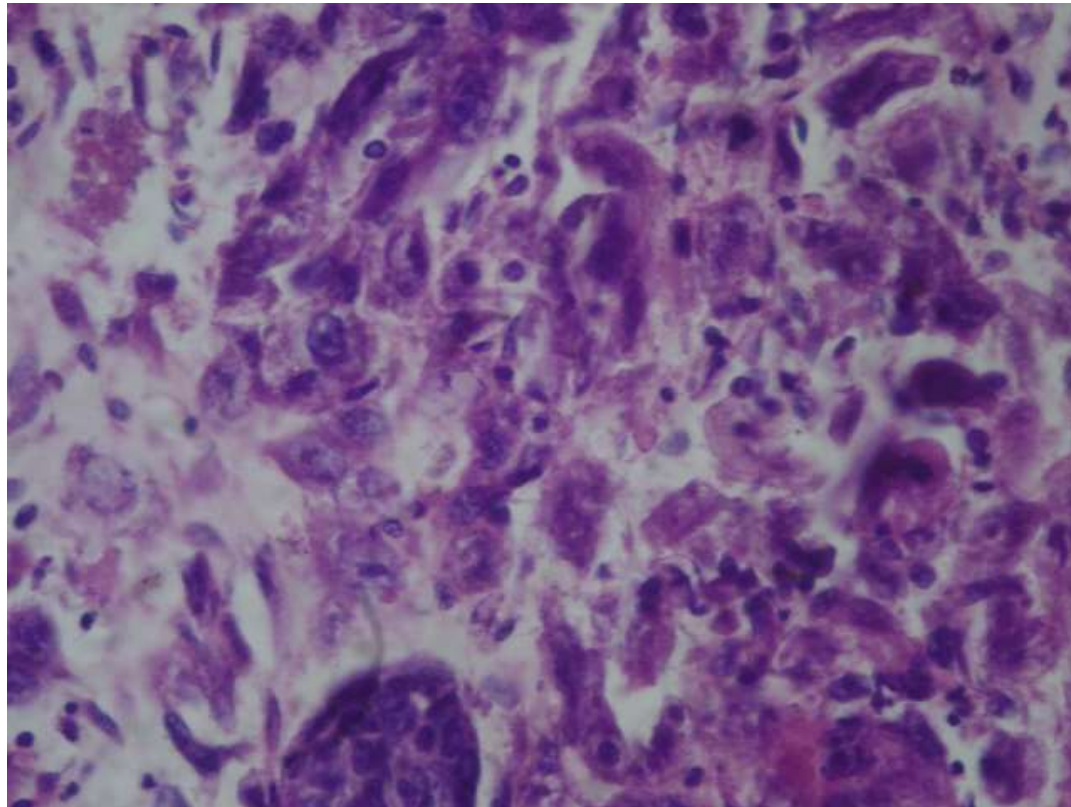


**Figure 6.3** Shows an H&E slide and the paraffin block area are matched.

Table 6.1 Overnight processing schedule				
Station	Reagents	Time	P/V	Temp
1	10% Formalin	1 h	On	38°C
2	10% Formalin	1 h	On	38°C
3	50% Alcohol/formalin	1 h	On	38°C
4	70% Alcohol	1 h	On	38°C
5	95% Alcohol	1 h	On	38°C
6	95% Alcohol	40 min	On	38°C
7	100% Alcohol	1 h	On	38°C
8	100% Alcohol	40 min	On	38°C
9	Xylene	1 h	On	38°C
10	Xylene	30 min	On	38°C
11	Paraffin	30 min	On	60°C
12	Paraffin	30 min	On	60°C
13	Paraffin	30 min	On	60°C
14	Paraffin	30 min	On	60°C

# PEWARNAAN

## 1. Hematoxylin & Eosin



### Hematoxylin and eosin stain for paraffin sections

#### Method

1. Dewax sections, rehydrate through descending grades of alcohol to water.
2. Remove fixation pigments if necessary.
3. Stain in an alum hematoxylin of choice for a suitable time.
4. Wash well in running tap water until sections 'blue' for 5 minutes or less.
5. Differentiate in 1% acid alcohol (1% HCl in 70% alcohol) for 5–10 seconds
6. Wash well in tap water until sections are again 'blue' (10–15 minutes), or
7. Blue by dipping in an alkaline solution (e.g. ammonia water), followed by a 5-minute tap water wash.
8. Stain in 1% eosin Y for 10 minutes.
9. Wash in running tap water for 1–5 minutes.
10. Dehydrate through alcohols, clear, and mount.

#### Results

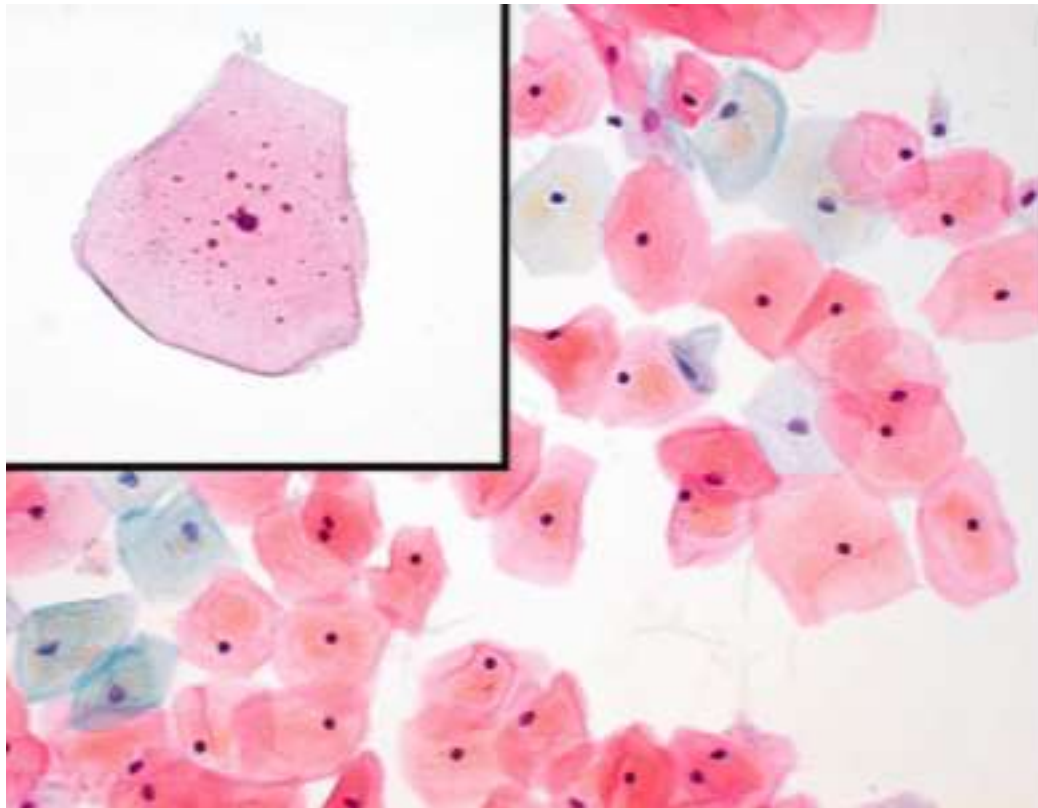
Nuclei	blue/black
Cytoplasm	varying shades of pink
Muscle fibers	deep pink/red
Red blood cells	orange/red
Fibrin	deep pink

#### Notes

Note that structures and substances other than nuclei may be hematoxyphilic to varying degrees. Examples include fungal hyphae, which are faintly hematoxyphilic, and calcium deposits, which are often deep blue-black.



## 2. PAPANICOLAOU



### Papanicolaou staining method

1. Remove polyethylene glycol fixative in 50% alcohol, 2 minutes.
2. Hydrate in 95% alcohol, 2 minutes, and 70% alcohol, 2 minutes.
3. Rinse in water, 1 minute.
4. Stain in Harris's hematoxylin, 5 minutes.
5. Rinse in water, 2 minutes.
6. Differentiate in 0.5% aqueous hydrochloric acid, 10 seconds approx.
7. Rinse in water, 2 minutes.
8. 'Blue' in Scott's tap water substitute, 2 minutes.
9. Rinse in water, 2 minutes.
10. Dehydrate, 70% alcohol for 2 minutes.
11. Dehydrate, 95% alcohol, 2 minutes.
12. Dehydrate, 95% alcohol, 2 minutes.
13. Stain in OG 6, 2 minutes.
14. Rinse in 95% alcohol, 2 minutes.
15. Rinse in 95% alcohol, 2 minutes.
16. Stain in EA 50, 3 minutes.
17. Rinse in 95% alcohol, 1 minute.

The staining times can be adjusted to suit personal preference for a darker or paler stain. Alternatives to Scott's tap water substitute include 0.1% ammoniated water or a weak aqueous solution of lithium carbonate.

### Results

The nuclei should appear	blue/black
Cytoplasm (non-keratinizing squamous cells)	blue/green
Keratinizing cells	pink/orange

### Note

Change stains frequently.

