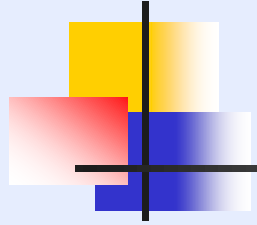


Some aspects of Tumour Immunology of Oral Cancer



NK cell – Interferon System
Revisited



Dr Arun Jamkar
Professor and Head
Department Of Surgery
B J M C Pune



Department
of Surgery
Presentation

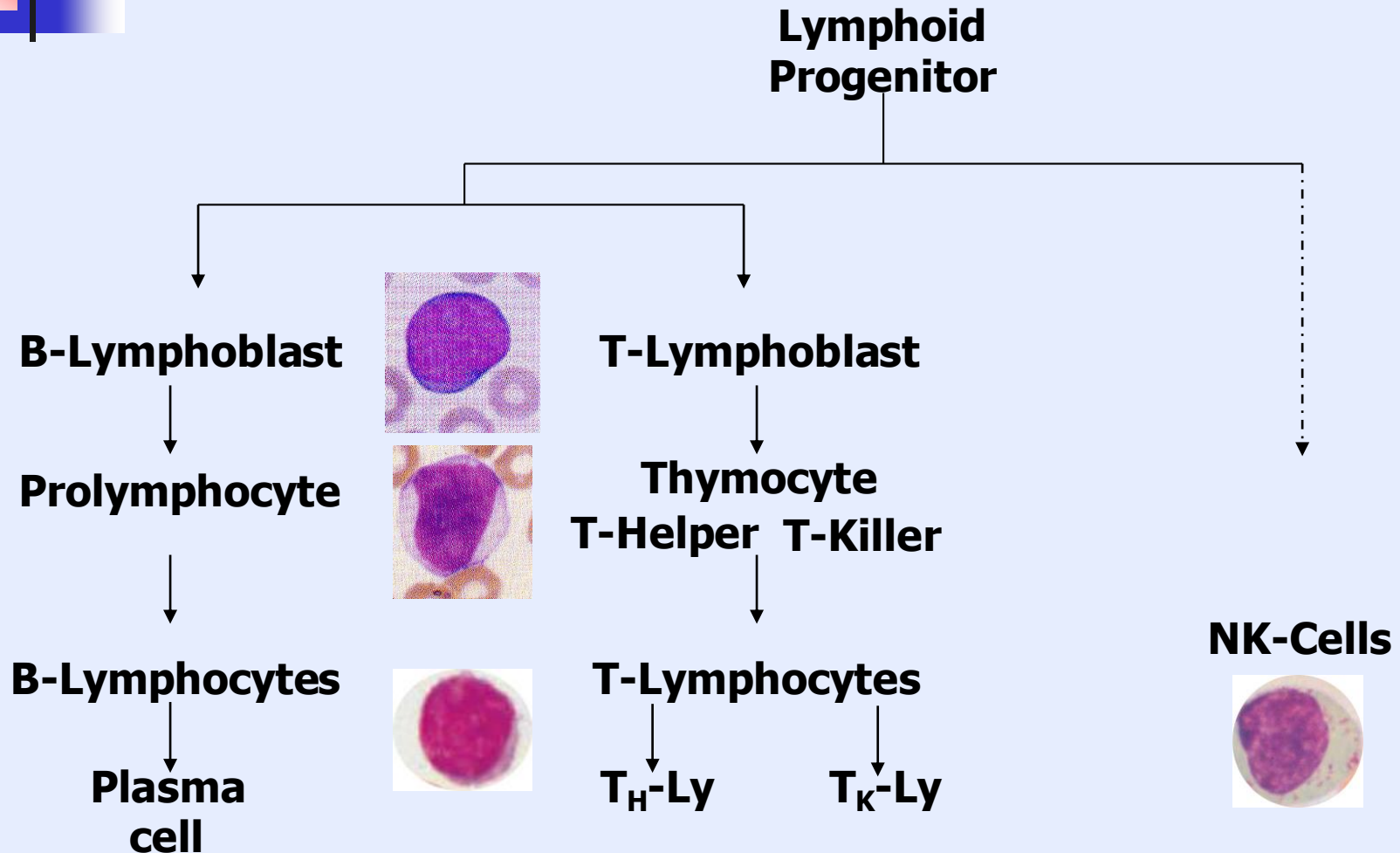


The Key Players

	Innate	Adaptive
Cellular	Phagocytes Epithelial Cells NK-Cells	Lymphocytes
Humoral	Complement Antimicrobial (Poly)Peptides	Antibodies



Lymphoid Lineage Gives Rise to Both NK-Cells and Lymphocytes



T Lymphocytes: Cell Mediated

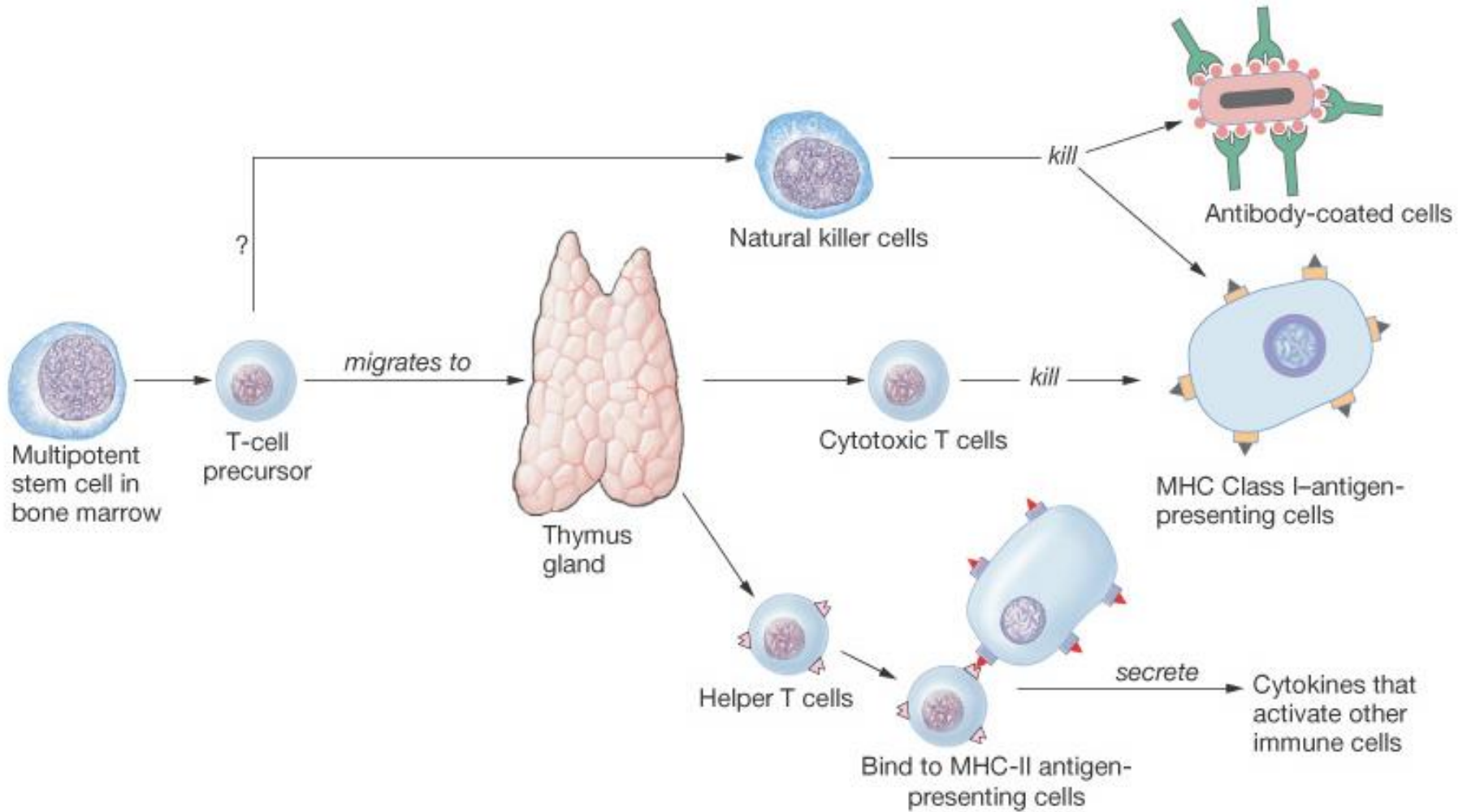
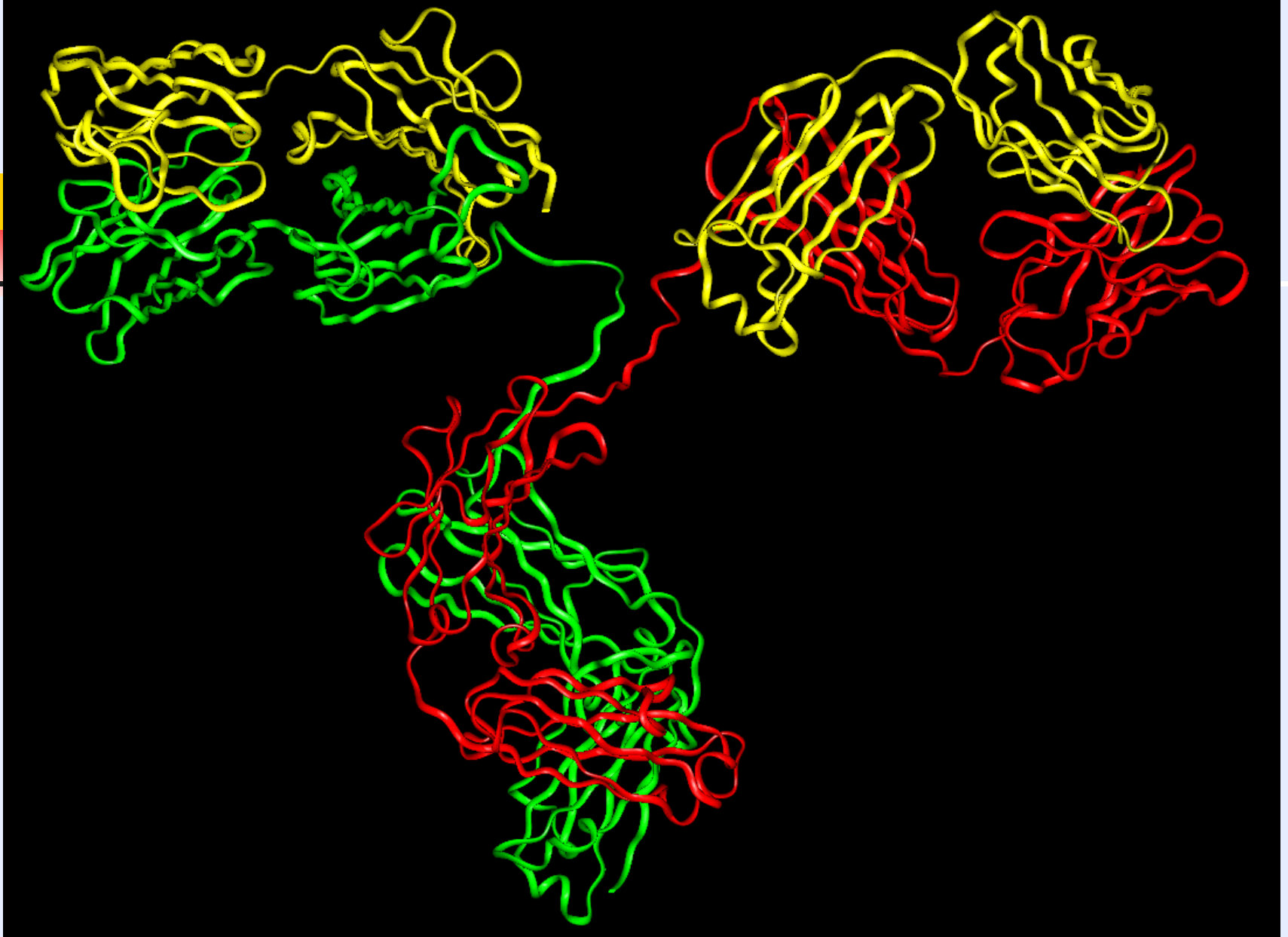


Figure 24-16: T lymphocytes and NK cells



NK-Cells Form Part of The Innate Immune System

- Large granular lymphocytes
- No specific antigen Recognition
- Recognize “altered self”
 - Altered MHC I molecules
 - virus infection
 - Intracellular pathogens
 - Altered surface glycoproteins
 - Tumor cells
- Recognize antibody-covered target cells
 - Fc γ III receptor (CD16)



Mouse IgG (McPherson, 1987)



*Human MHC Class I
 α -chain and β -2m*



Activated NK-Cells Are Cytotoxic And Stimulated Macrophages

- Activated by cytokines
 - IFN- α
 - IFN- β
 - IL-12 } made by virus infected cells
- Release their large granules containing
 - Pore-forming toxins
 - Enzymes that induce suicide of target cell
- Secrete the potent macrophage activator IFN- γ

NK-Cells in Action

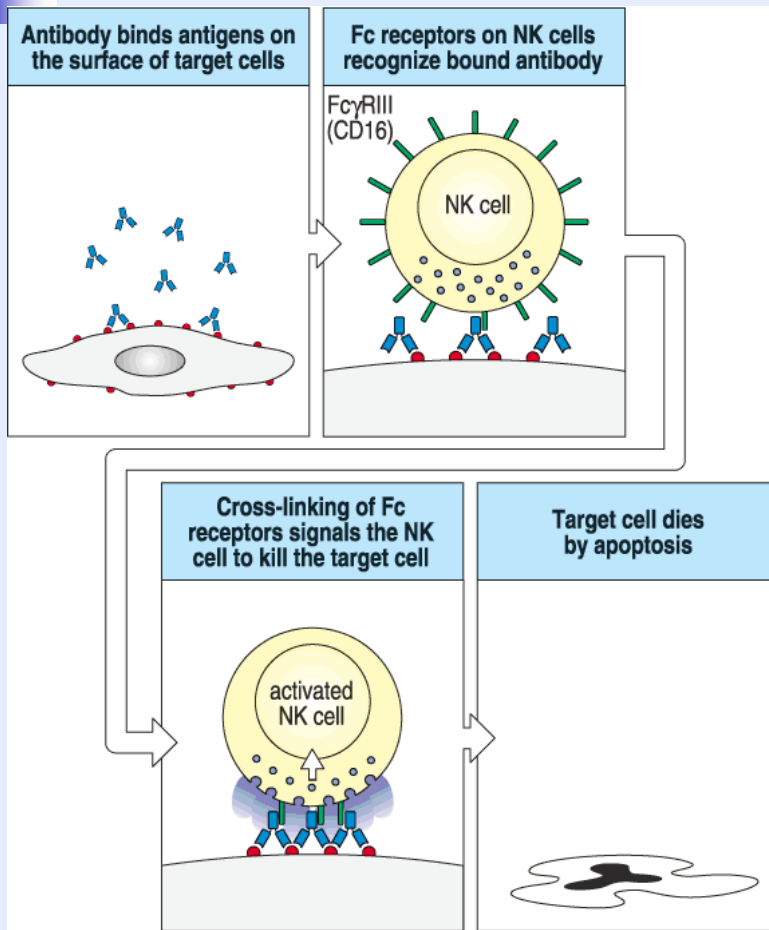
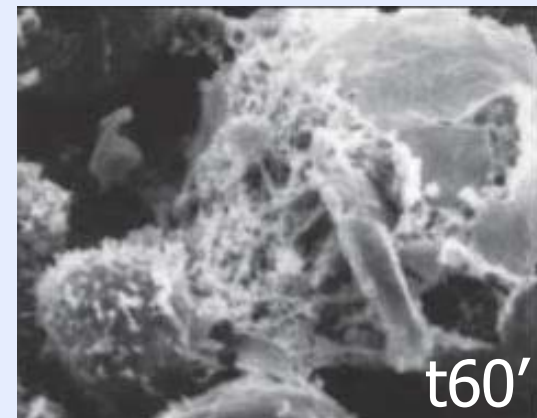
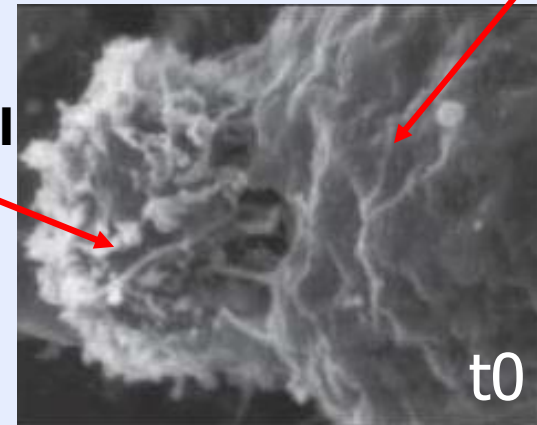