# CYTOLOGICAL METHODS

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SITOLOGI → ilmu yang mempelajari morfologi sel

- Sitoplasma → kualitas dan kuantitas
- Nucleus → kromatin, ukuran, nucleoli

Pewarnaan yang umum digunakan

- Papanicolaou
- HE

EXFOLIATIVE CYTOLOGY

- Pap smear
- Sitologi urine, pleura, ascites, brochus (washing/brushing)

FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)

# Sampel untuk Sitologi

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Cervical / Vaginal smear

Sputum

Bronchial washing / brushing

Nasopharyngeal smear/washing/brushing

Urine

Cairan lambung/pleura/ascites/sendiri

Liquor serebrospinal

Aspirasi Jarum Halus

Inprint neoplasma



# Pembuatan Sediaan

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Bahan cair :

Sampel + Fiksatif → sentrifuge → endapan di smear pada objek glass → pengecatan

Cairan : Ascites, Pleura, Urine tamping, BALL, Washing

Pemeriksaan sel-sel yang terlepas

# SITOLOGI EKSFOLIATIF

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# PAP SMEAR

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- Pap Smear adalah pemeriksaan sitologi abrasif ginekologi dari serviks untuk deteksi dini kanker serviks
- 1947, seorang ahli ginekologi dari Kanada J. Ernest Ayre memperkenalkan alat spatula untuk memperoleh sampel Pap Smear lebih baik dan dapat dengan mudah mencapai target. Spatula tersebut dari kayu yang dipotong sesuai bentuk yang diinginkan. Spatula tersebut dikenal sebagai Spatula Ayre.



# Tujuan Pemeriksaan Pap Smear

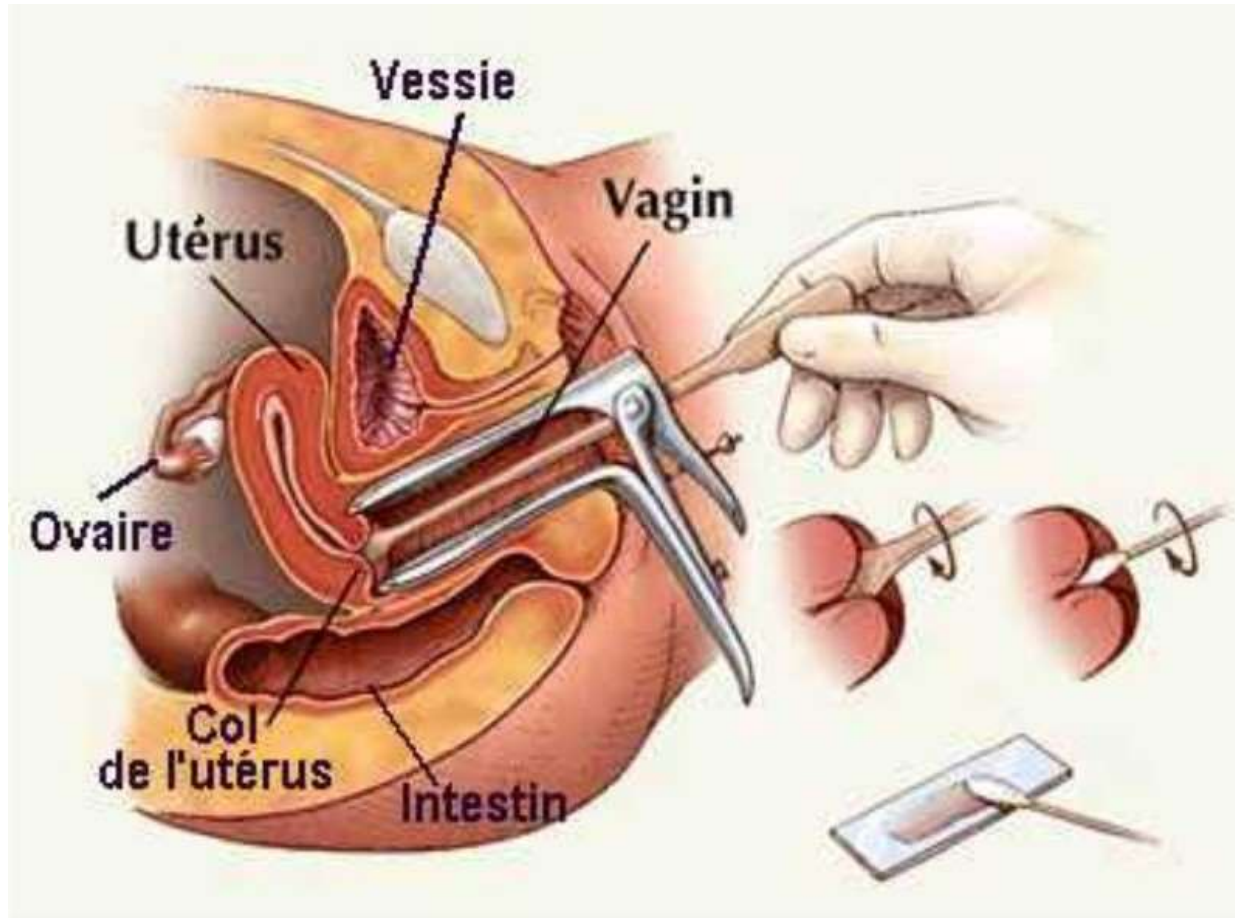
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- Deteksi dini kanker serviks → proses radang pada serviks dan vagina

## Jenis-jenis Pap Smear

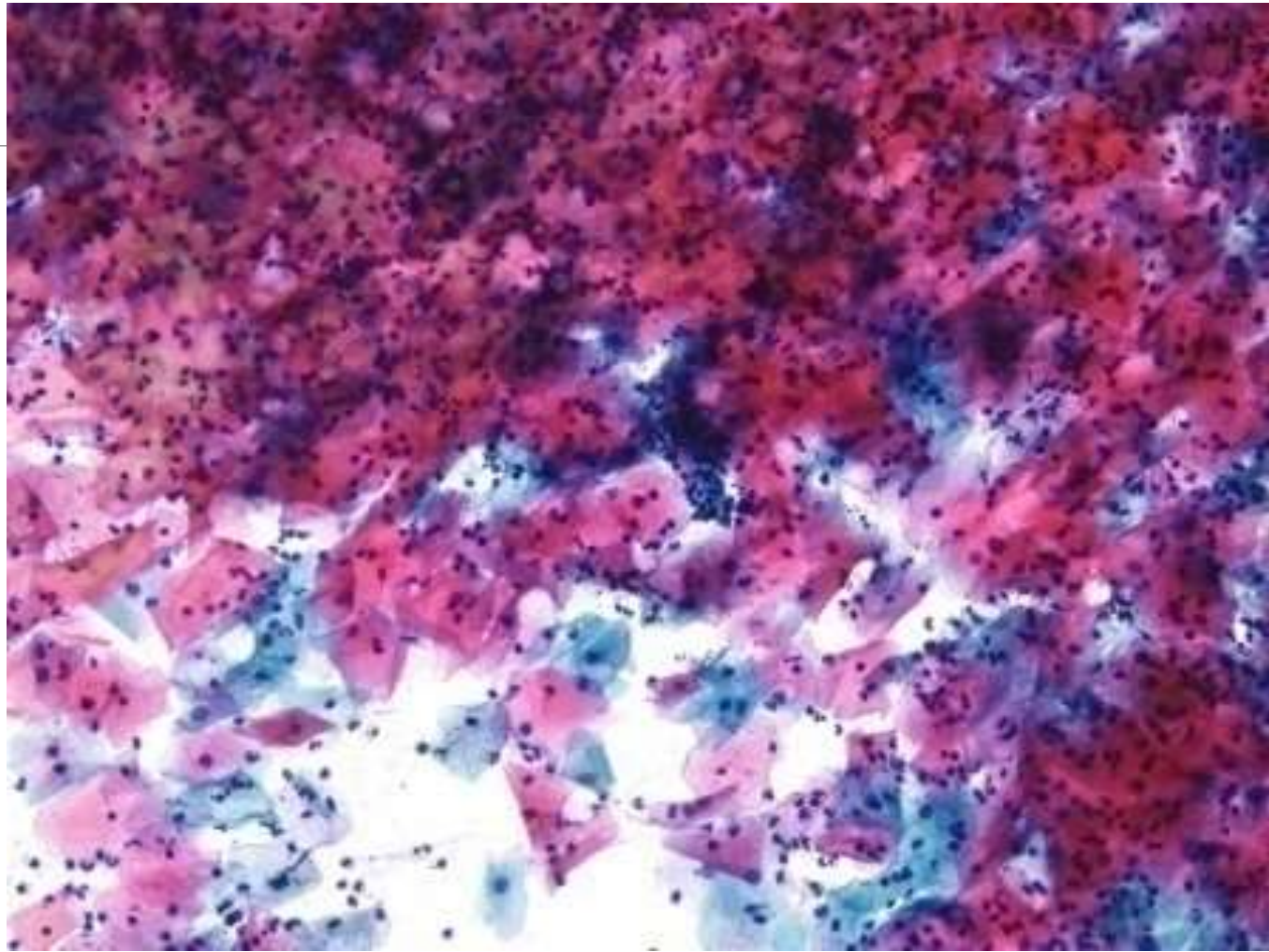
- Pap smear Konvensional
- Pap smear Liquid Base

# PAP SMEAR KONVENSSIONAL

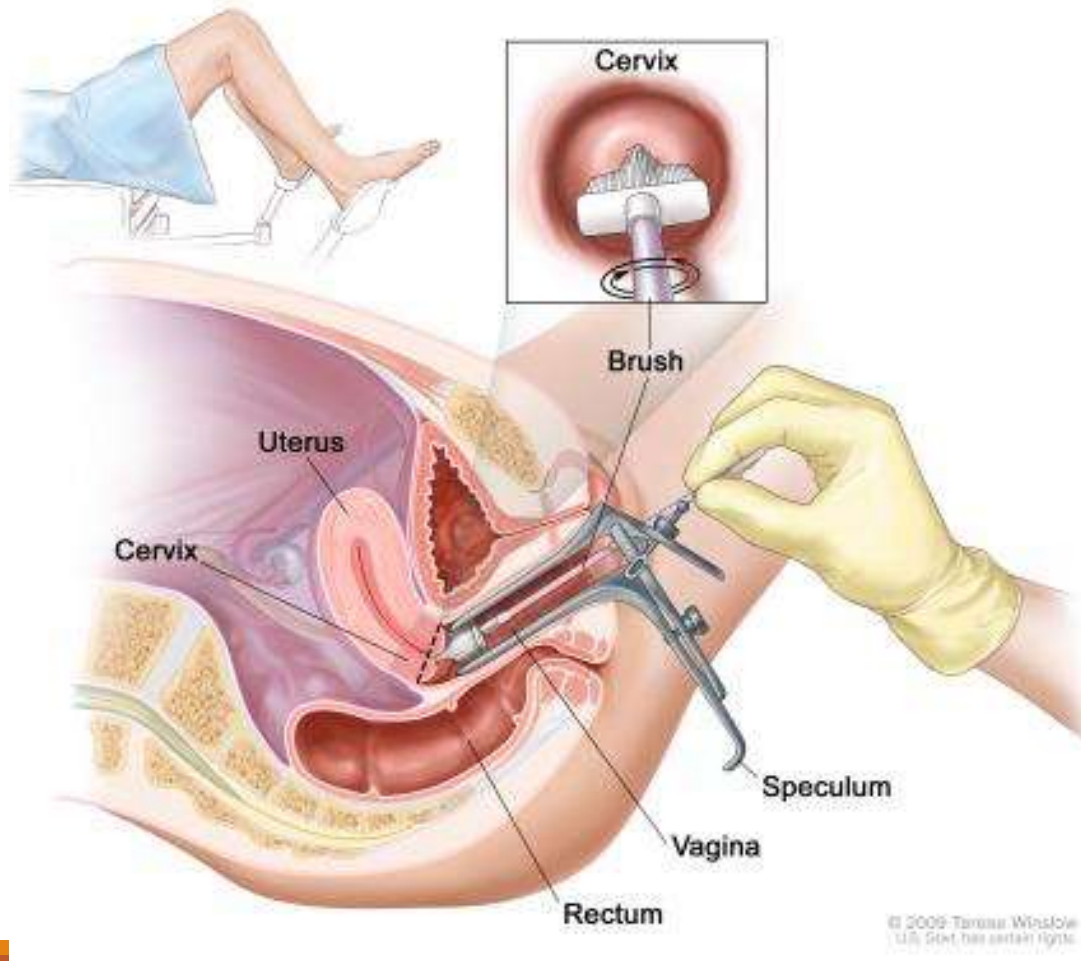


- 
- Sel-sel yang diperoleh sering saling menumpuk
  - Kabur oleh karena mengandung darah atau lendir.
  - Selain itu tidak seluruh sample yang diperoleh dilakukan pemeriksaan. Sisa sel yang masih melekat pada spatula akan terbang.
  - Akurasi sekitar 76,4 %.





# PAP SMEAR LIQUID BASED



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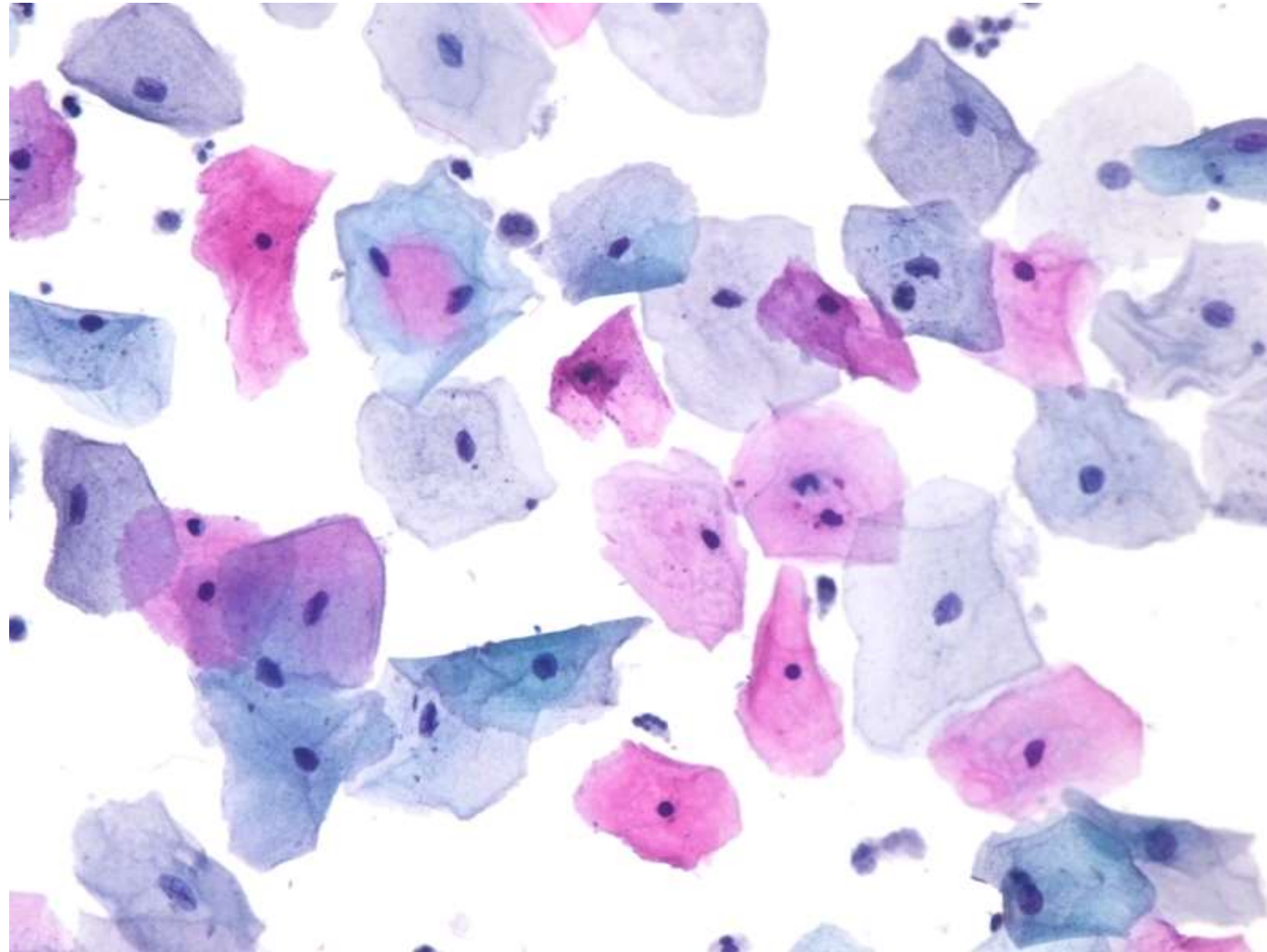
Sel tidak bertumpuk

Latar belakang lebih bersih

Seluruh sel yang diperoleh akan diproses dan tidak terbuang.

Evaluasi tambahan lebih lanjut.

Akurasi sekitar 98 %.





# FNAB

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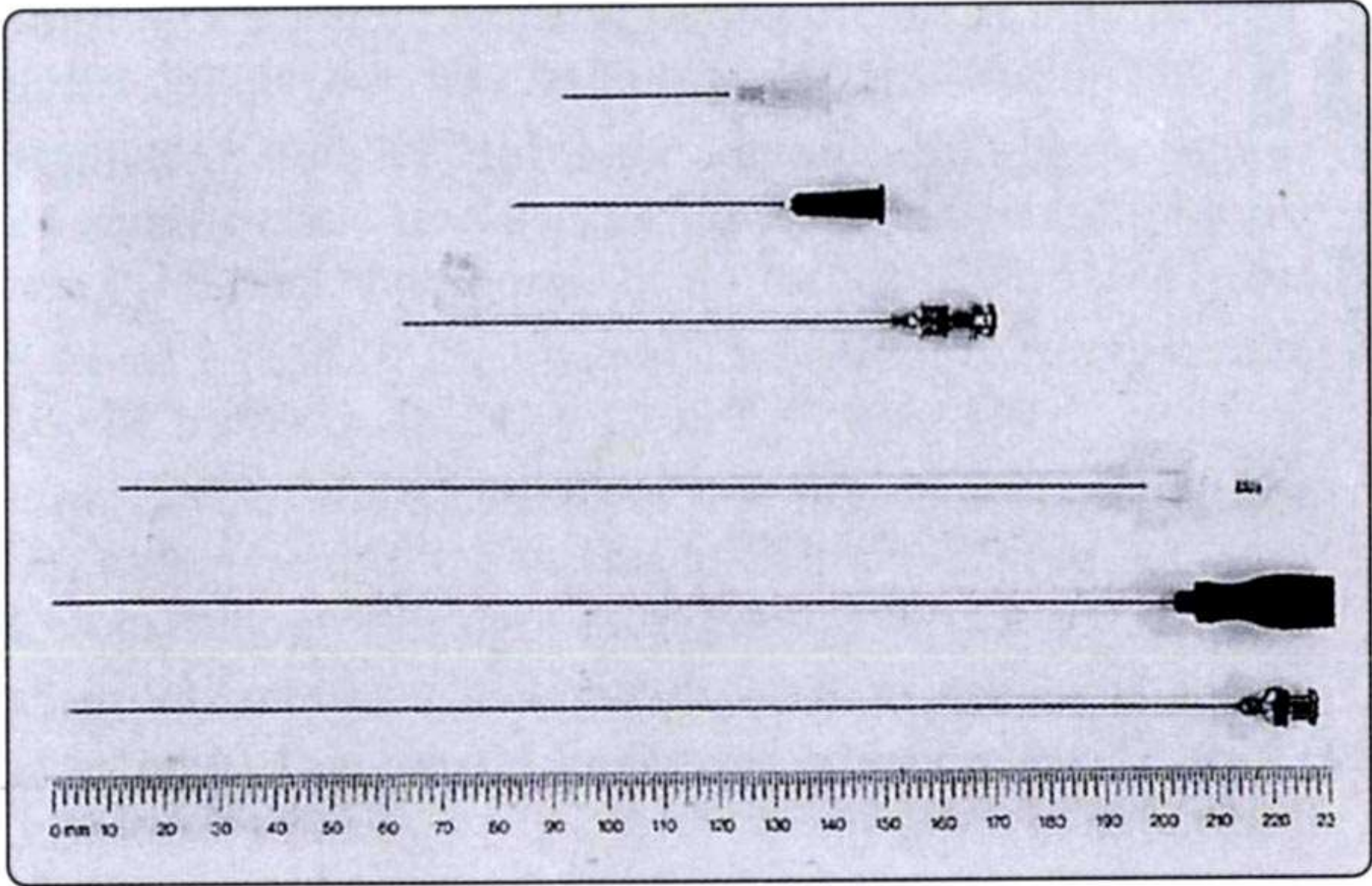
Jarum Halus → 25 G atau lebih besar (26G, 27G)