Fig 9.34 © 2001 Garland Science

Tumor Cell

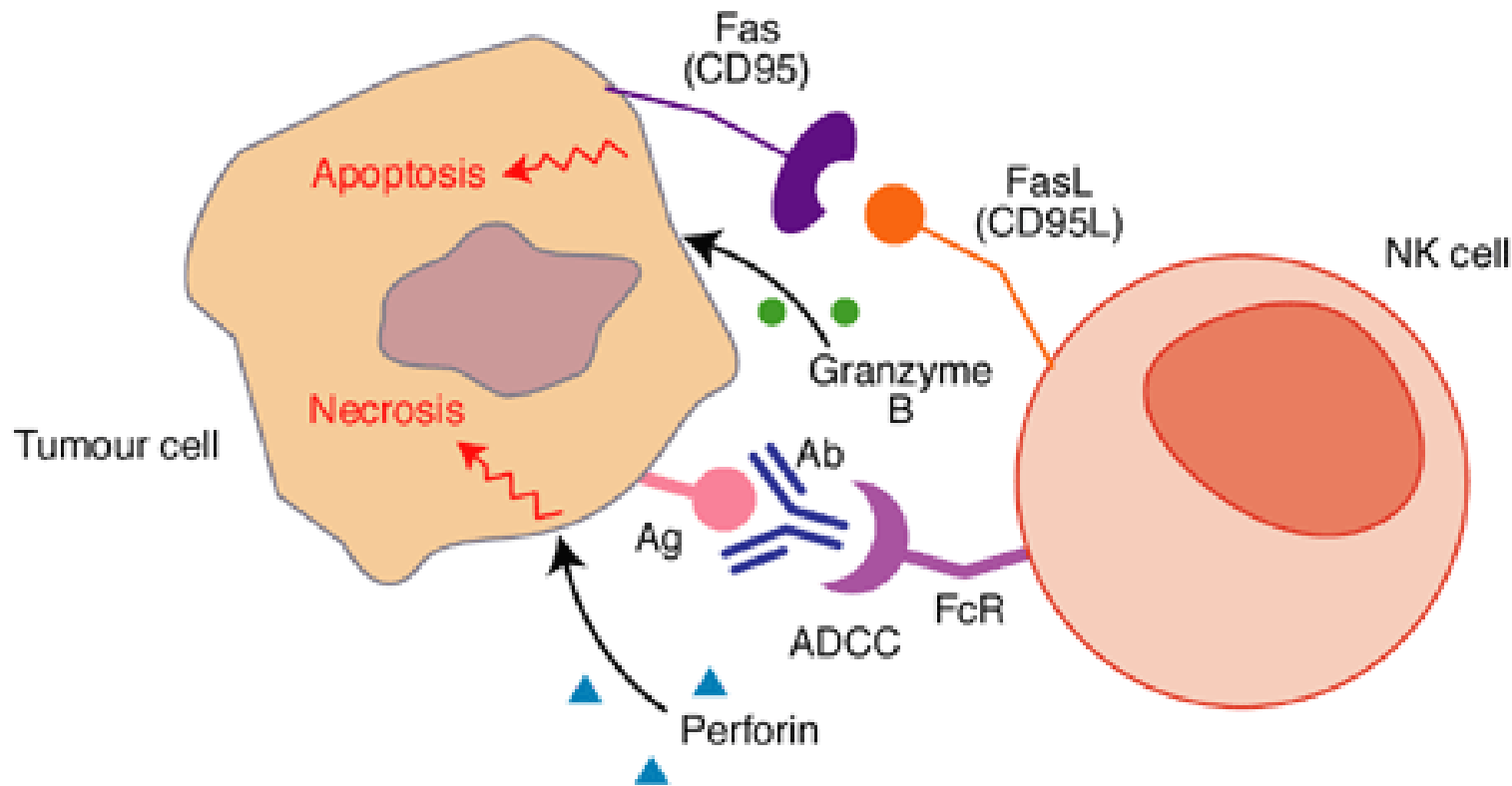
NK-Cell



Natural Killer cells : Characteristics



- Natural Killer (NK) Cells are an important first line of defense against newly arising malignant cells and cells infected with viruses, bacteria, and protozoa.
- They form a distinct group of lymphocytes with no immunological memory and are independent of the adaptive immune system.
- NK cells constitute 5 to 16 percent of the total lymphocyte population.
- Natural killer cells exhibit cytotoxic activity against a number of tumor cell lines,



The natural killer (NK)-cell response to tumour cells

Expert Reviews in Molecular Medicine © 2003 Cambridge University Press

- The natural killer (NK)-cell response to tumour cells.** NK cells kill tumour cells through mechanisms that involve: antibody (Ab)-dependent cellular cytotoxicity (ADCC), in which the Fc portion of an Ab bound to antigen (Ag) on the tumour cell surface binds to Fc receptor (FcR) on the NK cell; Fas (CD95)–Fas ligand (CD95L) interaction; and release of perforin and granzyme B molecules, which cause apoptosis/necrosis of the tumour cell



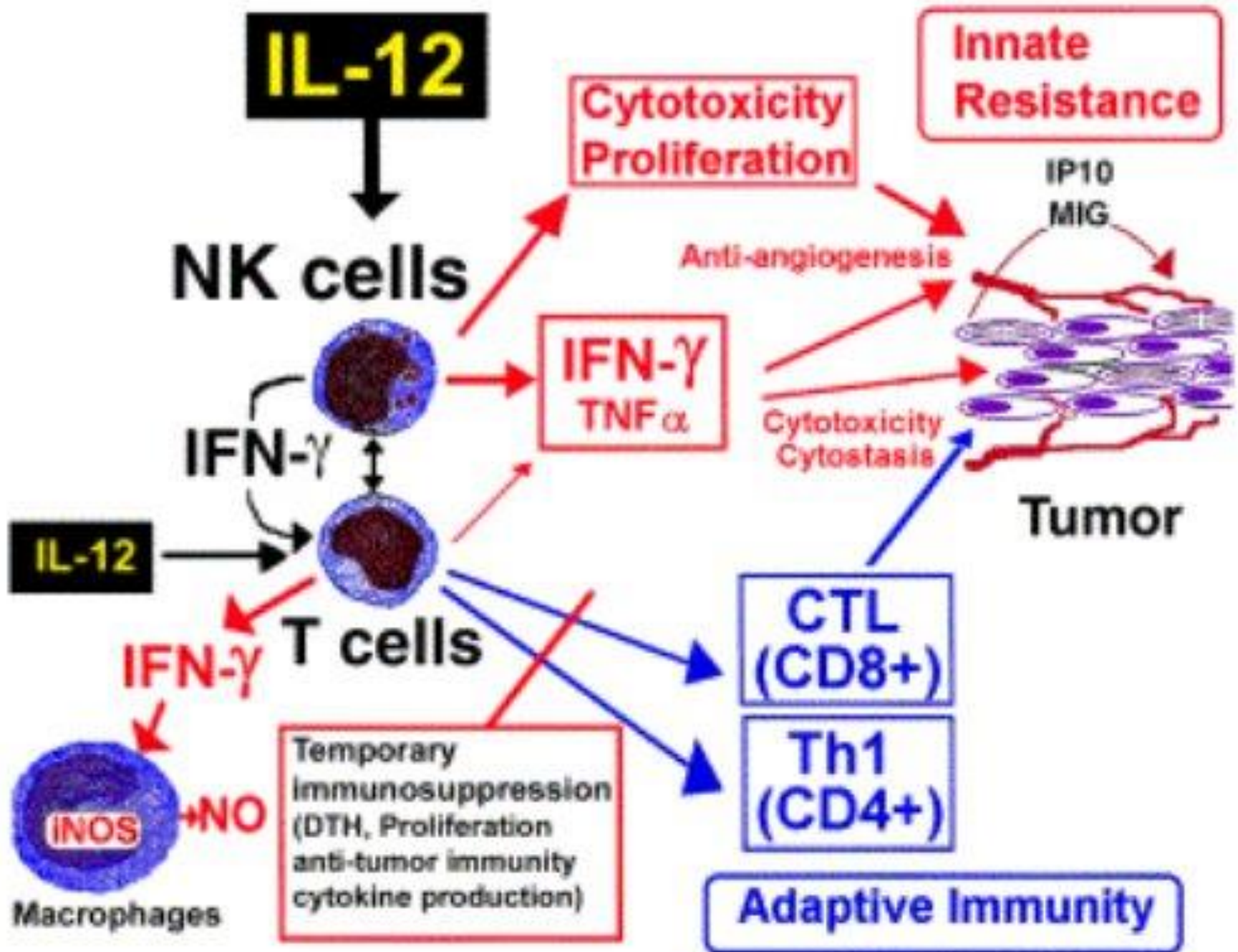
Natural Killer cells: @

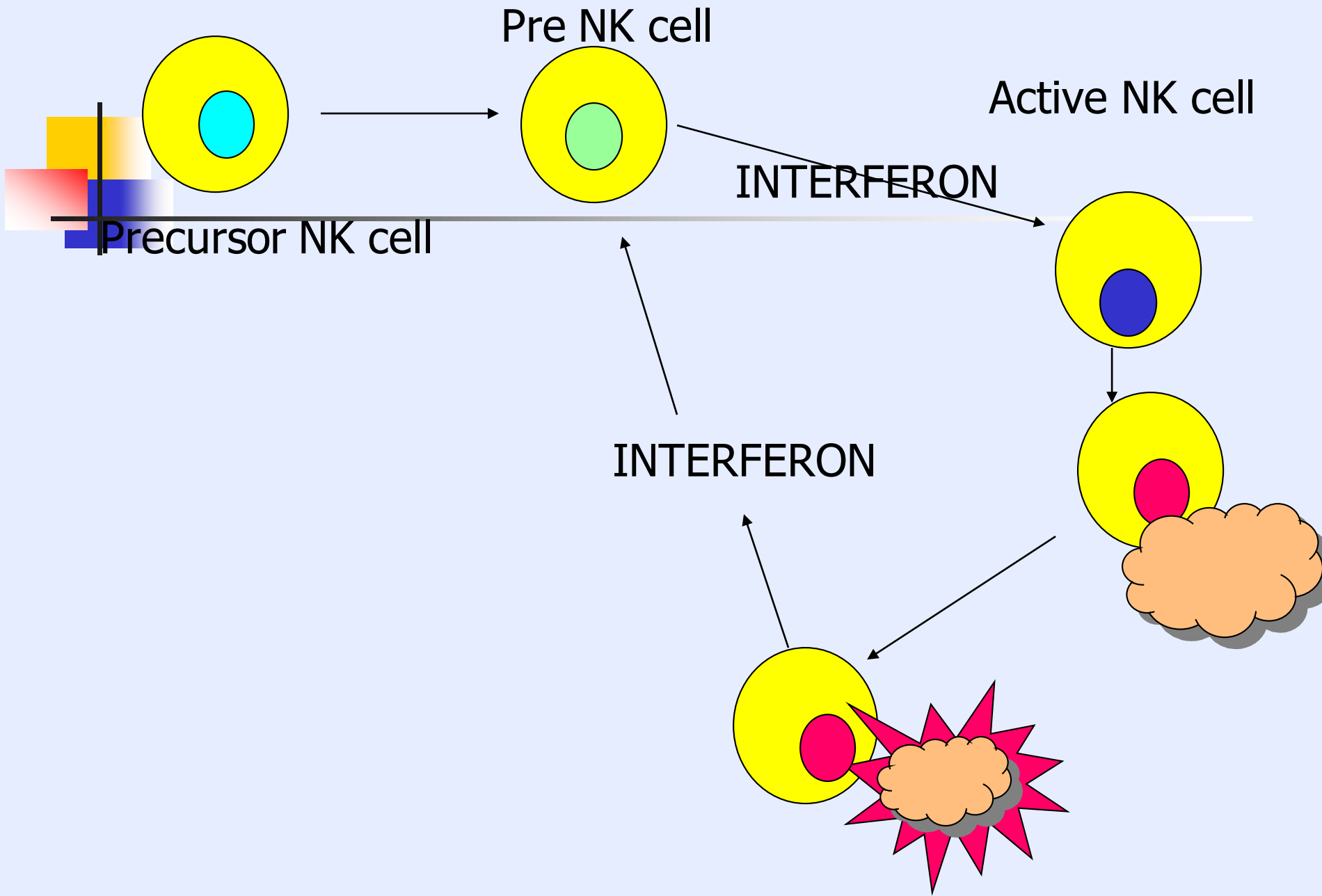
- Natural Killer (NK) cells are a type of lethal lymphocyte sometimes called large granular lymphocytes.
- Like cytotoxic T cells, they contain granules filled with potent chemicals.
- They are called "natural" killers because they, unlike cytotoxic T cells, do not need to recognize a specific antigen before moving into action.
- Natural killer cells may also contribute to immunoregulation by secreting high levels of influential lymphokines