Dapat Dilakukan pada :

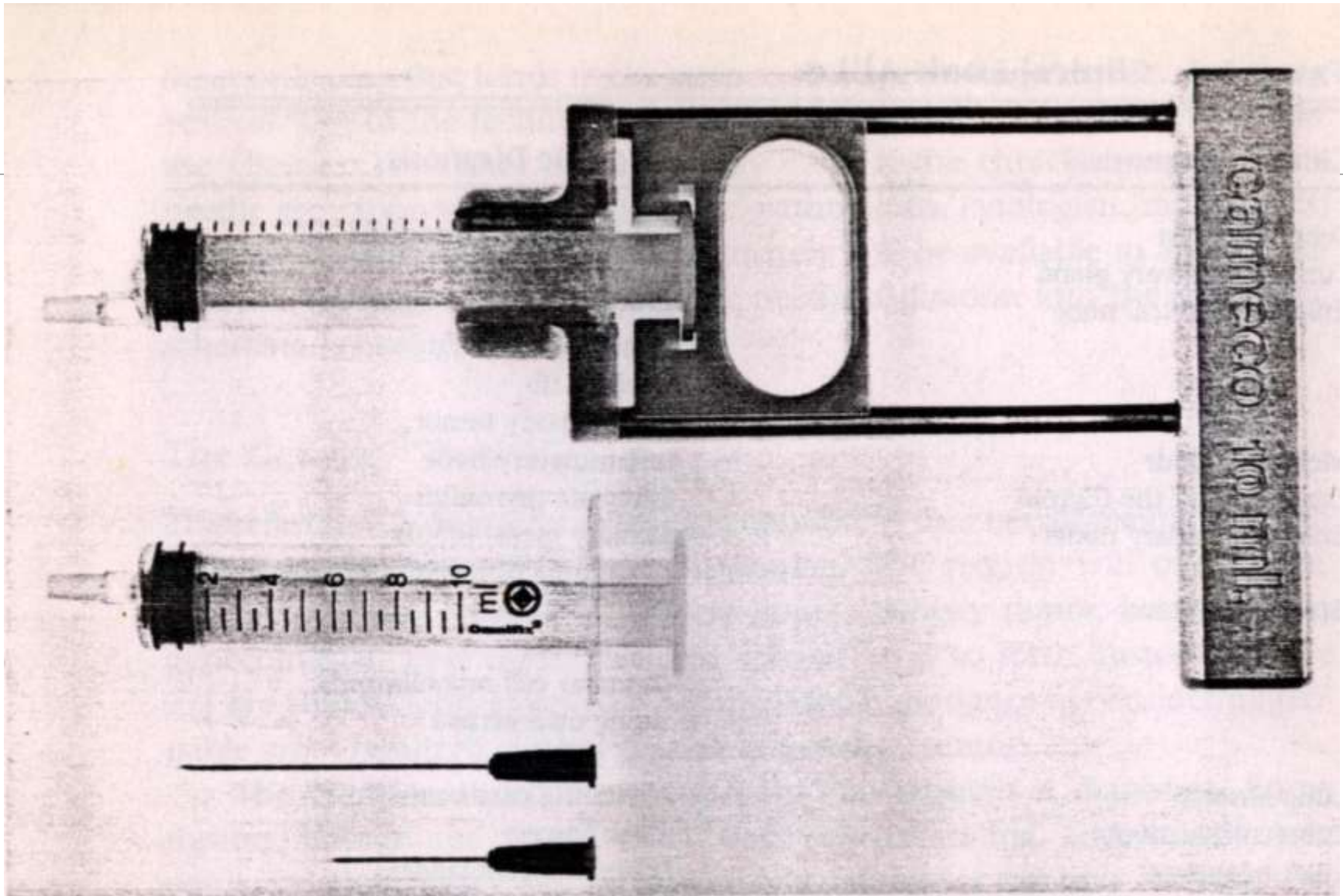
- Tumor-tumor permukaan
- Tumor organ dalam
  - → dengan tuntunan CT scan, USG

Keuntungan :

- Tidak traumatik
  - Tidak perlu anestesi
  - Tidak perlu ruangan khusus
- Diagnosis Pre Operatif



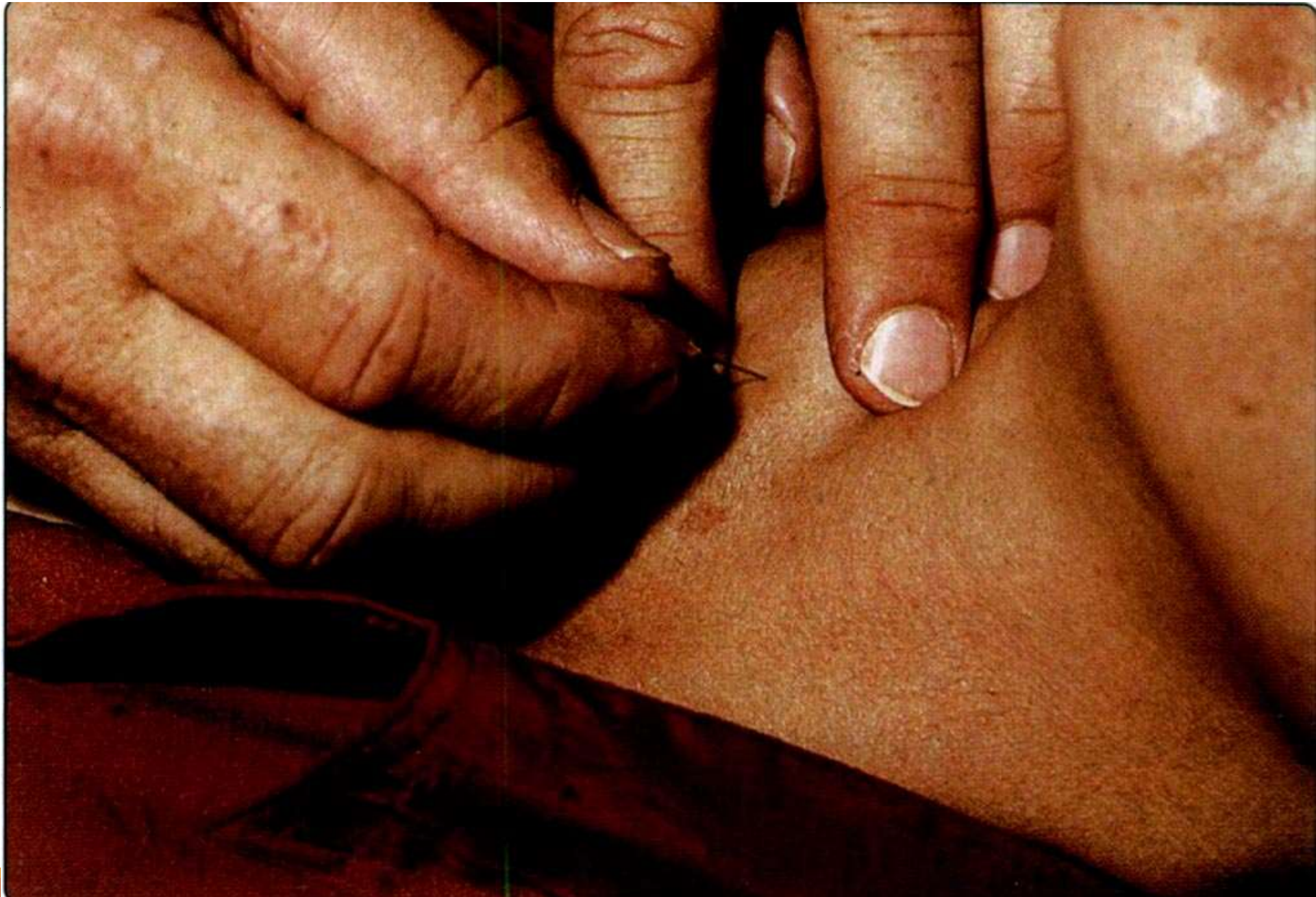


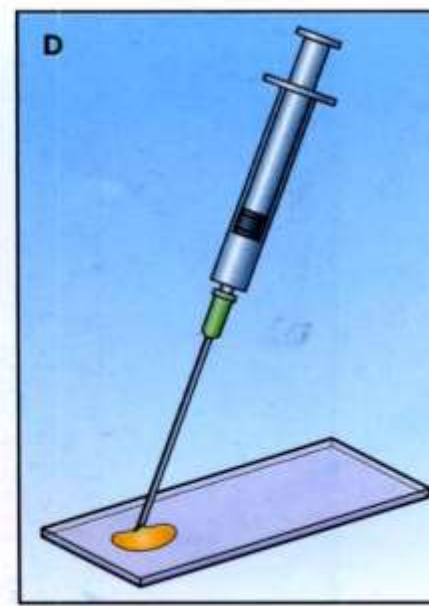
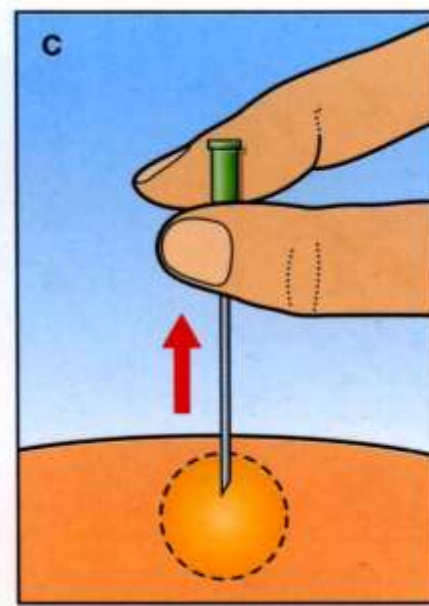
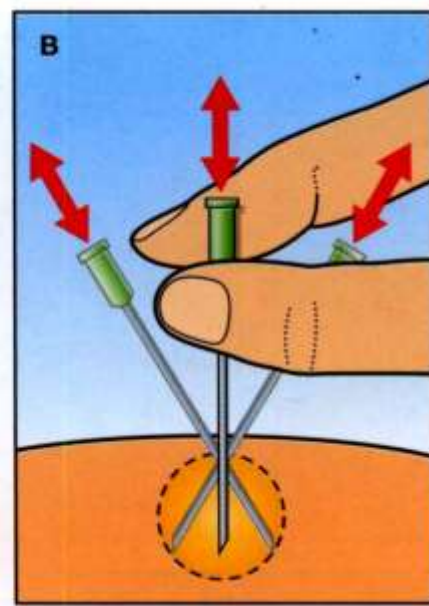
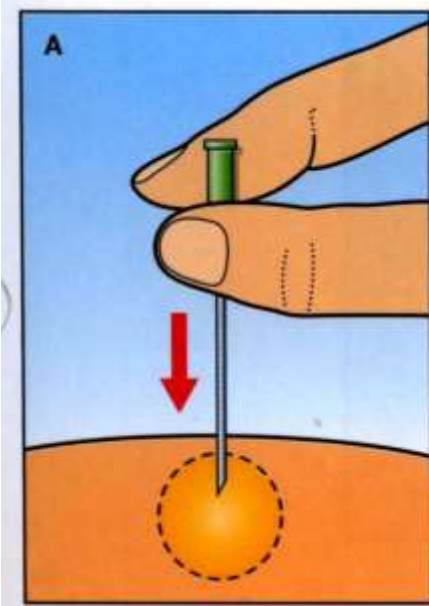