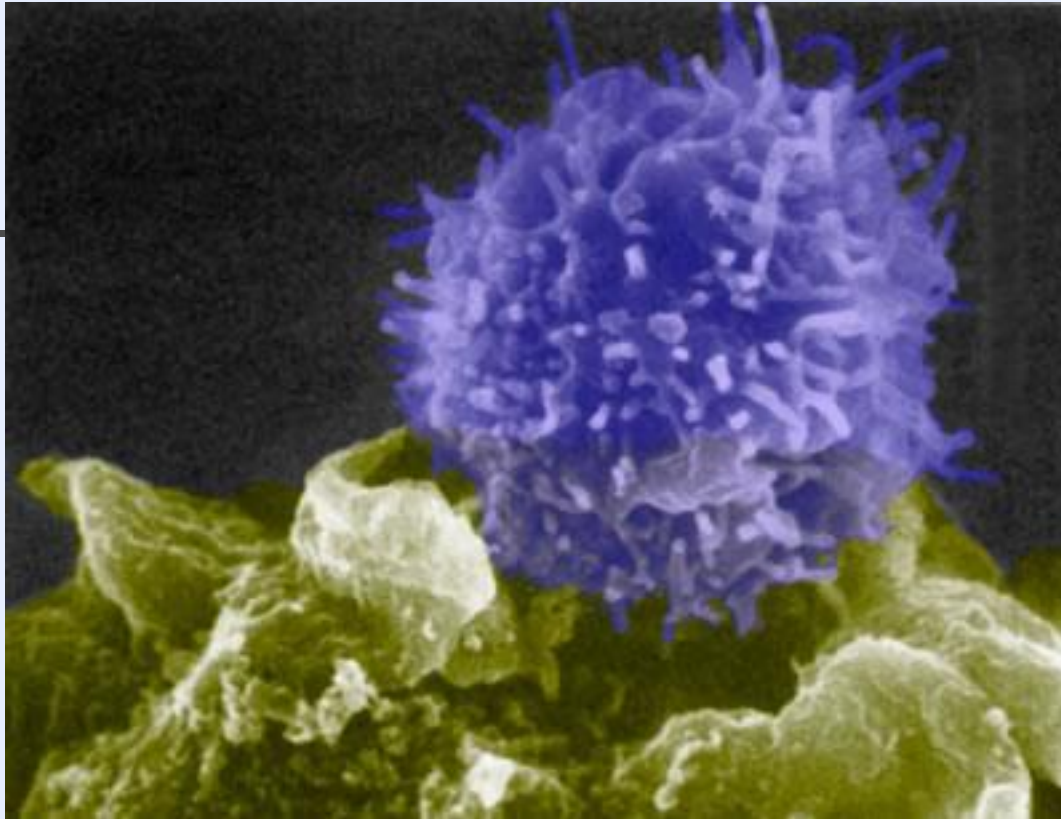


NK cell Action

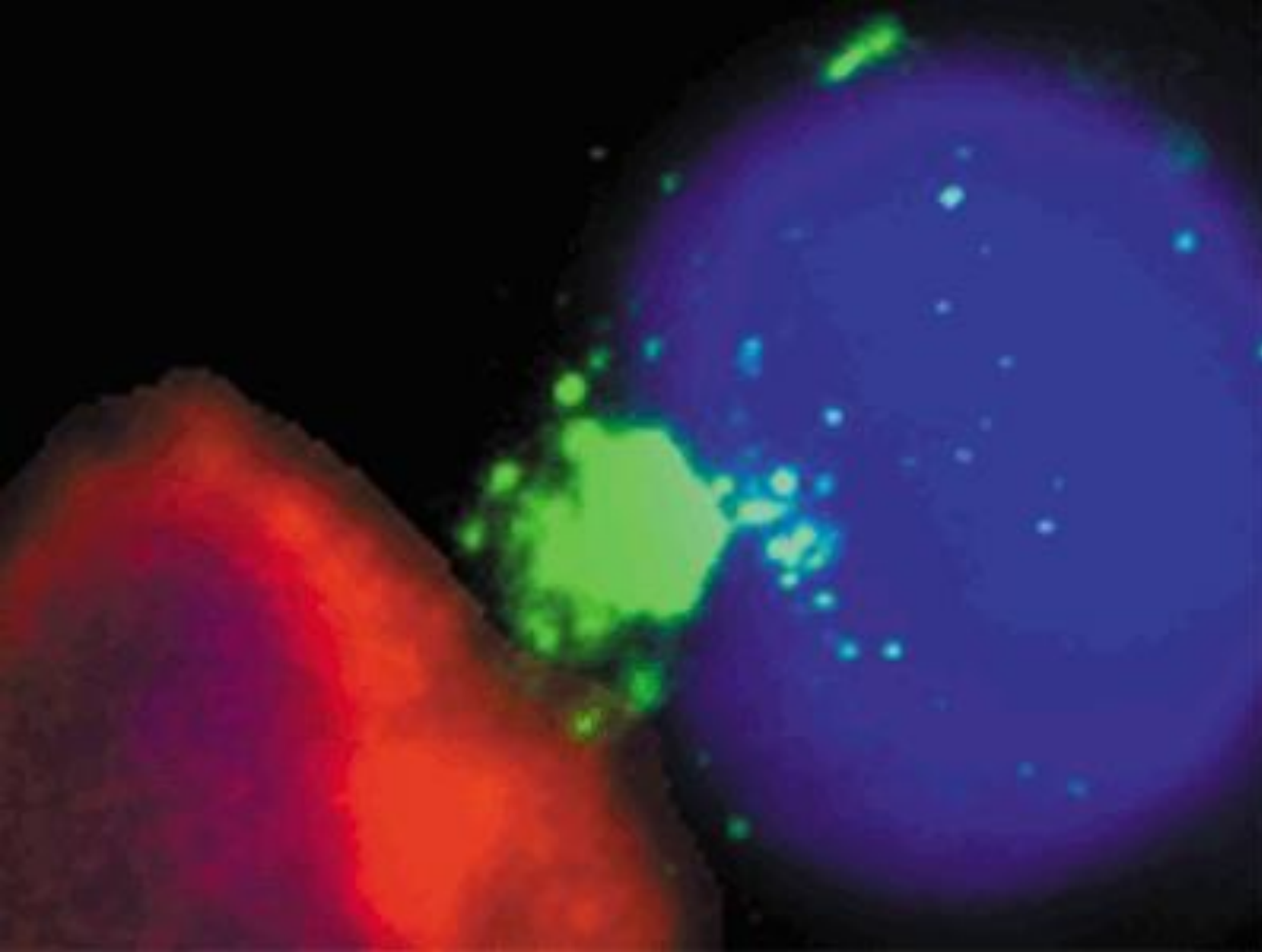
- Both cytotoxic T cells and natural killer cells kill on contact.
- An NK cell kills a target cell by releasing perforin or cytotoxic granules (and other molecules) found in the NK granules, which damages the target cell membrane forming channels in the target cell membrane resulting in changes in permeability and death in the target cell.
- The cytokine TNF alpha is released by the NK cells and may be involved in this process







This T cell (blue), one of the immune system's principle means of defense, identifies the molecular signature of a dendritic cell (green) at a junction between the two called the immunological synapse. If the immunological synapse signals the presence of a foe, the T cell will attack.

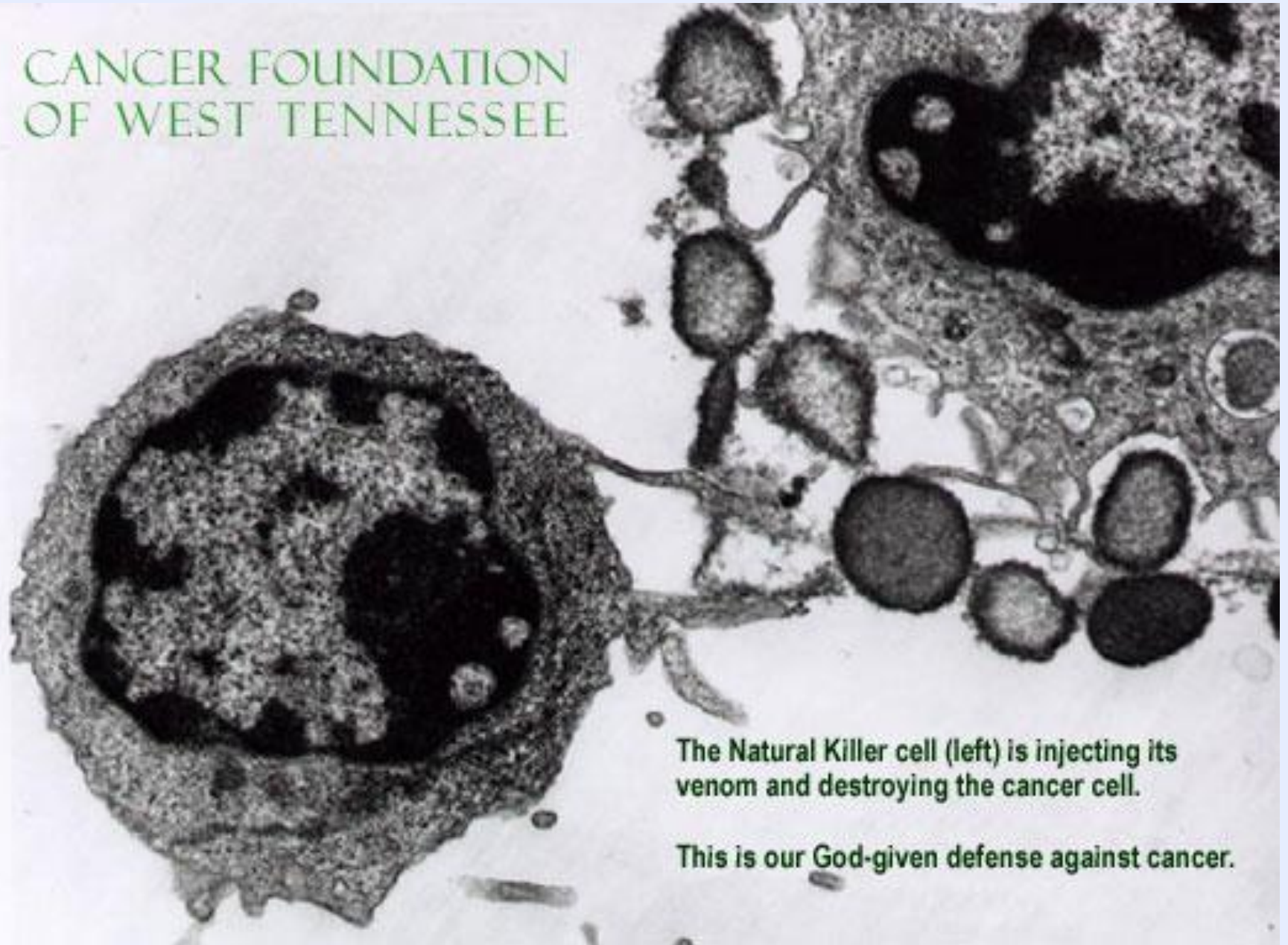


Natural killer cell (blue) contacting a Raji cell (red). [Djeu and colleagues](#) deciphered a PI3 kinase pathway that leads to ERK activation and perforin (green) mobilization in NK cells after they interact with their targets.



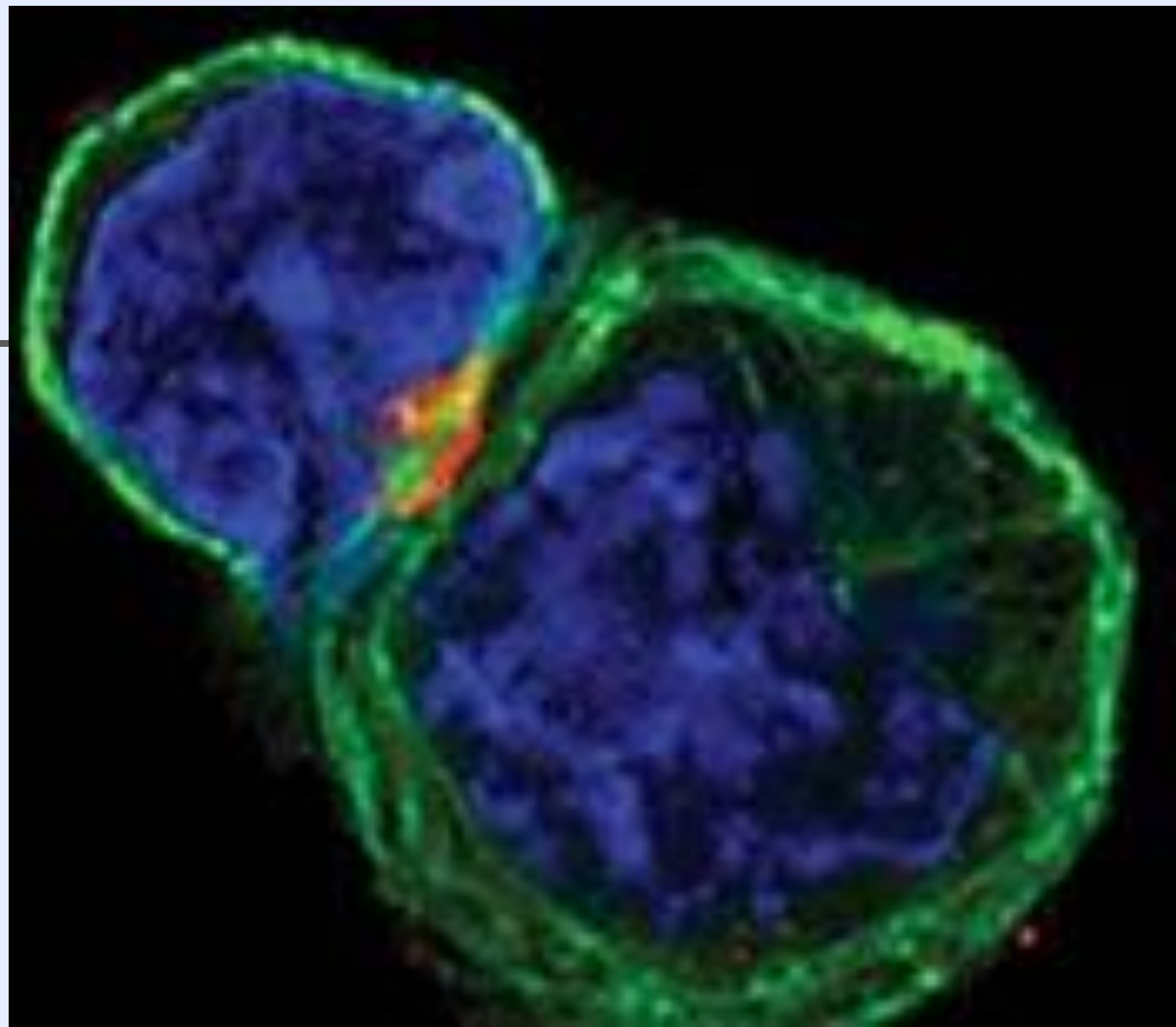
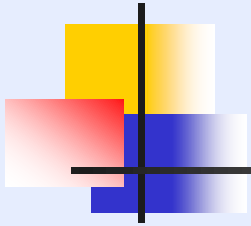
Painting by Christopher Cassidy in oil and acrylic on paper (27 x 27 cm)

CANCER FOUNDATION
OF WEST TENNESSEE



The Natural Killer cell (left) is injecting its venom and destroying the cancer cell.

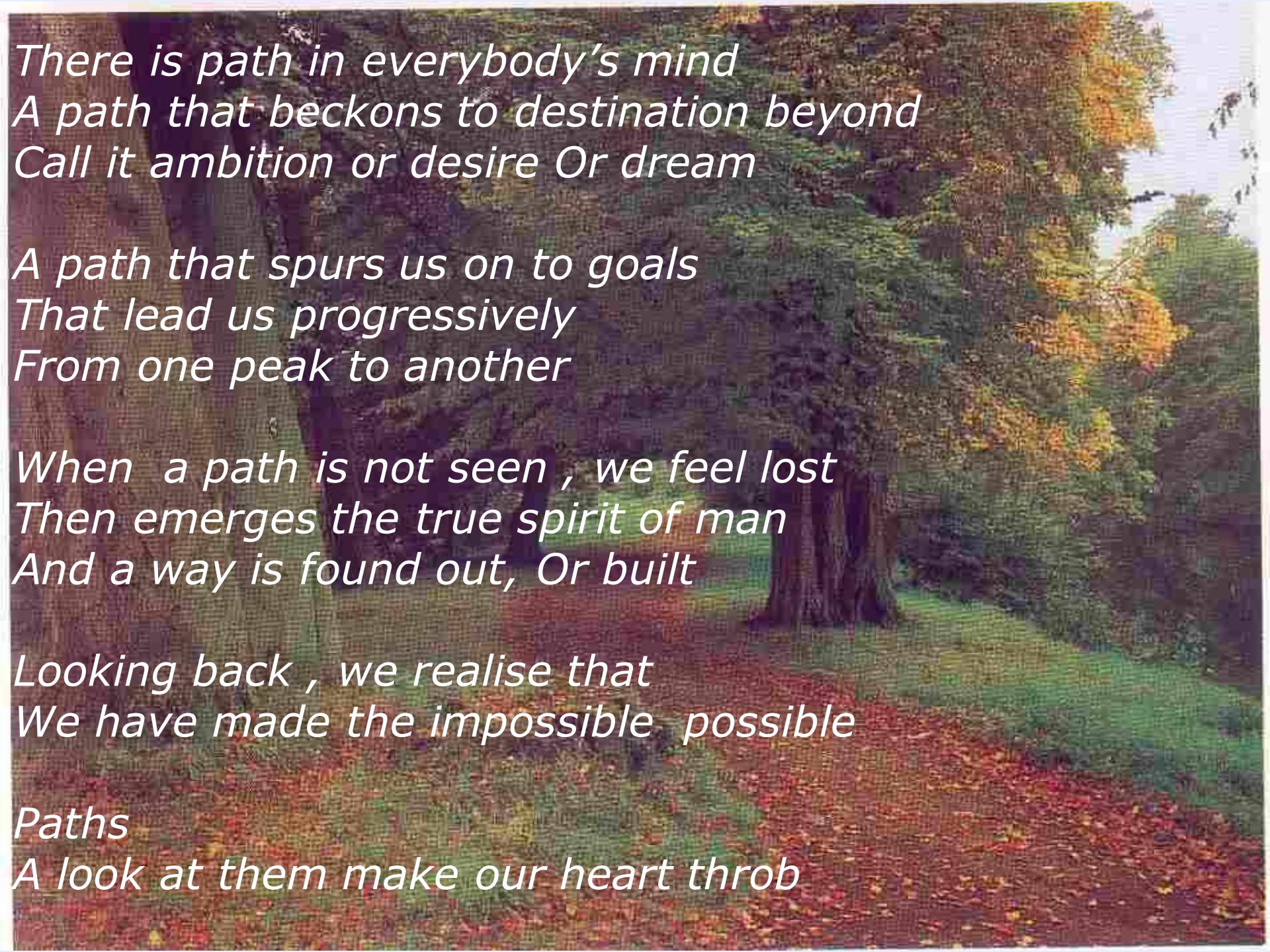
This is our God-given defense against cancer.



- An immune system T cell, left, in contact with an antigen-presenting cell, which primes the T cell to seek out and destroy an invader. A receptor called CTLA-4, in red, is now at the immunological synapse between the cells. Blocking CTLA-4 with specially made antibodies unleashes the killing power of T cells against cancer cells. (*Allison lab, UC Berkeley*)







*There is path in everybody's mind
A path that beckons to destination beyond
Call it ambition or desire Or dream*

*A path that spurs us on to goals
That lead us progressively
From one peak to another*

*When a path is not seen , we feel lost
Then emerges the true spirit of man
And a way is found out, Or built*

*Looking back , we realise that
We have made the impossible possible*

Paths

A look at them make our heart throb

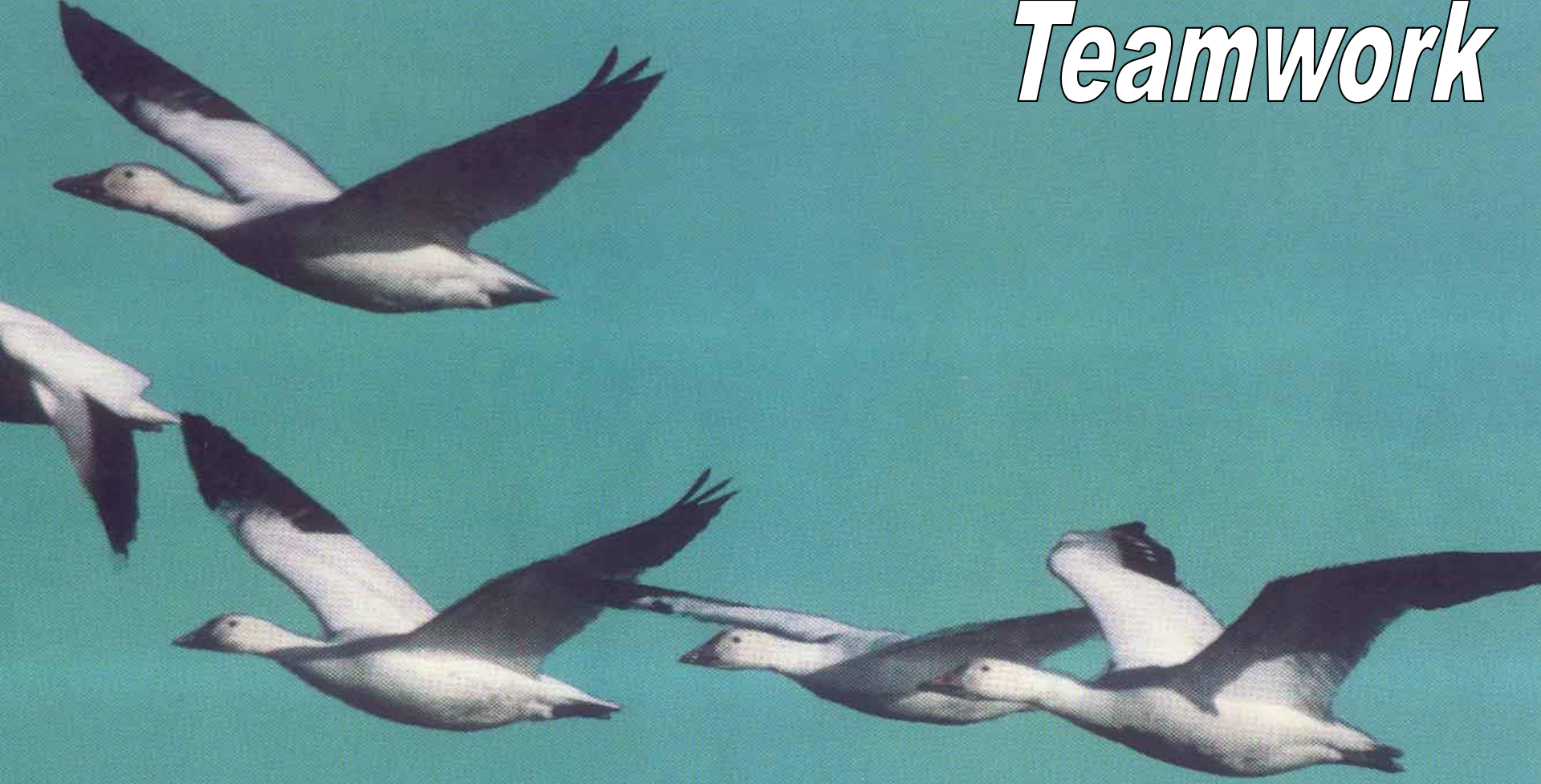


Vision

अनागतविधाता च प्रत्युत्पन्नमतिस्तथा ।
द्वैतौ सुखमेधेत यद्भविष्यो विनश्यति ॥

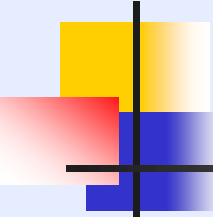
*He who plans (for the future) and takes care of the present, attains happiness;
he who is indifferent will meet with failure.*

Teamwork

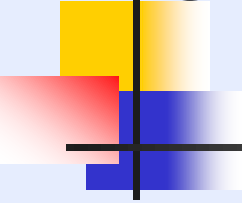


बहूनां चैव सत्त्वानां समवायो रिपुञ्जयः ।
वर्षाधाराधरो मेघस्तृणैरपि निवार्यते ॥

*The collective strength of many can together vanquish the enemy
even as a bunch of grass keeps off the pouring rain.*



**Specialised jobs are
best done by experts.**



***There is a wonderful joy of being sincere,
Every act of sincerity
in itself it's own reward***

***The feeling of purification, uplifting and
Liberation That one feels
when one rejects even if it be
Particle Of falsehood.***

***Sincerity is safety, protection, guide
Ultimately it is transforming power***

Interferon (Type- α and γ) Production by Fresh and Cryopreserved Human Mononuclear Cells

Brief Report

By

A. C. BANERJEA, N. KEDARNATH, M. M. GORE, C. DAYARAJ,
A. V. JAMKAR, and S. N. GHOSH

National Institute of Virology,
Pune, India

Accepted April 20, 1981

Summary

A comparative study of interferon (IFN) production (type- α and γ) was carried out using Ficoll-hypaque purified fresh and cryopreserved mononuclear cells from eight normal healthy individuals. Newcastle disease virus-NDV (R₂B strain) was used as an inducer for type- α and Staphylococcal enterotoxin-A-(SEA) for type- γ IFN production. There was no significant difference between the titres of type- α and γ -IFN and lymphocyte subpopulations of fresh and cryopreserved mononuclear cells studied under identical conditions.



Interferon Production by cryo-preserved Cells

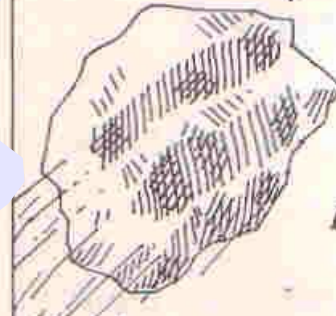
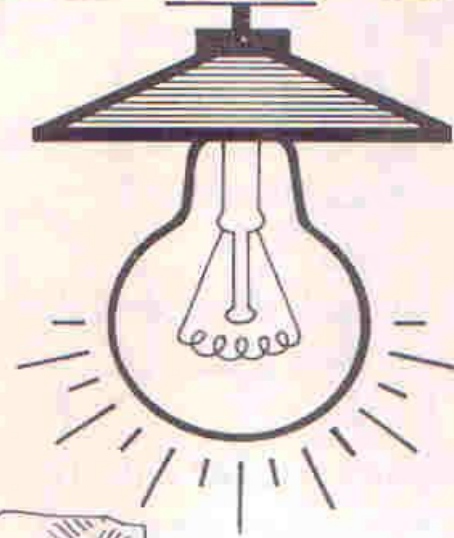
1. First paper by our group, prepared in my Presence
2. Seen Dr Ghosh in action
3. Remarkable research work by any standard
4. Very useful for day to day lab work



Clinical Trial of Interferon in Oral Cancer

- 1. It would have been First clinical trial of IFN in world.**
- 2. Not yet done in Oral cancer**
- 3. Cleared by Ethical Committee of BJMC and NIV ICMR never gave permission**
- 4. We have protocols ready to define responders and non responders.**
- 5. American companies were willing to provide at concession cost.**
- 6. I don't know what happened but Dr Ghosh had this pinching all the time life.**
- 7. We tried local IFN in superficial cancer Penis buy IFN produced in NIV**

HOW TO KILL GOOD IDEAS



Here are 10 tried and trusted ways to kill good Ideas and enthusiasm of your co-workers.

1. IT'S AGAINST COMPANY POLICY.
2. IT DOESN'T FIT THE SYSTEM.
3. IT WILL NEVER BE APPROVED.
4. THE TIMING JUST ISN'T RIGHT.
5. IT DIDN'T WORK BEFORE.
6. IT'S TOO WILD.
7. WE'RE NOT READY FOR THAT.
8. I WILL THINK ABOUT IT.
9. PUT SOMETHING IN WRITING AND GET BACK TO ME.
10. LET'S FORM A COMMITTEE.

*IDEAS ARE RUPEE A DOZEN! OR ONE DIAMOND EACH—
IT DEPENDS UPON YOU.*

When you kill somebody's good idea
you kill a little of that person too!







NK interferon System

- natural killer cell activity
- Augmentation of natural killer cell activity by interferon.
- IFN producing capacity of the peripheral mononuclear cell
 - Type Alpha IFN
 - Type Gamma IFN
- Circulating IFN



INTERFERON PRODUCING CAPACITY (IPCA) OF PERIPHERAL MONONUCLEAR CELL IN ORAL CANCER PATIENTS

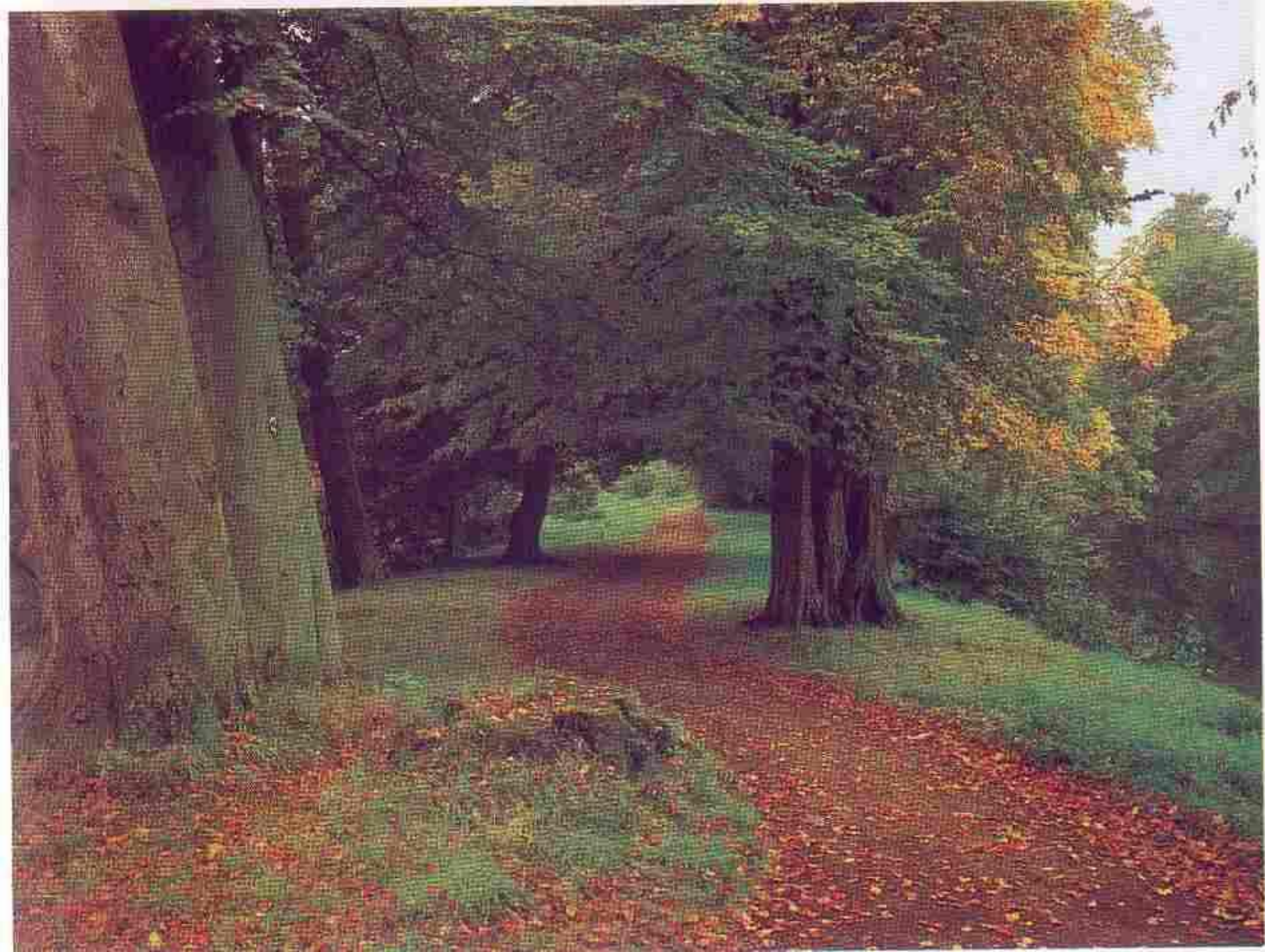
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M.S.,(Gen. Surg.) Ph.D.(Oncology)
A.C. BANERJAE, M.Sc., Ph.D.
M.M. GORE, M.Sc., Ph.D.
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* National Institute Of Virology , Pune.
* B.J.Medical College, Pune. Maharashtra,
* INDIA

SUMMARY

Interferon producing capacity (IPCA) of peripheral blood mononuclear cells is ability of these cells to produce IFN with suitable IFN inducer. In Vitro IPCA of cryopreserved mononuclear cells (MNC) from peripheral blood of 46 oral cancer patients was studied and was compared to that of healthy, age matched donors. New castle disease virus (NDV) and staphylococcal enterotoxin A (SEA) were used as inducers for evaluating Type alpha IPCA (AIPCA) and Type gamma IPCA (GIPCA) respectively. Age of healthy donors did not influence the AIPCA or GIPCA.

Oral cancer patients demonstrated significant low AIPCA ($P < 0.05$) (Range Healthy





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Volume

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INTERFERON PRODUCING CAPACITY (IPCA) OF PERIPHERAL MONONUCLEAR CELL IN ORAL CANCER PATIENTS

Correlation with postoperative
surgical and recurrence free
interval.

AV Jamkar,
AC Banerjee,
MM Bhore,
PS Sathe,
SN Ghosh

ABSTRACT

Interferon producing capacity (IPCA) of peripheral mononuclear cells is ability of those cells to produce interferon (IFN) with suitable IFN inducer. In our earlier communication type alpha IPCA (AIPCA), and type gamma IPCA (GIPCA) in 46 patients of oral cancer was found to be low compared to healthy donors. IPCA of less than 95% confidence limit was labelled as non-responders. These patients were managed surgically and followed up further.