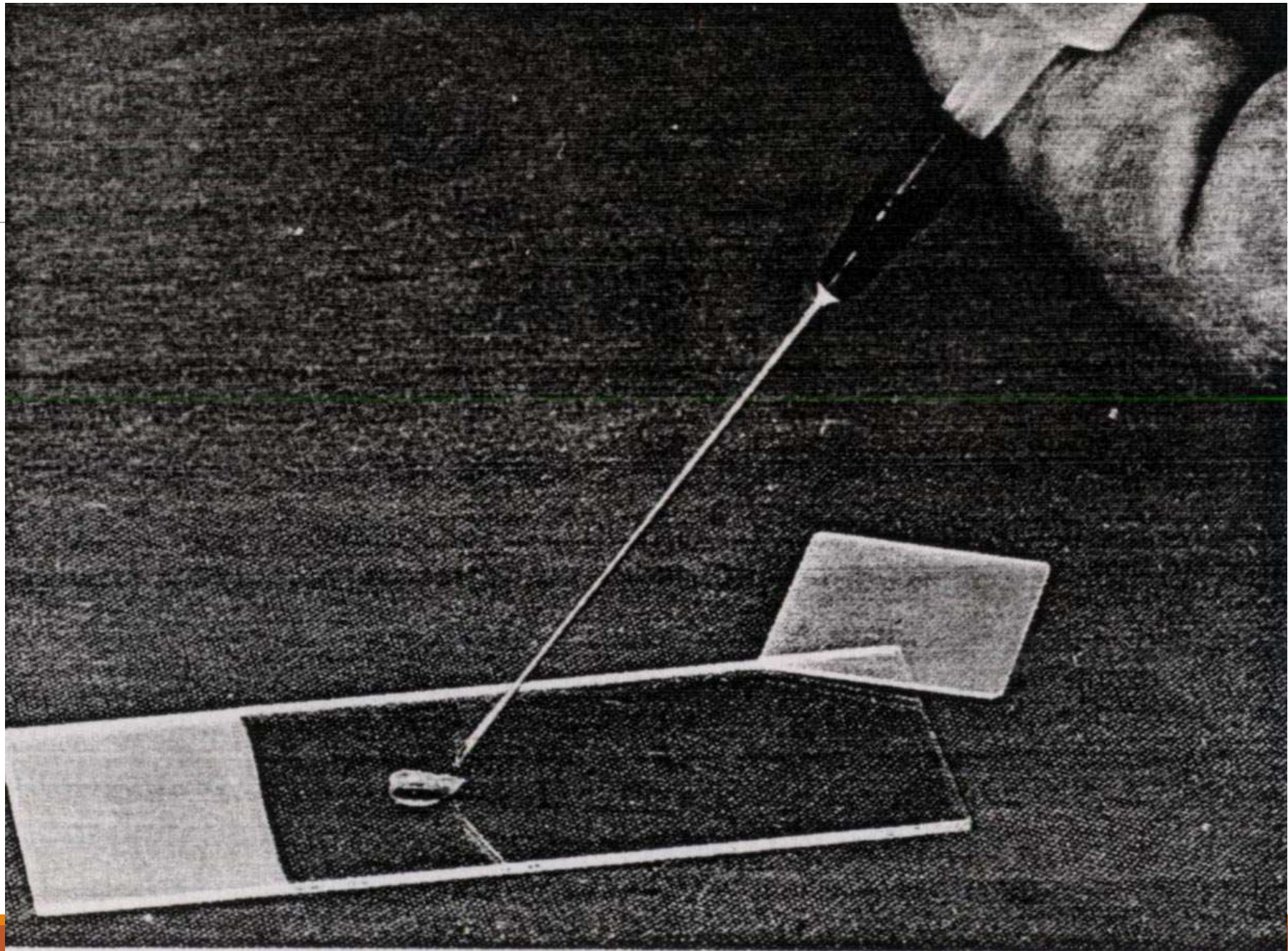




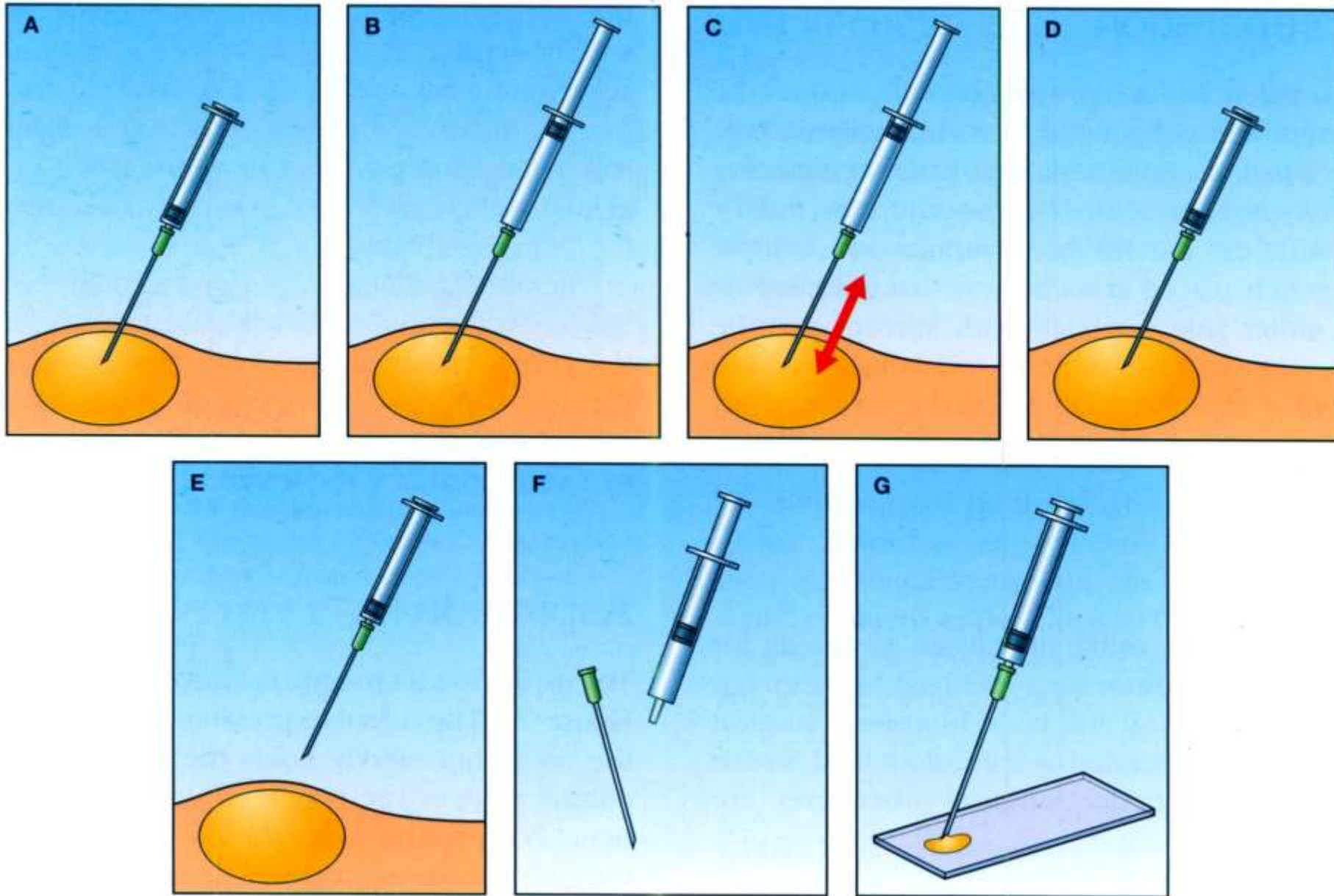


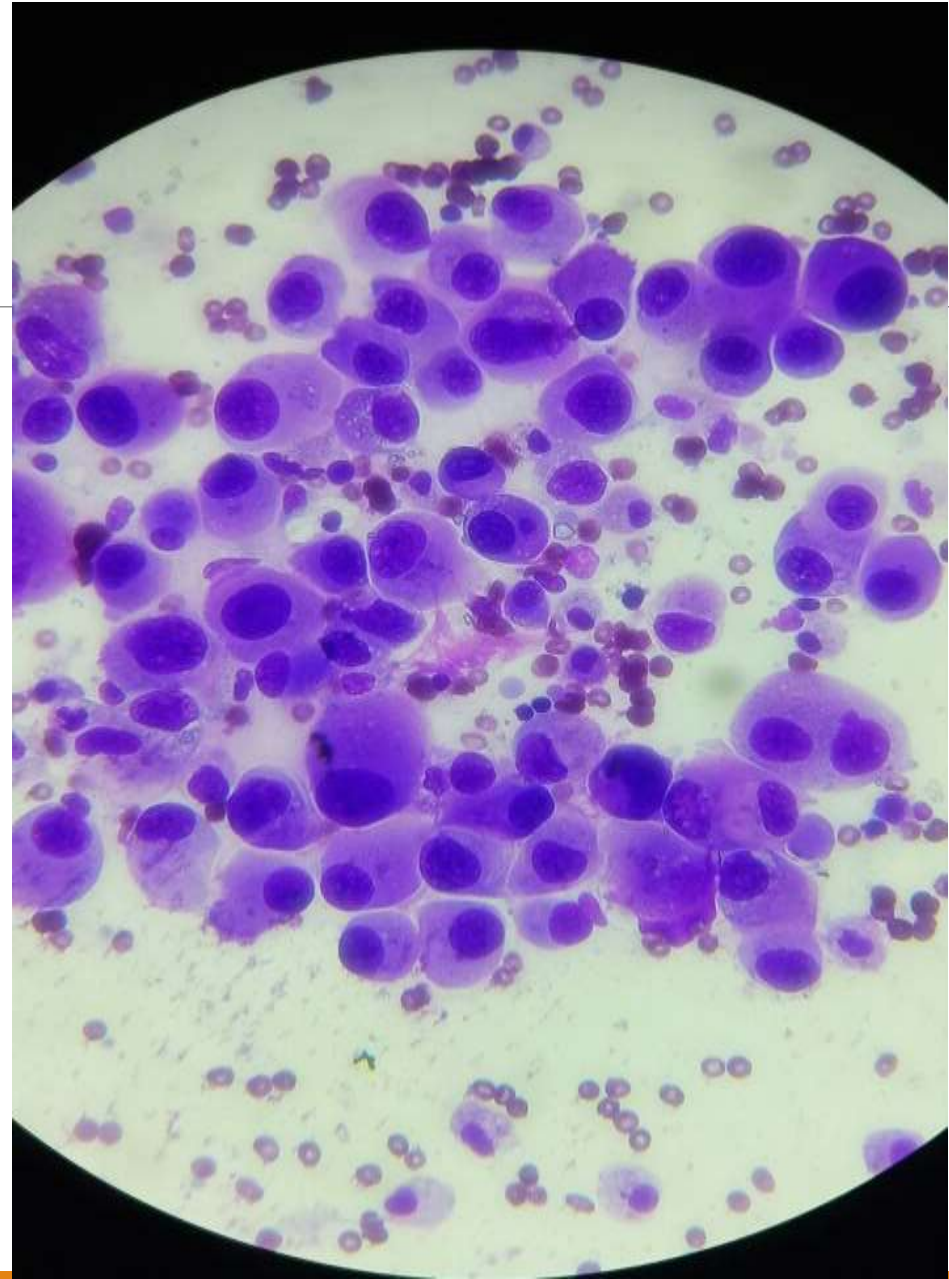
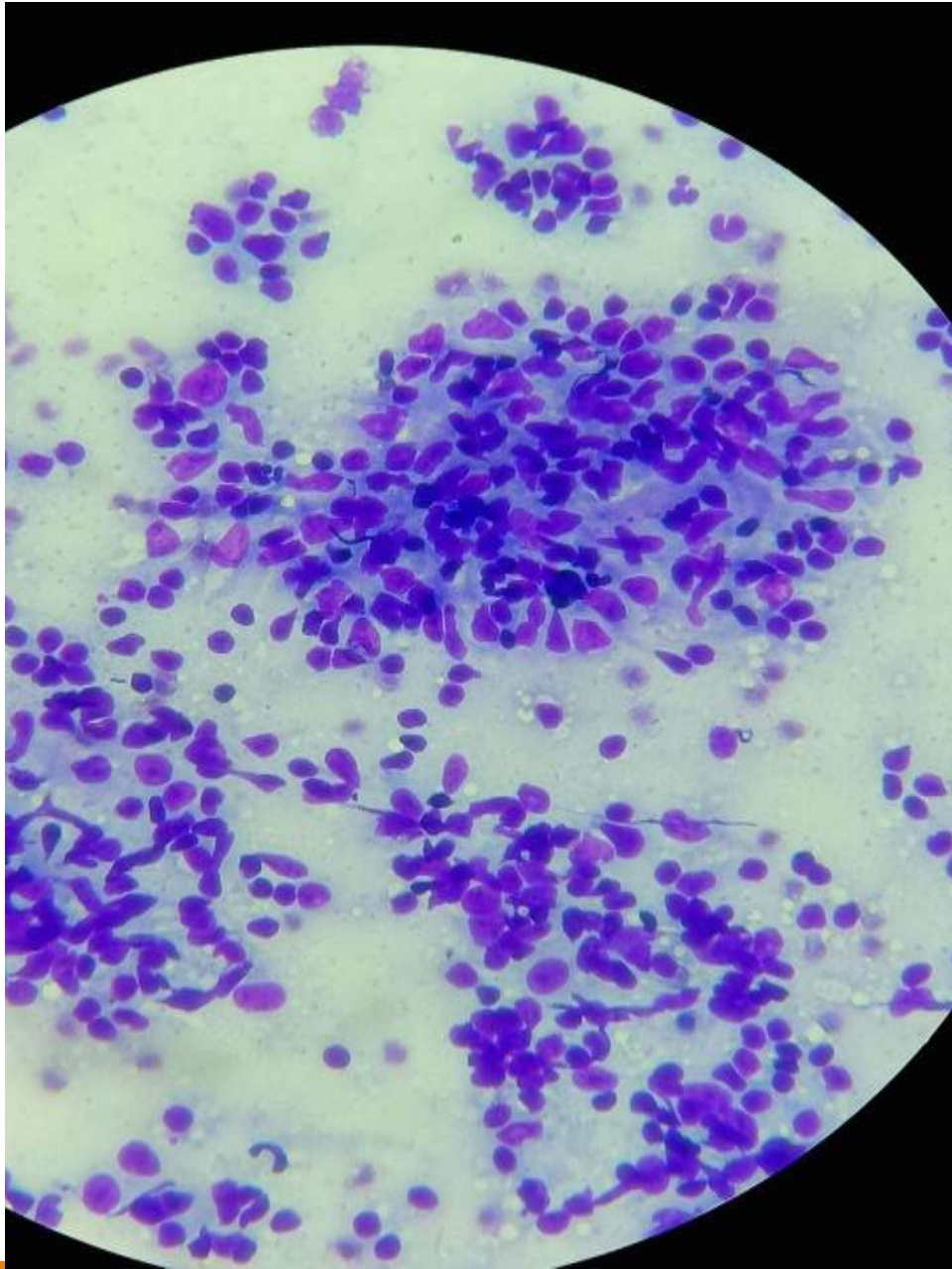












# HYSTOCHEMISTRY/CYTOCHEMISTRY

Additional diagnostic tools

Untuk identifikasi komposisi bahan kimia yang dihasilkan sel

Table 7.12

Common histochemical/cytochemical stains in tumour diagnosis.