After six years a follow up of only 16 patients was available. Postoperative survival period was analysed with IPCA levels. Those patients who died within one year had high AIPCA and significantly high GIPCA compared with those patients who were surviving more than one year upto six years. No correlation was found between recurrence free interval and IPCA. However, patients having early recurrence and who were high responders to GIPCA died within one year and non-responders survived for longer time. The outcome of these results raise a controversy "whether good immune response is really beneficial for patient".

KEY WORDS : *Interferon, type alpha-interferon, type gamma-interferon, peripheral mononuclear cells, interferon producing capacity, postoperative survival period, recurrence free interval.*

Dr.Ghosh is no more with us. This paper is dedicated to his memory.



Circulating Interferon in Oral Cancer Patients

A. V. Jamkar* P. S. Sathe** S. N. Ghosh***

Circulating Interferon (IFN) in one hundred and twenty two oral cancer patients and seventy healthy blood donors was estimated either by plaque reduction method or cytopathic effect inhibition method. Twenty percent of healthy blood donors and 24.5% oral cancer patients demonstrated more than 10 IU/ml of Interferon in circulation.

The IFN was predominantly type alpha variety with partial activity attributed to type beta variety. None of the patients of stage I oral cancer had circulating IFN as well as anti-IFN antibody. Percentage of IFN positive patients was maximum in stage II. Stage and site of oral cancer however had no effect on levels of circulating IFN.

Key Words: Oral Cancer, Interferon.

Introduction

Circulating Interferon (IFN) in cancer patients might reflect the interferon producing capacity of mononuclear cells. Interferon in addition to their antiviral action are supposed to be potent immune response modifier¹; therefore levels of circulating interferon may serve as an index of tumour immunity¹.

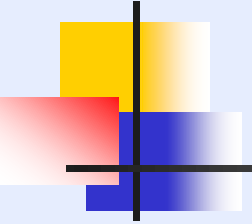
Trincheri et al²⁰ showed that human lymphocytes cultured with tumour cells *in vitro* for 18 to 24 hours produce a soluble factor, IFN, which augments natural killer

Circulating IFN was not detected in leukemias⁴. Elevated levels of circulating IFN have been reported in solid tumours and lymphoreticular malignancies⁷, carcinoma cervix¹⁵, carcinoma of breast and other tumours⁸, and head and neck cancer¹⁸.

Present study was undertaken as a part of assessment of NK cell - IFN system of oral cancer. We have found high NK cell activity⁹ and depressed IFN producing capacity of peripheral mononuclear cells¹⁰ and in present communication, circulating





- 
-
- NK-IFN SYSTEM IN ORAL CANCER
 - BASAL NK ACTIVITY INCREASED
 - AUGMENTATION AFTER IN VITRO IFN TREATMENT
 - TYPE ALPHA AND TYPE GAMMA IFN PRODUCING CAPACITY DECREASED
 - ADVANCED TUMOURS DECREASED
 - CIRCULATING IFN IN 24.6% PATIENTS

Natural Killer Cell Activity and *In Vitro* Modulation of NK Activity by Leukocyte Interferon in Oral Cancer Patients

A. V. Jamkar* M. M. Gore** and S. N. Ghosh**

*B. J. Medical College and Sassoon General Hospitals, Pune, **National Institute of Virology, Pune.

SUMMARY

Natural killer cell (NK) activity and its augmentation after *in vitro* treatment with human leukocyte interferon (IFN) was studied in 20 oral cancer patients and 12 normal healthy controls. Median basal NK activity was significantly higher in cancer patients than in the controls. After *in vitro* treatment with IFN all the control subjects showed augmentation of NK activity. Among the 20 cancer patients studied 2 did not show any augmentation and 4 showed a decrease after treatment with IFN. In view of conflicting reports regarding high or low NK activity in various stages of different cancers, an attempt was made to correlate NK activity with two different clinical parameters viz. tumour size expressed as T₁-T₄ and metastases in regional lymph nodes expressed as N₀-N₃ in the TNM classification. Median value plots of NK activity indicated an increasing trend with increasing tumour size whereas negative correlation was noticed with increasing metastases in lymph nodes.

THE INDIAN JOURNAL OF CANCER



A JOURNAL
OF
THE INDIAN CANCER SOCIETY
AND
THE INDIAN ASSOCIATION OF CANCER SURGEONS

Natural Killer Cell Activity in Oral Cancer Patients I. Correlation with Tumor Size and Metastasis in Regional Lymph Nodes

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N. Kedarnath, M.Sc.,
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SUMMARY

Natural killer cell (NK) activity was studied in 20 oral cancer patients and 12 normals. Oral cancer patients showed a higher NK activity than the age-matched controls. In view of conflicting reports regarding high or low NK activity in various stages of different cancers, an attempt was made to correlate NK activity with two different clinical parameters viz. tumour size expressed as $T_0 - T_4$ and metastases in regional lymph nodes expressed as $N_0 - N_4$ in the TNM classification. Median value plots of NK activity indicated an increasing trend with increasing tumour size whereas negative correlation was noticed with increasing metastases in lymph nodes. Significance of these findings have been discussed.

INTERFERONS IN BIOMEDICAL RESEARCH



EDITORS

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LUCKNOW (India)

1987

Natural Killer Cell Activity and *In Vitro* Modulation of NK Activity by Leukocyte Interferon in Oral Cancer Patients

A. V. Jamkar* M. M. Gore** and S. N. Ghosh**

*B. J. Medical College and Sassoon General Hospitals, Pune, **National Institute of Virology, Pune.

SUMMARY

Natural killer cell (NK) activity and its augmentation after *in vitro* treatment with human leukocyte interferon (IFN) was studied in 20 oral cancer patients and 12 normal healthy controls. Median basal NK activity was significantly higher in cancer patients than in the controls. After *in vitro* treatment with IFN all the control subjects showed augmentation of NK activity. Among the 20 cancer patients studied 2 did not show any augmentation and 4 showed a decrease after treatment with IFN. In view of conflicting reports regarding high or low NK activity in various stages of different cancers, an attempt was made to correlate NK activity with two different clinical parameters viz. tumour size expressed as T_1 - T_4 and metastases in regional lymph nodes expressed as N_0 - N_3 in the TNM classification. Median value plots of NK activity indicated an increasing trend with increasing tumour size whereas negative correlation was noticed with increasing metastases in lymph nodes.

INTRODUCTION

A sub-population of lymphocytes called natural killer cells (NK) have the ability to spontaneously lyse a variety of tumour cells, virus-infected cells and normal cells^{6,10}. It is well known that interferon (IFN) augments NK activity by activating pre-NK cells. These activated cells, after coming into contact with tumour cells, secrete IFN leading to further recruitment of pre-NK cells^{15,16}. Exogenous IFN therapy in cancer cases has yielded variable results^{8,12}. It has been suggested that before IFN therapy, cancer patients may be screened for their basal and IFN mediated augmentation of NK activity¹¹. The present communication reports the IFN mediated augmentation of NK activity in oral cancer patients. These results suggest that similar approach could be used as a possible guideline for selection of cases for IFN therapy.

TABLE III

**NK ACTIVITY IN THE PERIPHERAL BLOOD OF
ORAL CANCER PATIENTS IN DIFFERENT STAGES
OF THE DISEASE**

	No. of cases	NK activity ^a	
		Range	Mean log ₁₀ ± S.D.
Stage I	2	40 - 71	1.72 ± 0.17
Stage II	1	-	1.73
Stage III	8	9 - 190	1.75 ± 0.41
Stage IV	2	159 - 317	2.34 ± 0.21
Moderate Recurrence	4	10 - 501	1.73 ± 0.80
Extensive Recurrence	3	6 - 631	1.84 ± 1.03
Total	20	6 - 631	1.82 ± 0.56

^a Lytic units/10⁷ lymphocytes.

Natural Killer Cell Activity in Oral Cancer Patients : II. Correlation of In-Vitro Modulation by Leukocyte Interferon with Circulating Interferon and Interferon Induction by K 562 Cells

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N. Kedarnath, M.Sc.,

A. C. Banerjea, M.Sc.,

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* B. J. Medical College, Pune-400 001, India.

SUMMARY

Natural killer cell (NK) activity and its augmentation after in vitro treatment with human leukocyte interferon (IFN) was studied in 18 oral cancer patients and 12 normal healthy controls. Median basal NK activity was significantly higher in cancer patients than in the controls. After in vitro treatment with IFN all controls showed augmentation of NK activity. Among the 18 cancer patients studied two did not show any augmentation and four showed decreased activity below their respective basal NK activity, after treatment with IFN. Three out of these six patients showed detectable levels of circulating IFN. When lymphocytes of either group were co-cultivated with K 562 cells, a decreased IFN induction was observed in lymphocytes of cancer patients, especially at the lowest ratio of lymphocytes to K 562 cells. The significance of these observations in the ability of patients to respond to IFN therapy is discussed.



Responder and Nonresponder hypothesis

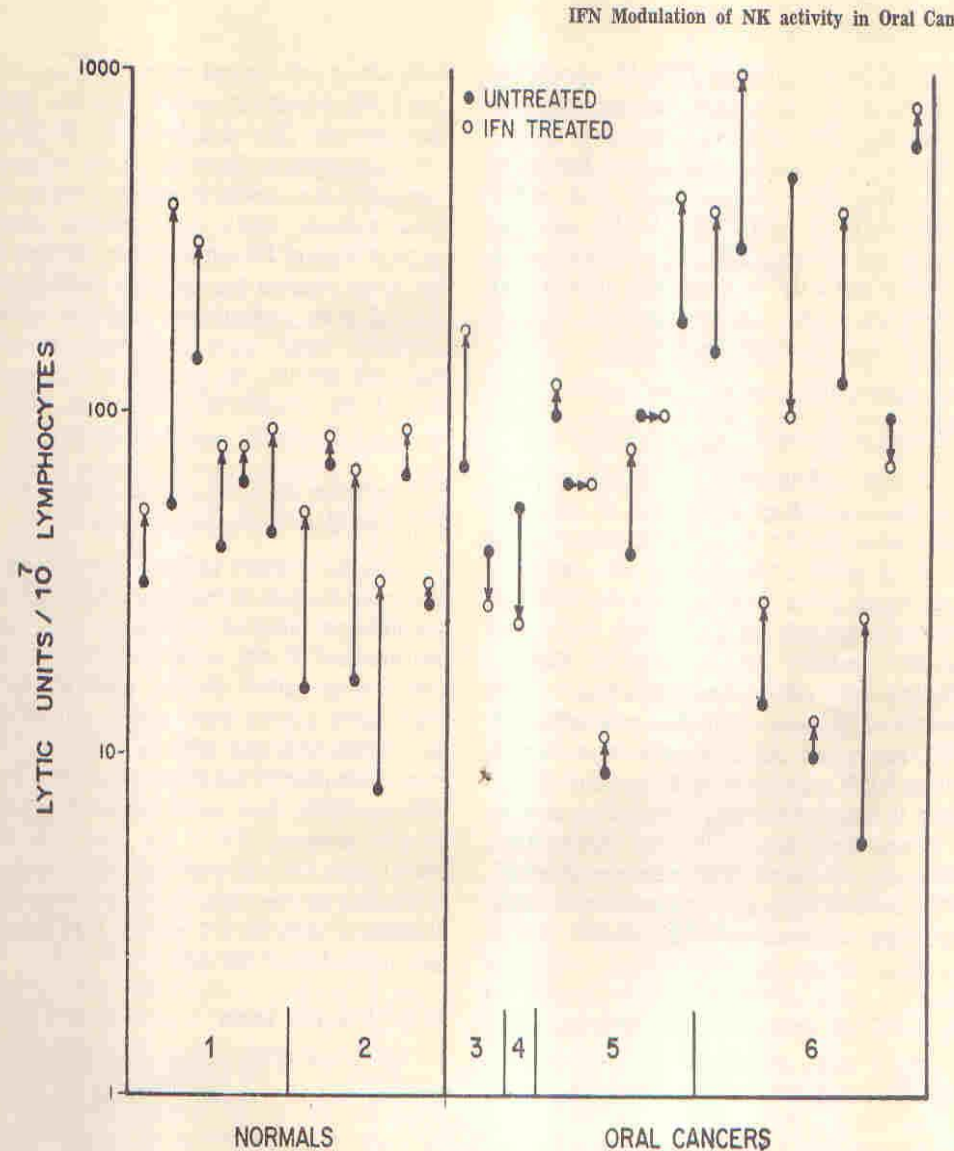


Fig. 1: NK activity and its modulation after *in vitro* IFN treatment. Controls (1) Below 35 yrs., (2) Above 45 yrs. Cancer patients, (3) Stage I, (4) Stage II, (5) Stage III, (6) Stage IV and Recurrence.

TABLE IV

NK ACTIVITY IN THE PERIPHERAL BLOOD OF ORAL CANCER PATIENTS: RELATIONSHIP WITH SIZE OF TUMOUR AND NO. OF METASTATIC LYMPH NODES

Tumour size	No. of cases studied	NK cell activity*	
		Geometric mean	Range
T ₁	2	53.07	40 - 71
T ₂	8	54.76	9 - 501
T _n	7	59.07	6 - 631
T ₄	2	171.13	100 - 316.2
Metastatic lymph nodes			
N ₀	5	93.33	10 - 631
N _{1n} †	4	49.50	11 - 54
N _{1b}	4	156.50	100 - 316.2
N ₂	5	45.69	9 - 125.9
N ₃	2	23.70	6 - 100

* Lytic units/10⁷ lymphocytes.

† N_{1n} represents lymph nodes which are inflammatory and clinically non-malignant.

Nk Cell Activity TNM effect



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Anaest

Official journal of the Indian

Ind. J. Anaesth., 35(5), 350, 1987

EFFECT OF OPERATION AND ANAESTHESIA ON THE NATURAL KILLER CELL ACTIVITY IN ORAL CANCER

M.B. Bhaskarwar*, A.V. Jamkar**, M.M. Gore***, S.N. Ghosh****

SUMMARY

Natural killer (NK) cells present in human circulation have the capacity to kill any foreign cell including tumour cells without prior sensitisation. NK-cell activity was measured in six oral cancer patients before and after surgery. NK-cell activity was found to be significantly depressed after operation. The implications of results are discussed.

Key Words

Natural killer cells: Interferon, Oral cancer.

Effect of anaesthesia & surgery: On NK-cell activity.

A subpopulation of lymphocytes called 'Natural Killer Cells' (NK-cells) has the ability to spontaneously lyse a variety of tumour cells, virus infected cells and normal cells. It is postulated that they have a role in 'immune surveillance' and destruction of malignant cells *in vivo*. It is well known that 'Interferon' (IFN) augments NK-cell activity by activating dormant NK-cells. These activated NK-cells after coming in contact with tumour cells, secrete IFN leading to further recruitment of pre-

Human NK-cell activity is attributed almost exclusively to cells with large granular morphology with characteristic azurophilic cytoplasmic granules. They differ from cytotoxic 'T' cells in that NK-cells do not express antigens detectable by OKT-3 and other related monoclo-

*M.D., Registrar in Anaesthesia; **M.S.(Gen.Surgery), Ph.D.(Surgery), Head of General Surgical Unit and Reader in Surgery; B.J. Medical College, Pune-411001; ***M.Sc., Ph.D., Senior Research Officer; ****Ph.D., Director Grade Scientist, Division of Immunology, National Institute of Virology, Pune, INDIA.

Reprint requests to: Dr A.V. Jamkar.

The Effect of Cyclophosphamide – Methotrexate Chemotherapy on Natural Killer Cell – Interferon System (NK–IFN System) in Oral Cancer

A. V. JAMKAR¹, M. M. GORE², A. C. BANERJAE³, P. S. SATHE⁴, S. N. GHOSH⁵

ABSTRACT

Natural Killer (NK) cell interferon (IFN) is supposed to be first line attack against developing tumour.

The effect of cyclophosphamide – Methotrexate chemotherapy on this system was evaluated in oral cancer. Sixty patients were divided into two groups (19 chemotherapy group, 41 control group). Chemotherapy group received cyclophosphamide and or Methotrexate for a period of 14 days. Natural Killer Cell activity and Interferon producing capacity was evaluated in both the groups. These parameters of NK–IFN system were found unaffected by chemotherapy. Implications of these results are discussed.

Key words : Natural Killer Cell, IPCA Interferon Producing Capacity, Cyclophosphamide, Methotrexate.

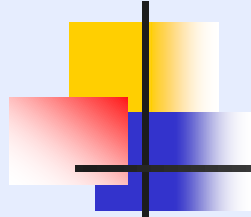
INTRODUCTION

A subpopulation of Lymphocytes called 'Natural Killer Cells – NK Cells' have the ability to spontaneously lyse a variety of tumour cells, virus infected cells and normal cells. It is postulated that they have a role in immune surveillance and destruction of malignant cells *in vivo*.

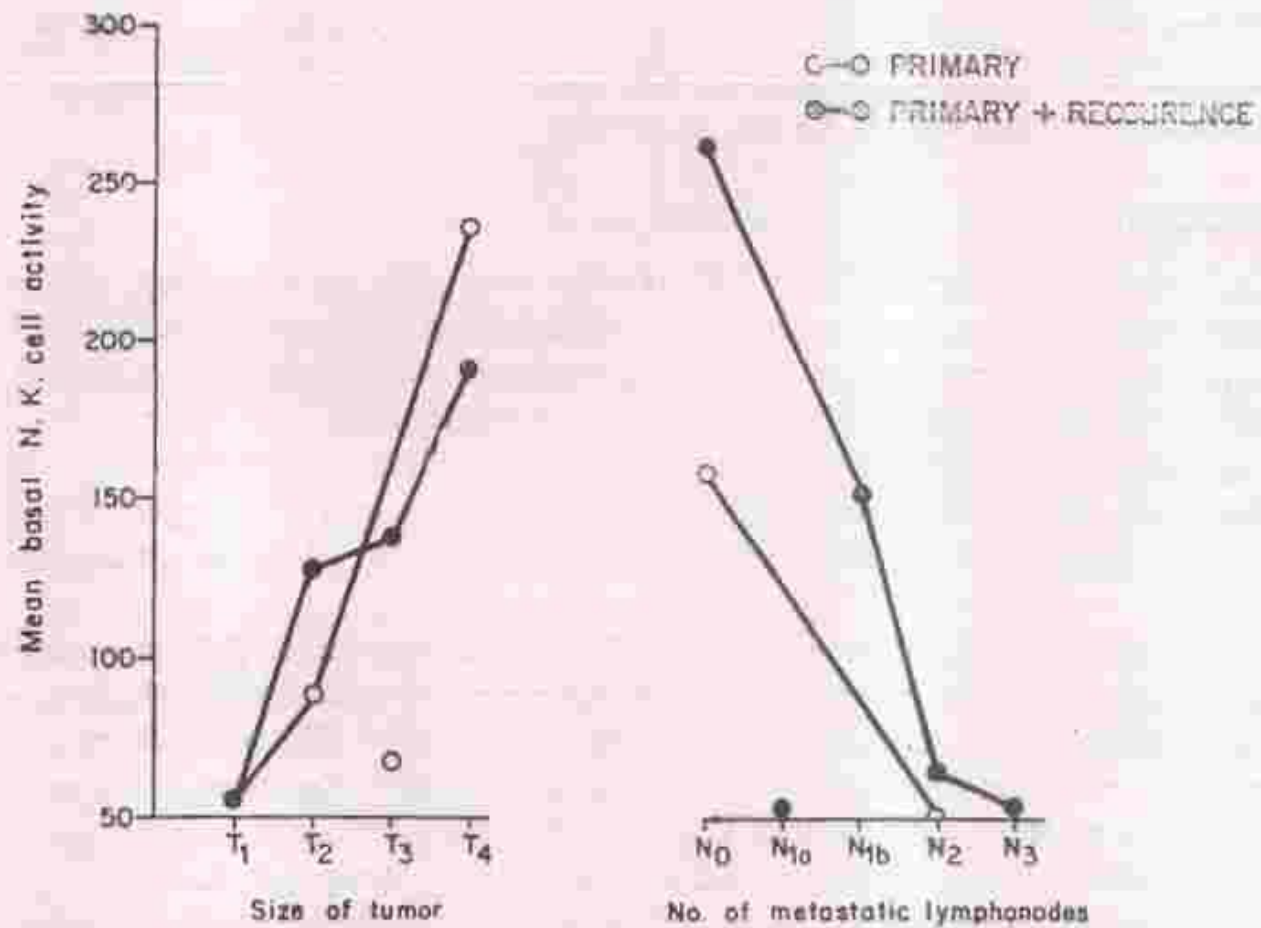


CONCLUSIONS Of NK cell Activity

1. Young Normals Have More Nk Cell Activity Than Old Normals. Ifn Augmentation Was Almost Equal.
2. Cancer Patients Have High Basal Nk Cell Activity.
3. Ifn Augmentation Occurred In Almost All Normals But Not In All Cancers (12/18).
4. Suggested Interferon Augmentation Index More Than 150 Could Be Ifn Responders.
5. Suggestive Indication That Basal Nk Cell Activity Increases Proportionately With Size Of Tumour And Inversely With Number Of Metastatic Lymph Nodes.



BASAL NATURAL KILLER CELL ACTIVITY





ONCOLOGY OVERVIEW

Selected Abstracts on

Mechanisms of Metastasis

September 1984

U.S. DEPARTMENT OF
HEALTH AND
HUMAN SERVICES

Public Health Service

National Institutes
of Health

abstract)

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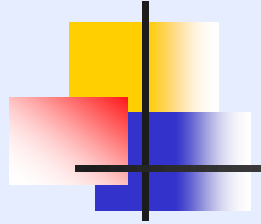
Immune defense mechanism and metastasis in humans

261. NATURAL KILLER CELL ACTIVITY IN ORAL CANCER PATIENTS. I. CORRELATION WITH TUMOR SIZE AND METASTASIS IN REGIONAL LYMPH NODES.

Jankar AV, Gore MM, Kedarnath N, Banerjee AC, Mehta MJ,
Ghosh SN

Natl. Inst. Virology, 20-A, Dr. Ambedkar Rd., Pune 411 001, India
Indian J Cancer; 20(1A):49-53 1983

Natural killer cell (NK) activity was studied in 20 patients (16 men, 4 women; 35-60 yr old) with oral cancer and 12 healthy, age-matched subjects. Primary carcinomas were observed in 13/20 patients, and the other seven patients had recurrent cancer. Anti-metabolite therapy consisting of cyclophosphamide (CCP) was administered to six and CCP and methotrexate to one patient. No statistical difference in NK activity was observed in patients on the basis of age (less than 30 yr old vs greater than 45 yr old). NK activity in oral cancer patients was higher than in age-matched controls. The geometric mean of the lytic units was higher in the patients with advanced cancer than in those with early cancer, but no proportionate correlation was observed with clinical stages of the disease. Primary and recurrent cancer showed similar trends of NK activity when TNM (tumor, node, metastasis) staging was applied. Thus, NK activity was higher in patients with large tumors than in those with small tumors. A decreasing trend was seen when only regional lymph node metastasis was considered. Thus, NK activity appeared to show opposite trends with respect to tumor size and nodal metastasis. (14 Refs)



Oral Cancer
Is
Definitely
Different



Fig. 4 *Gingivo-buccal cancer extending to retromolar region.*

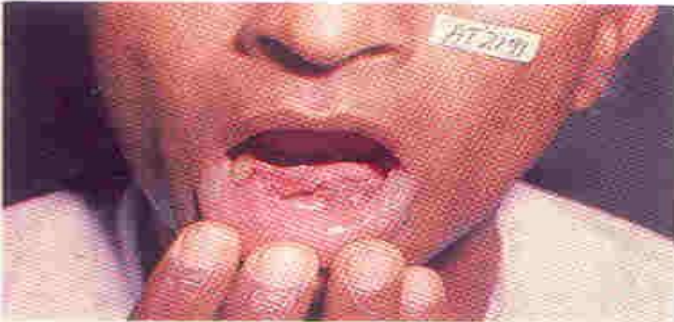
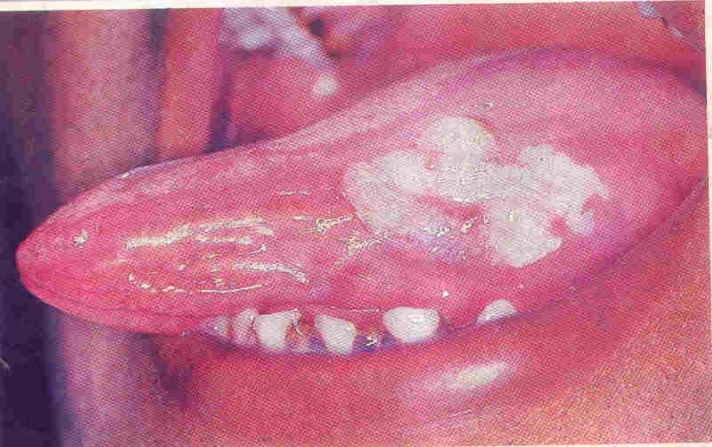


Fig. 3 *Anteriorly placed gingivo-buccal cancer ("Khaini" cancer).*



CANCER OF THE ORAL CAVITY:

SITE DISTRIBUTION

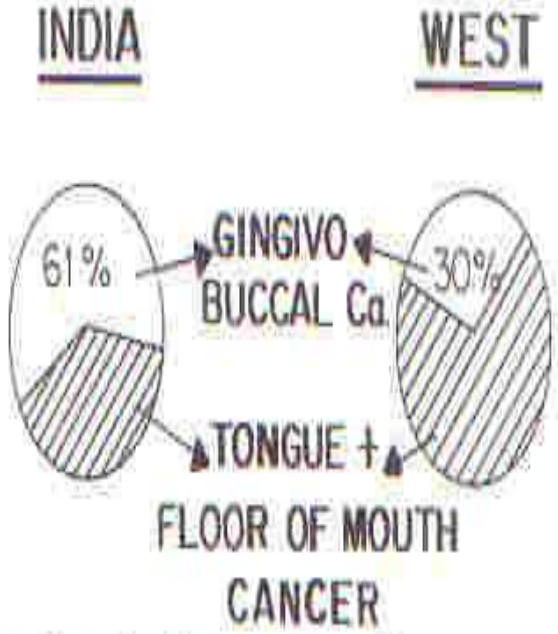


Fig. 2 *Oral Cavity Cancer: Site distribution in India and in the West.*

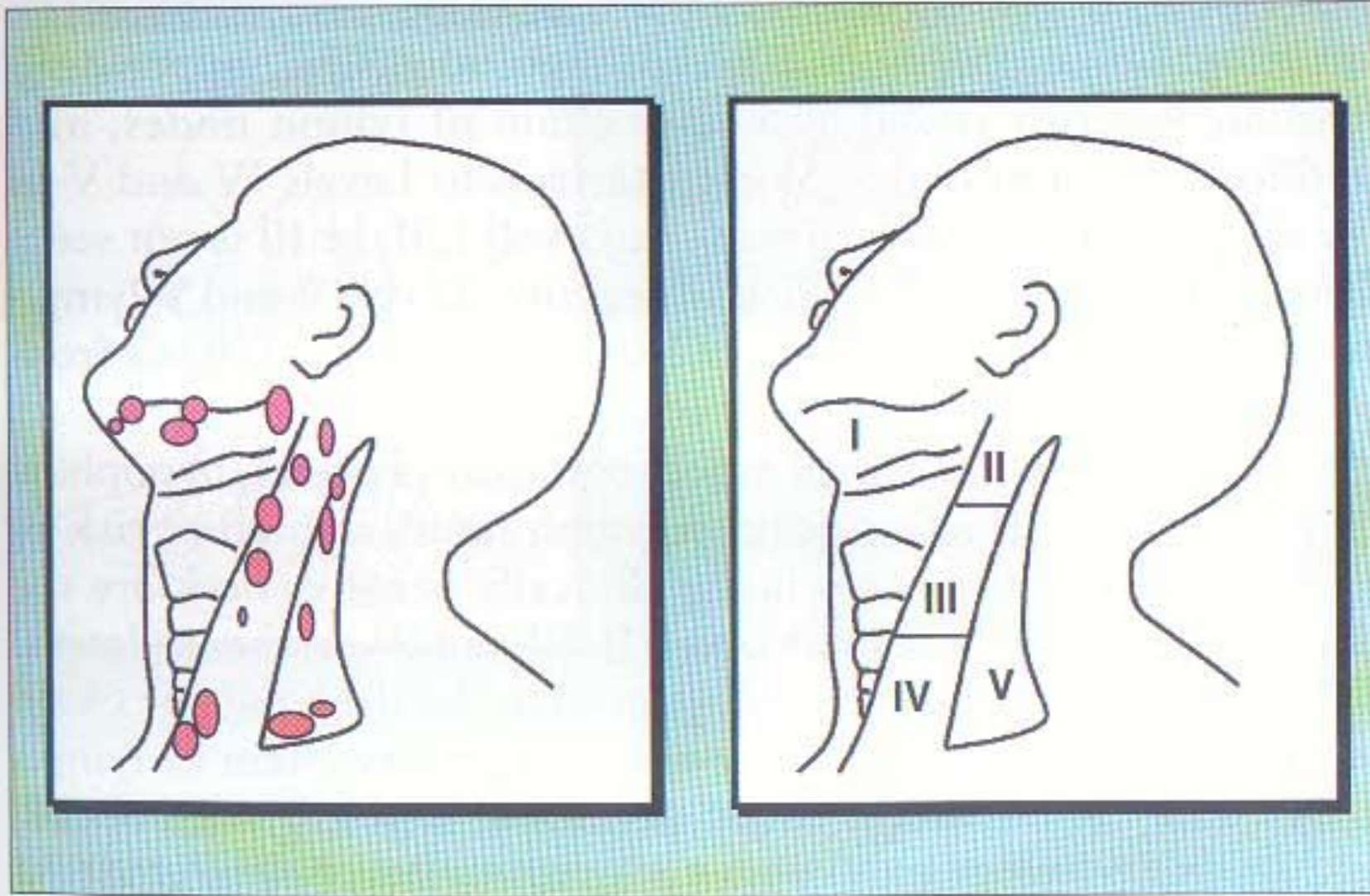


Fig. 9.5 Memorial Sloan-Kettering Cancer Center leveling system of cervical lymph nodes.



Fig. 3 Anteriorly placed gingivo-buccal cancer ("Khaini" cancer)



Fig. 4 Gingivo-buccal cancer extending to retromolar region.



BIOLOGICAL DISTINCTIONS IN ORAL CANCER

	GINGIVO-BUCCAL Ca	TONGUE Ca
STAGE AT PRESENTATION	<p>Detailed description: A pie chart for GINGIVO-BUCCAL Ca. The largest slice is IV (72%) with diagonal hatching. A smaller slice is I & II (13%) with a dotted pattern. The smallest slice is III (15%) with a cross-hatch pattern.</p>	<p>Detailed description: A pie chart for TONGUE Ca. The largest slice is I & II (40%) with a dotted pattern. The next largest is III (33%) with a cross-hatch pattern. The smallest is IV (27%) with diagonal hatching.</p>
PROPENSITY TO NECK METASTASES	N_0 — 54% N_+ — 46%	N_0 — 29% N_+ — 71%
FIRST NODAL STATION	LEVEL I	LEVELS II/III
PATTERN OF FAILURE	PREDOMINANTLY AT THE PRIMARY SITE	PREDOMINANTLY IN THE NECK

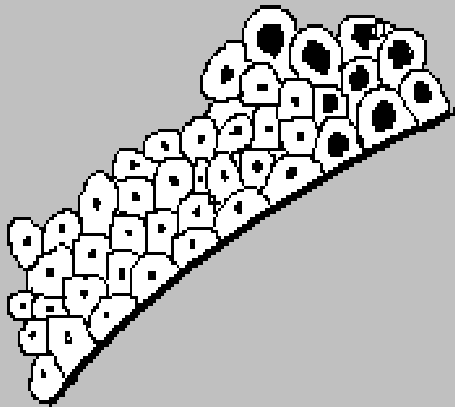
Fig. 5 Differences in the biological behaviour of oral cavity cancers.