SUBSTANCE	STAIN
1. <i>Basement membrane/ collagen</i>	Periodic acid-Schif (PAS) Reticulin Van Gieson Masson's trichrome
2. <i>Glycogen</i>	PAS with diastase loss
3. <i>Glycoproteins, glycolipids, glycomucins (epithelial origin)</i>	PAS with diastase persistence
4. <i>Acid mucin (mesenchymal origin)</i>	Alcian blue
5. <i>Mucin (in general)</i>	Combined Alcian blue-PAS
6. <i>Argyrophilic/ argentaffin granules</i>	Silver stains
7. <i>Cross striations</i>	PTAH stain
8. <i>Enzymes</i>	Myeloperoxidase Acid phosphatase Alkaline phosphatase
9. <i>Nucleolar organiser regions (NORs)</i>	Colloidal silver stain



# IMMUNOHISTOCHEMISTRY

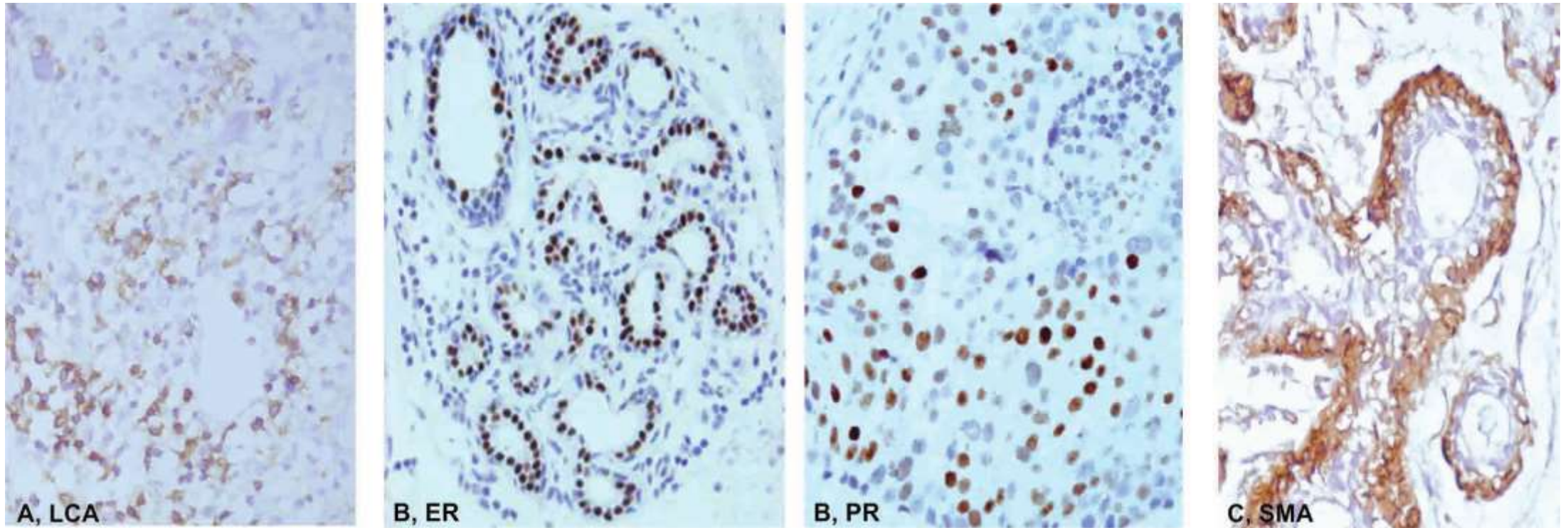
## FUNGSI:

- TUMOR OF UNCERTAIN HISTOGENESIS (DIAGNOSIS)
  - KATEGORISASI UNDIFF MALIGNANT TUMOR
  - ASAL TUMOR METASTASIS
- PROGNOSTIC MARKER
- PREDIKSI RESPON TERAPI
- INFEKSI

Table 7.13

Common panel of immunohistochemical stains for tumours of uncertain origin.

TUMOUR	IMMUNOSTAIN
1. <i>Epithelial tumours (Carcinomas)</i>	i) Pankeratin (fractions: high and low molecular weight keratins, HMW-K, LMW-K) ii) Epithelial membrane antigen (EMA) iii) Carcinoembryonic antigen (CEA) iv) Neuron-specific enolase (NSE)
2. <i>Mesenchymal tumours (Sarcomas)</i>	i) Vimentin (general mesenchymal) ii) Desmin (for general myogenic) iii) Muscle specific actin (for general myogenic) iv) Myoglobin (for skeletal myogenic) v) $\alpha$ -1-anti-chymotrypsin (for malignant fibrous histiocytoma) vi) Factor VIII (for vascular tumours) vii) CD34 (endothelial marker)
3. <i>Special groups</i>	
a) Melanoma	i) HMB-45 (most specific) ii) Vimentin iii) S-100
b) Lymphoma	i) Leucocyte common antigen (LCA/CD45) ii) Pan-B (Immunoglobulins, CD20) iii) Pan-T (CD3) iv) CD15, CD30 (RSCell marker for Hodgkin's)
c) Neural and neuro-endocrine tumours	i) Neurofilaments (NF) ii) NSE iii) GFAP (for glial tumours) iv) Chromogranin (for neuroendocrine)



**Figure 7.32** Examples of IHC staining at different sites in the tumour cells. A, Membranous staining for leucocyte common antigen (LCA) or CD45 in lymphomas. B, Cytoplasmic staining for smooth muscle actin (SMA) in myoepithelium on breast acinus. C, Nuclear staining for breast ER-PR receptor studies in breast cancer.

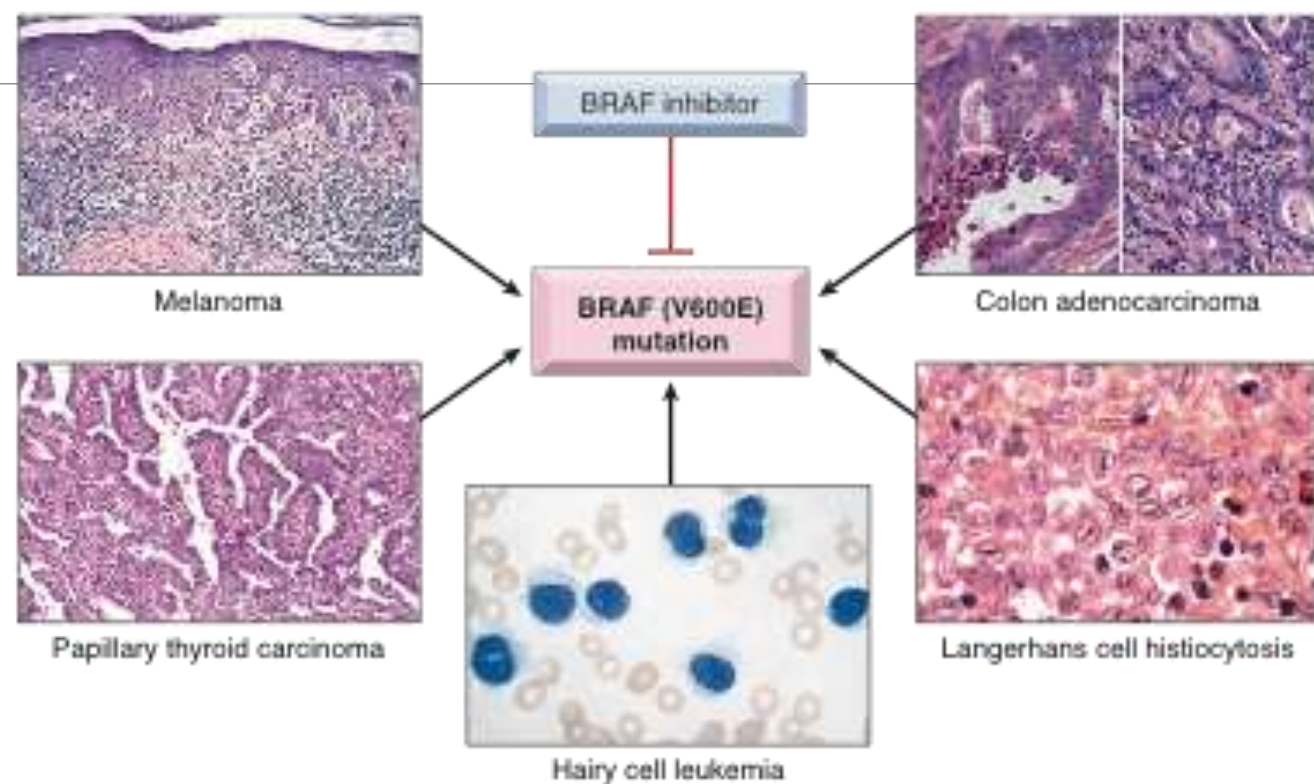
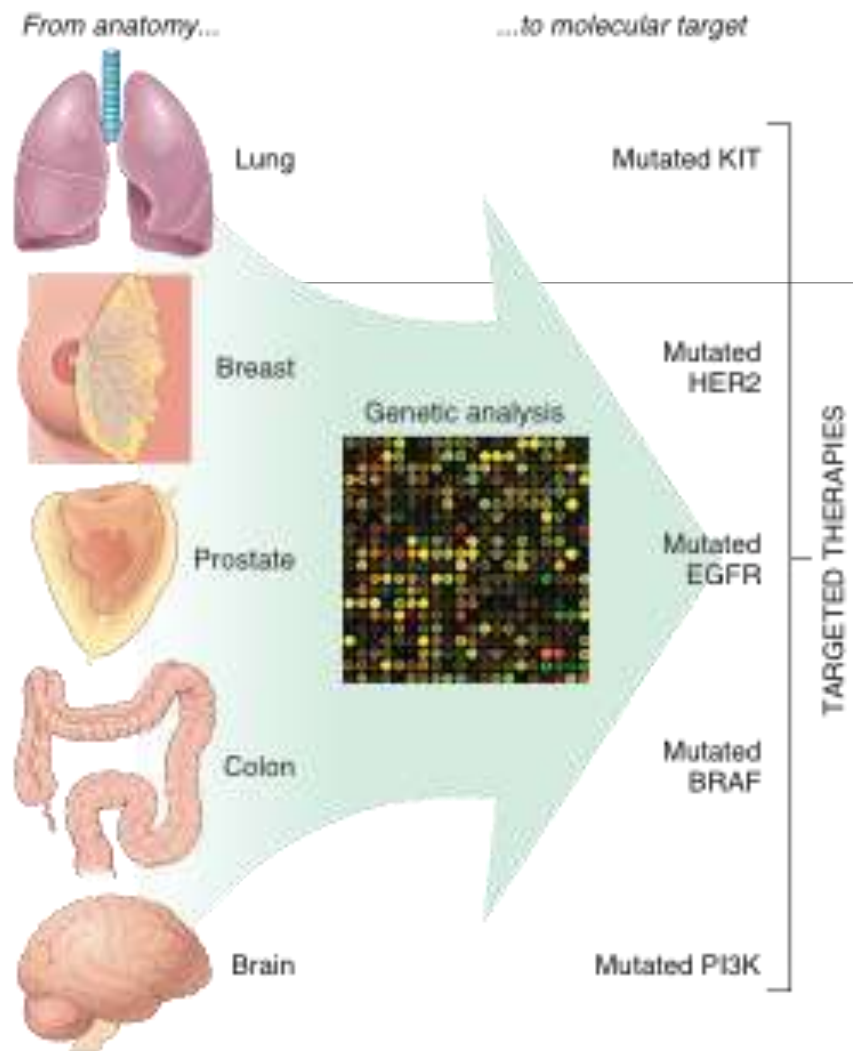


Figure 7-52 Diverse tumor types with a common molecular pathogenesis.