Mechanism of Metastasis

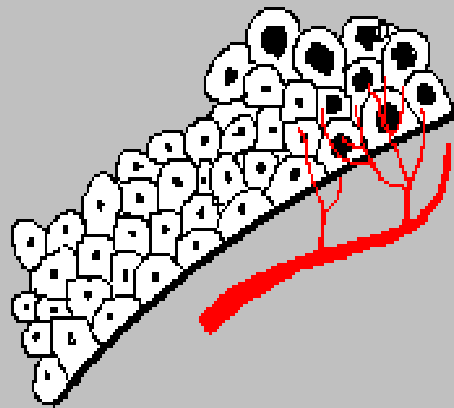
Halstedian Principle

- Lymphatic Spread by Permeation along the Lymphatic canaliculi
- Lymph node offer Protective role and acts like a filter
- Sentinel node and Sequential lymph node involvement
- Concept of Block dissection and En block dissection to remove micro metastasis

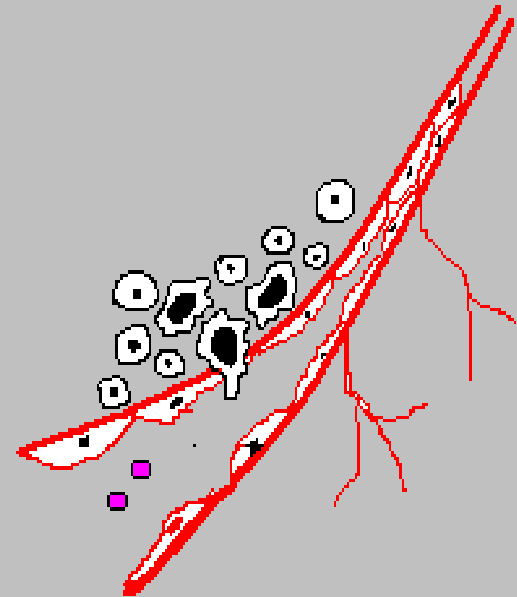
Phases of Metastasis



Transformation

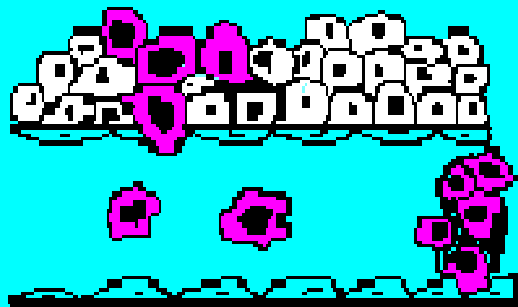


Angiogenesis

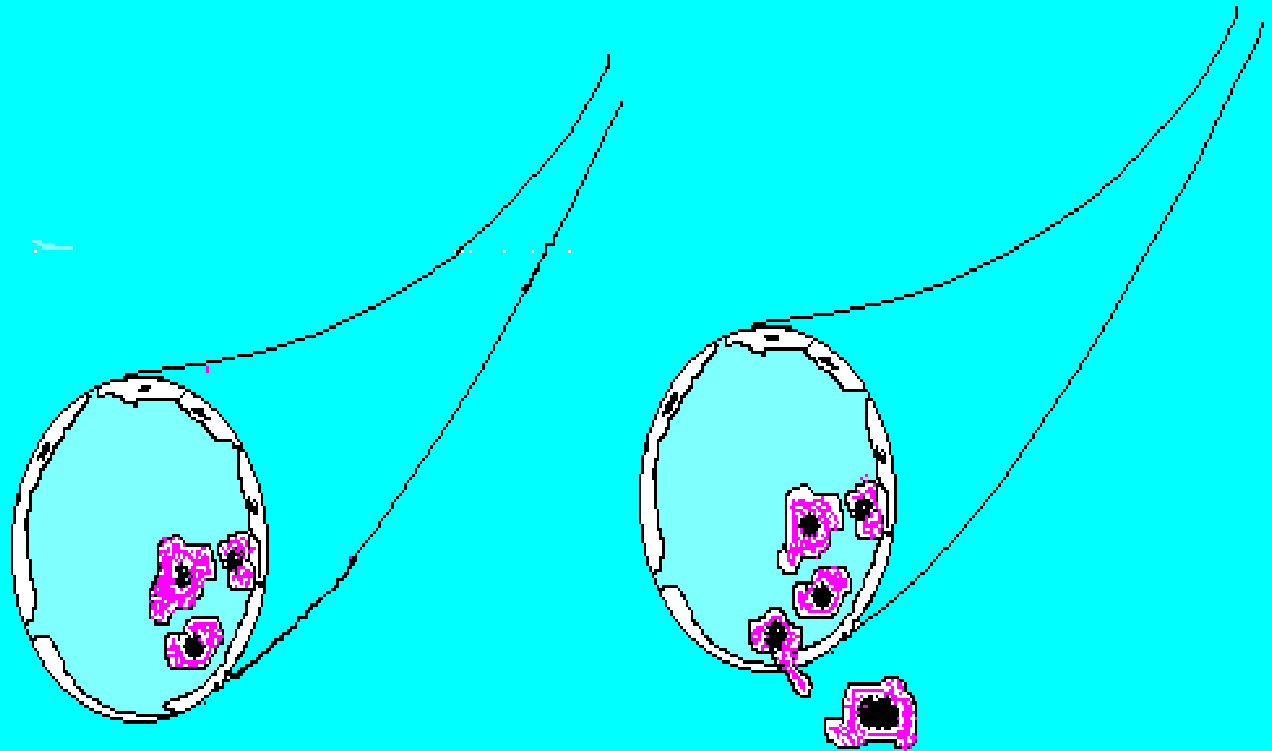


Detachment
Motility /
invasion

Phases of Metastasis



Embolism,
Circulation,
Survival



Adherence

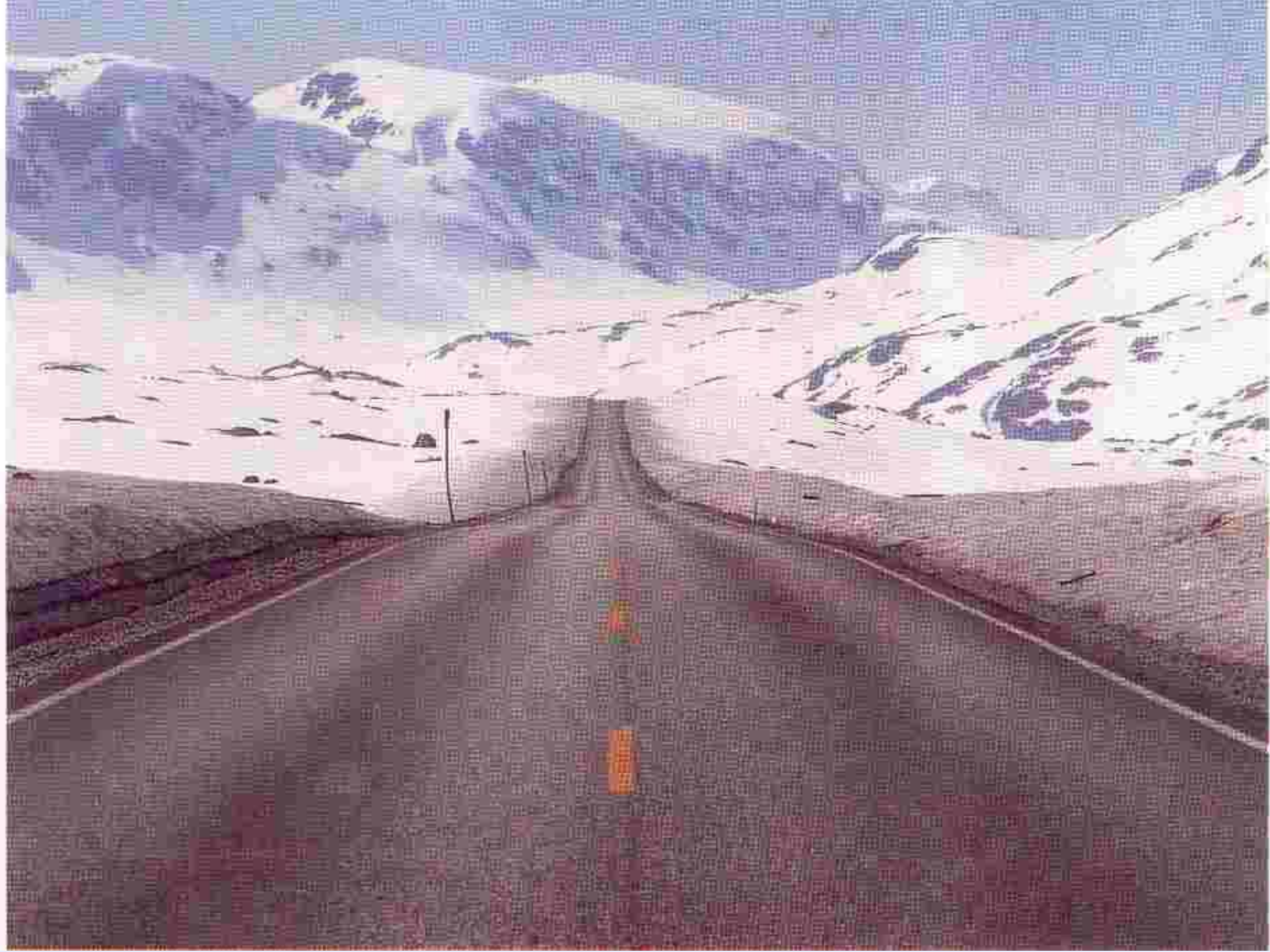
Extravasation



Mechanism of Metastasis

Newer Concepts

- Lymphatic metastasis by Embolisation
- No role for lymphnodes to play
- skip lesion possible
- Block dissection questioned