Figure 7-51 A paradigm shift: classification of cancer according to therapeutic targets rather than cell of origin and morphology. (Courtesy Dr. Levi Garraway, Dana Farber Cancer Institute.)



# ELECTRON MICROSCOPY

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- i) Cell junctions, their presence and type.
- ii) Cell surface, e.g. presence of microvilli.
- iii) Cell shape and cytoplasmic extensions.
- iv) Shape of the nucleus and features of nuclear membrane.
- v) Nucleoli, their size and density.
- vi) Cytoplasmic organelles—their number is generally reduced.
- vii) Dense bodies in the cytoplasm.
- viii) Any other secretory product in the cytoplasm e.g. melanosomes in melanoma and membrane-bound granules in endocrine tumours.

# TUMOR MARKER (BIOCHEMICAL ASSAY)

Table 7.14 Important tumour markers.

MARKER	CANCER
1. ONCOFOETAL ANTIGENS	
<i>i. Alpha-foetoprotein (AFP)</i>	Hepatocellular carcinoma, non-seminomatous germ cell tumours of testis
<i>ii. Carcinoembryonic antigen (CEA)</i>	Cancer of bowel, pancreas, breast
2. Enzymes	
<i>i. Prostate acid phosphatase (PAP)</i>	Prostatic carcinoma
<i>ii. Neuron-specific enolase (NSE)</i>	Neuroblastoma, oat cell carcinoma lung
<i>iii. Lactic dehydrogenase (LDH)</i>	Lymphoma, Ewing's sarcoma
3. HORMONES	
<i>i. Human chorionic gonadotropin (hCG)</i>	Trophoblastic tumours, non-seminomatous germ cell tumours of testis
<i>ii. Calcitonin</i>	Medullary carcinoma thyroid
<i>iii. Catecholamines and vanillylmandelic acid (VMA)</i>	Neuroblastoma, pheochromocytoma
<i>iv. Ectopic hormone production</i>	Paraneoplastic syndromes
4. CANCER ASSOCIATED PROTEINS	
<i>i. CA-125</i>	Ovary
<i>ii. CA 15-3</i>	Breast
<i>iii. CA 19-9</i>	Colon, pancreas, breast
<i>iv. CD30</i>	Hodgkin's disease, anaplastic large cell lymphoma (ALCL)
<i>v. CD25</i>	Hairy cell leukaemia (HCL), adult T cell leukaemia lymphoma (ATLL)
<i>vi. Monoclonal immunoglobulins</i>	Multiple myeloma, other gammopathies
<i>vii. Prostate specific antigen (PSA)</i>	Prostate carcinoma

# OTHER MODERN AIDS

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FLOW CYTOMETRY

IN SITU HYBRIDISATION (FISH/CISH)

CELL PROLIFERATION ANALYSIS (mitotic count, Ki-67, MIB)

IMAGE ANALYZER AND MORPHOMETRY

MOLECULAR DIAGNOSTIC TECHNIQUE

DNA MICROARRAY ANALYSIS TUMOR

# TEKNIK PENGIRIMAN BAHAN

**RS UNIVERSITAS MUHAMMADIYAH MALANG**  
**INSTALASI LABORATORIUM**  
 Jl. Raya Tlogomas No. 45 Telp. 0341 - 50 1000 Malang 65144

No. RM: 1802145  
 Nama: [Redacted] 1802145  
 J.K: Perempuan  
 Tgl. Lahir: 14-06-1996  
 Usia: 21 Thn - 7 Bln - 22 Hr  
 Alamat: [Redacted]

Spesialis: DC-02-2018  
 Dokter Pengirim: dr. Moch. Aliq S. M.Kes., SpB, FinaCS  
 Dokter Spesialis Bidan: dr. Moch. Aliq S. M.Kes., SpB, FinaCS  
 SIP: 503.1/22.01/000001/1996  
 As/Ruang: Mawati A

LOKASI PENGAMBILAN: *Mawati Lu Madoran Sentral*  
 DIAGNOSA KLINIS: *S. F. B. k.*  
 FIXASI: *penali 10%*

KETERANGAN KLINIS:  
*DD: massa 0.5 cm, padat, licin  
 basal tegas, keanehan.  
 Bagaimana gambaran PA?*

Dokter Pengirim,  
 dr. Moch. Aliq S. M.Kes., SpB, FinaCS  
 DOKTER SPESIALIS BIDAN  
 SIP: 503.1/22.01/000001/1996

**FORMULIR PERMINTAAN SITOLOGI APUSAN PAP**

RM: 1802145 Tanggal: 21/1/18  
 Nama (Ny/Nn): [Redacted] Dokter/Pengirim: dr. Andri W. S.  
 umur: 27 th No. 7 Haryono XI / 376 Dimado No. Telp.:  
 alamat: [Redacted]

**PEMERIKSAAN SITOLOGI YANG DIKEHENDAKI**  
 a. Hormonal : a. Hormonal sewaktu b. Hormonal serial c. Postmaturia  
 s. Ginekologi : a. Infeksi b. Keganasan c. lain-lain :  
 Apakah pasien pernah diperiksa sitologi/PA? YA / TIDAK  
 Jika YA, hasil pemeriksaan yang lalu : .....

**BAHAN PEMERIKSAAN**  
 Asal Sekret : a. Vaginal b. Eksoserviks c. Endoserviks  
 d. Endometrial e. Fornik Posterior f. Lain-lain :  
 Tanggal Pengambilan: 21/1/18

Keluhan Utama : *fluor albus + keanehan post tangi TGA*  
 Diagnosis Klinis : *fluor albus + keanehan post tangi*

**KETERANGAN KLINIS**  
 MPHT: 1/1/18  
 Status Pasien : a. Belum kawin b. Kawin c. Partus: G..... P..... A.....  
 d. Belum Hamil e. Hamil f. Postpartum g. Menopause  
 h. Lain-lain :  
 Kontrasepsi : a. PIU b. IUD c. Suntikan d. Lain-lain :  
 Pernah Operasi :  
 Pernah Radiasi :  
 Inspeksi :  
 Permukaan Porsio : a. Normal b. Erosi c. Mencurigakan

Malang, 21/1/18  
 Pengirim,

# Formulir PA

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Harus Berisi:

- No PA
- Identitas Pasien dan dokter pengirim
- Lokasi tumor (kp dengan gambar)
- Diagnosis Klinis
- Keterangan Kinis lainnya



No. Pendaftaran / No. PA : 40.1801007.82036 / H.019/18

Nama Pasien

[REDACTED]

No. RM : 1801007

Tgl. Dikirim : 17-01-2018

Umur : 44 Tahun / P

Tgl. Hasil : 29-01-2018

Diagnosis Klinis : CA MAMMA

Lokasi : Mamma sinistra

#### HASIL PEMERIKSAAN PA

##### MAKROSKOPIS

Diterima 1 potong jaringan berat 260 gram, ukuran 15x12x5 cm, dilapisi kulit. Pada irisan tampak massa putih abu-abu ukuran 2,5x2x2 cm, putih abu-abu, padat kenyal. Jarak massa dengan dasar 1 cm. Jarak massa dengan kulit 1,5 cm. Pada eksplorasi tidak didapatkan pembesaran nodul KGB.

##### MIKROSKOPIS

Sediaan menunjukkan potongan jaringan mamma dengan proliferasi epitel anaplastik, inti bulat oval, pleomorfik berat, hiperkromatik, tersusun solid (tubular formation < 10%), tumbuh invasif ke dalam stroma. Mitosis 18/10 HpF. Papilla mamma dalam batas normal. Didapatkan angioinvasi. Jarak tumor dengan dasar (fascia) berhimpit. Jarak tumor dengan kulit 10 mm.

##### KESIMPULAN

Mamma Dekstra, Operasi

INVASIVE CARCINOMA (IDC), NO SPECIAL TYPE, WHO GRADE III

DIAMETER TUMOR 2,5 CM

JARAK TUMOR DENGAN DASAR (FASCIA) BERHIMPIT (< 1 MM)

JARAK TUMOR DENGAN KULIT 10 MM

DIDAPATKAN ANGIOINVASI

PADA EKSPLORASI KGB TIDAK DITEMUKAN PEMBESARAN NODUL

pT<sub>3</sub>N<sub>0</sub>M<sub>0</sub>

Pemeriksa

dr. Dian Y. Lestari, Sp.PA

INSTALASI



# FIKSASI

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Tindakan merendam bahan pemeriksaan yang berasal dari jaringan tubuh kedalam cairan fiksasi

Tujuan Fiksasi:

- Mencegah terjadinya proses autolisis
- Mencegah proses pembusukan
- Memadatkan dan mengeraskan agar mudah dipotong
- Memadatkan cairan koloid
- Mencegah kerusakan struktur jaringan

# JENIS FIKSASI

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Untuk cairan → urine, cairan pleura, bronchial washing

- alkohol 50% dengan volume perbandingan 1:1

Untuk sputum tampung

- Alkohol 70%

Bahan pap smear

- Alkohol 96%

Bahan Histopatologi

- Formaline 10% (buffer formalin), volume 5-10x ukuran jaringan

# TRIMS

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