Myocutaneous flaps in Head and Neck Oncology

Dr Pradip Sharma

M S , DNB

Consultant surgeon

Inlacs & Budharani Hospital Pune

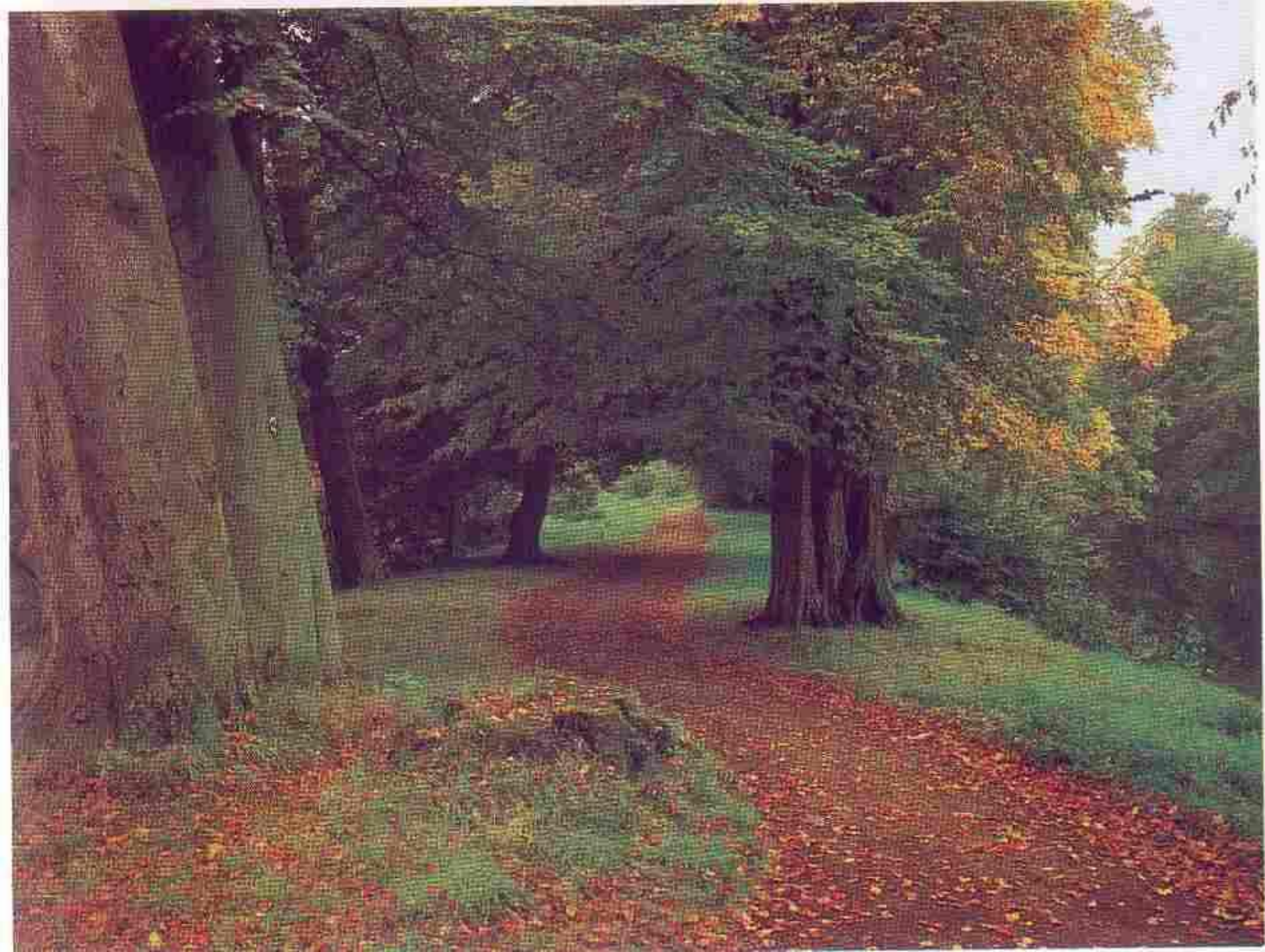
and

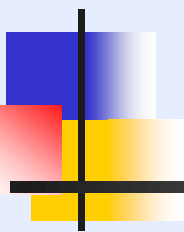
Dr Arun Jamkar

Professor and Head

Department Of Surgery

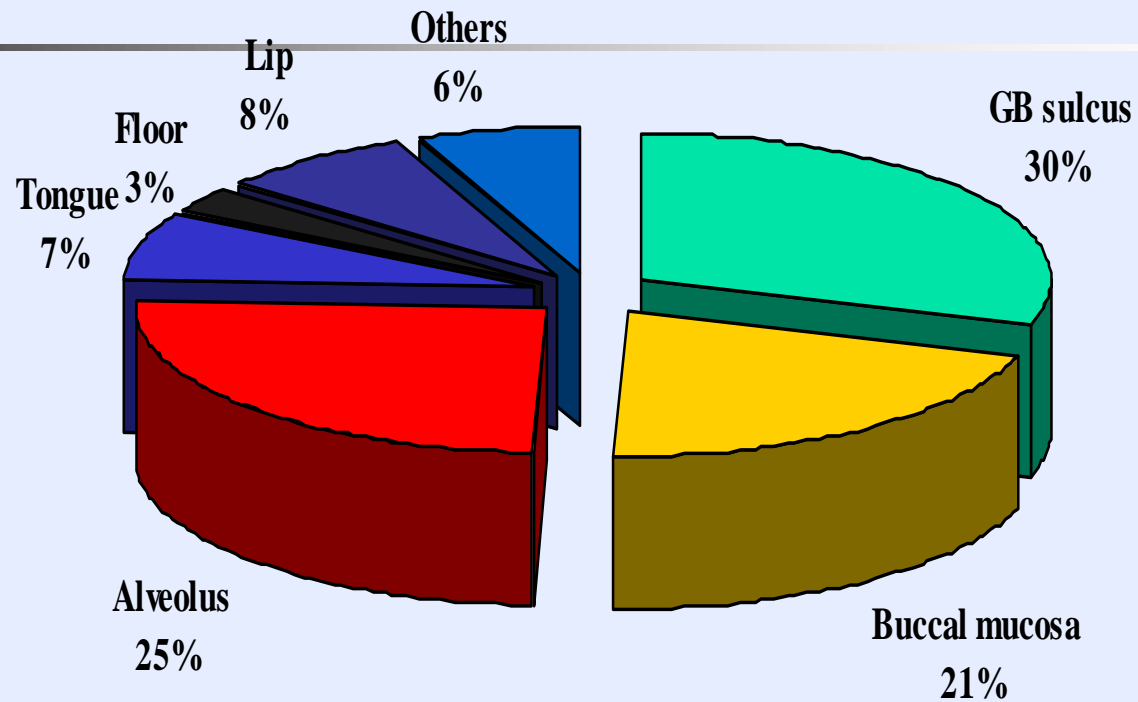
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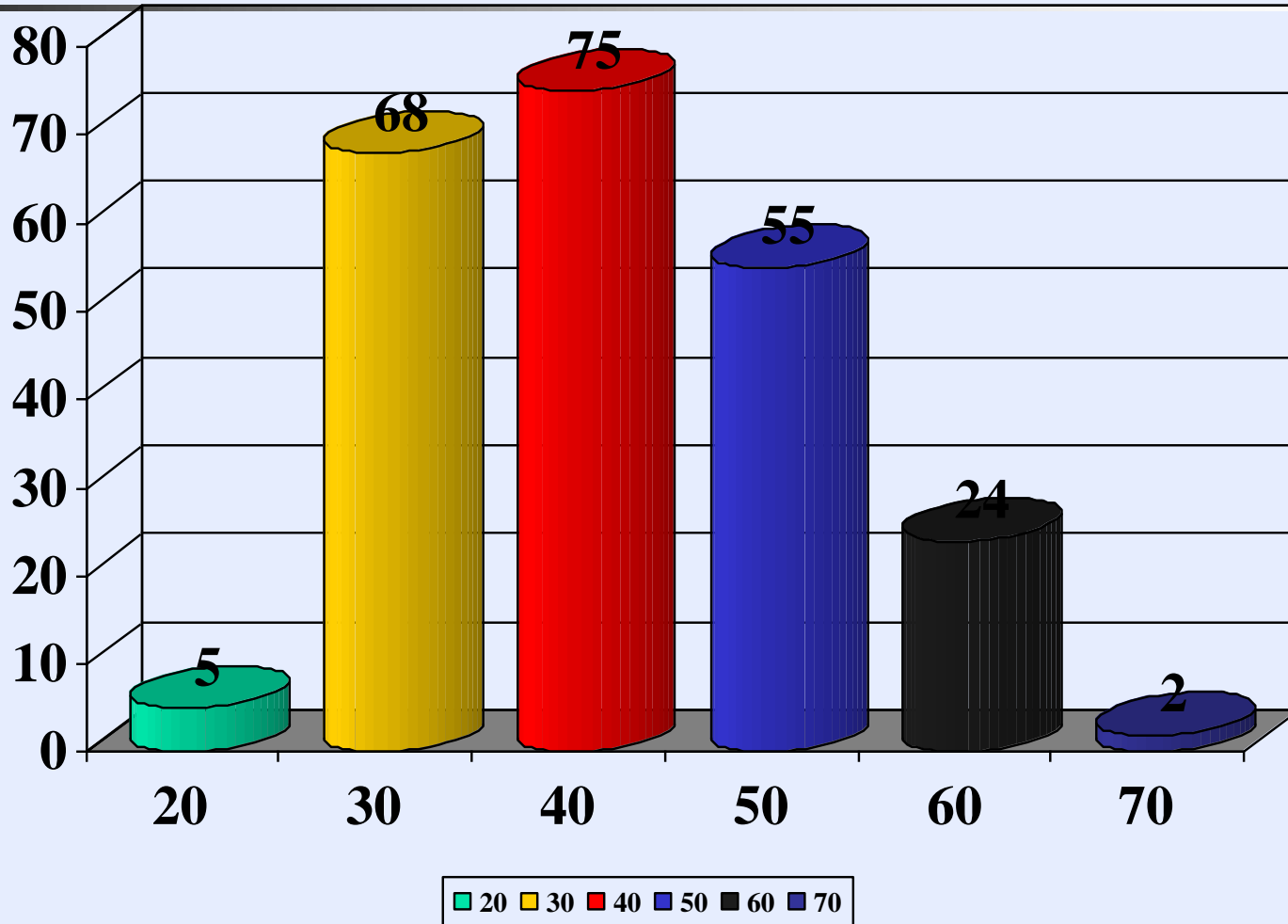
All oral cancer surgery
produce Oral Cripple
Greatest challenge is
Functional, Cosmetic and
Structural rehabilitation

Oral cancer : Site distribution



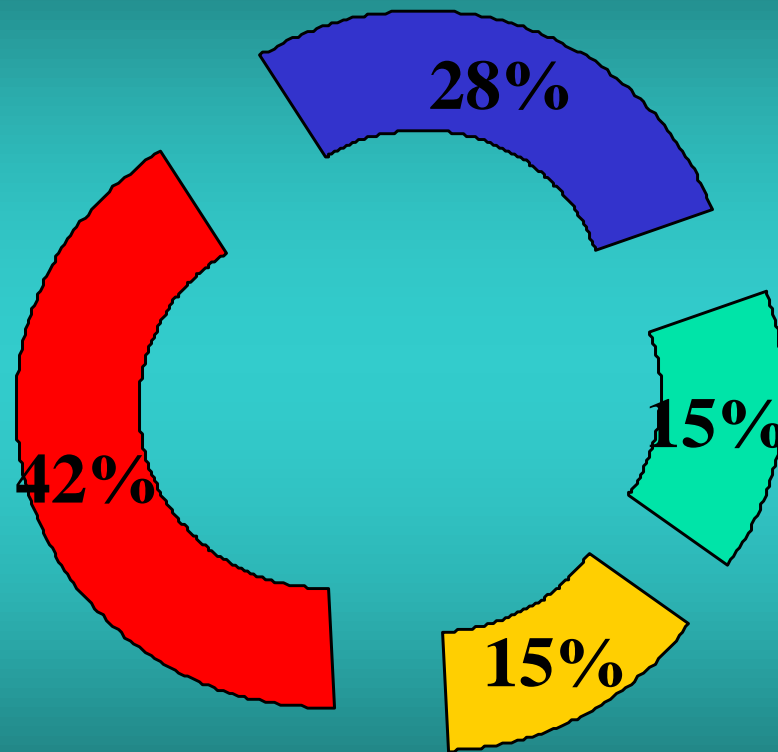
■ GB sulcus ■ Buccal mucosa ■ Alveolus ■ Tongue ■ Floor ■ Lip ■ Others

Oral Cancer reconstruction Age distribution



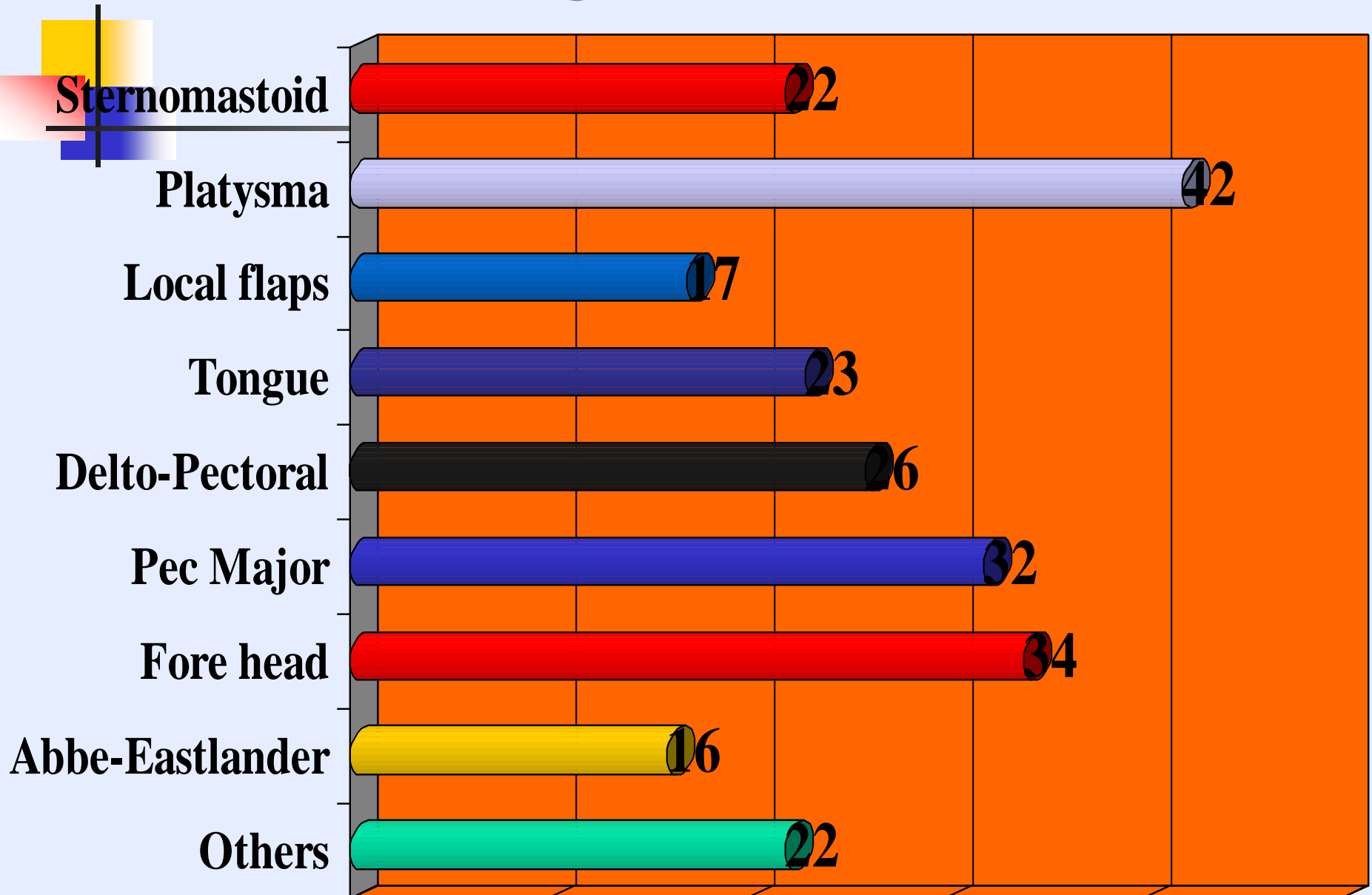
Oral cancer reconstruction

Stage Distribution

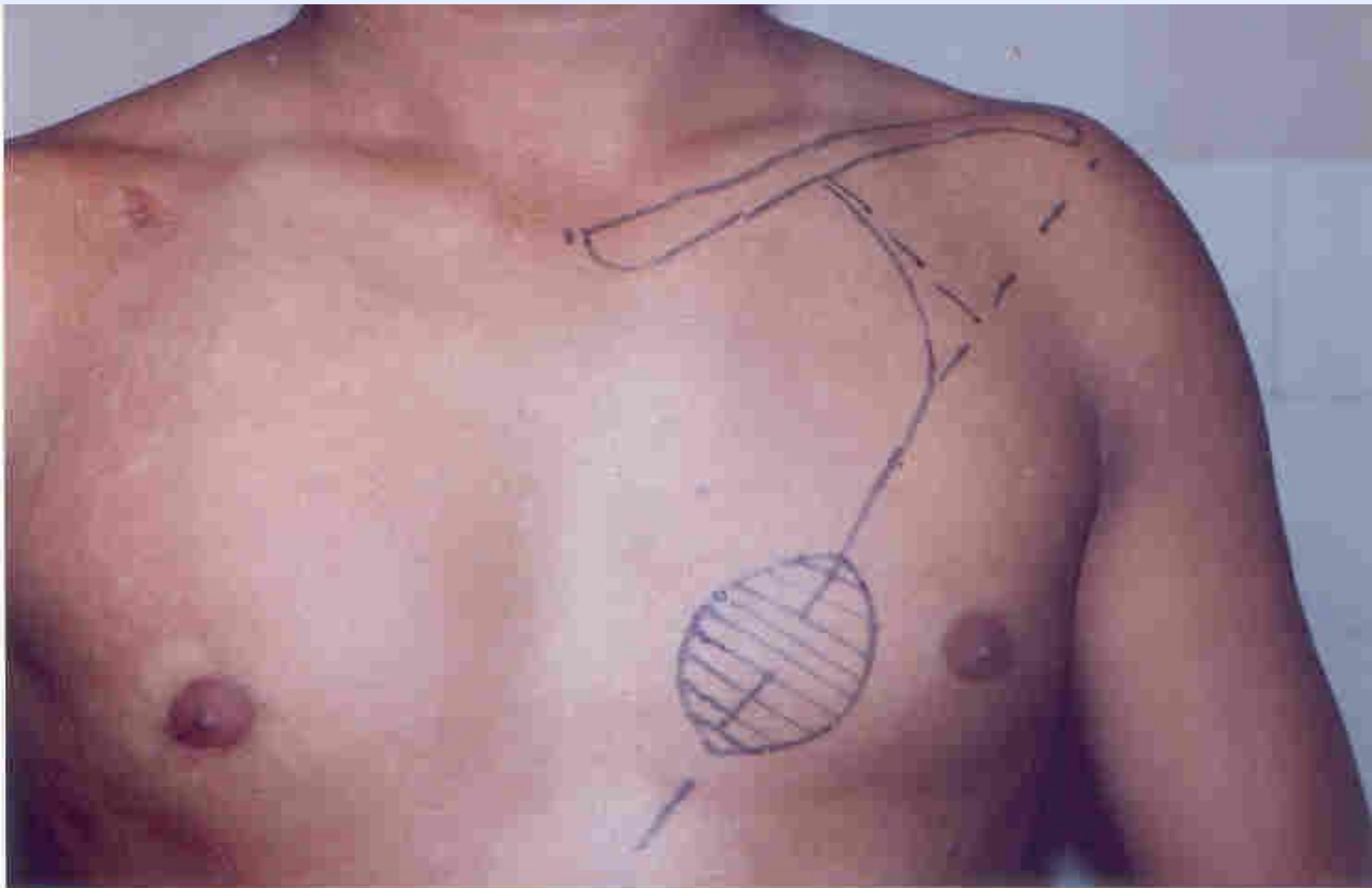


■ Stage 1 ■ Stage 2 ■ Stage 3 ■ Stage 4

Details of Myo-cutaneous flaps



Skin marking of the flap



Simple Fore head Flap



USE OF ISLAND DELTOPECTORAL FLAP IN RECONSTRUCTIVE HEAD NECK ONCOLOGY

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SUMMARY

Deltpectoral flap is commonly used to reconstruct defects resulting from abalative head neck cancer surgery. Standard Deltpectoral flap has its own inherent technical drawbacks. Herewith we describe a technique by which these are obviated.

INTRODUCTION

Deltpectoral flap was first described in 1965 by V.Y Bakamjian for the pharyngo-oesophageal reconstruction. Thereafter its utility was expanded to cover other areas in the head and neck region.

However the standard Deltpectoral flap has its own inherent technical drawbacks. It is a three stage procedure: involving harvesting the flap, division of the flap pedicle and inseting of the flap. Its use inside the oral cavity as a lining is limited due to formation of oro-cutaneous salivary fistula with its associated morbidity. The effect of gravity on the down draining fistula also prevents spontaneous closure of the fistula.

The effect of gravity on the down draining fistula also prevents spontaneous closure of the fistula.

METHOD

The Deltpectoral flap is marked in the standard fashion. The dimensions of the defect resulting from the abalative surgery are noted and marked

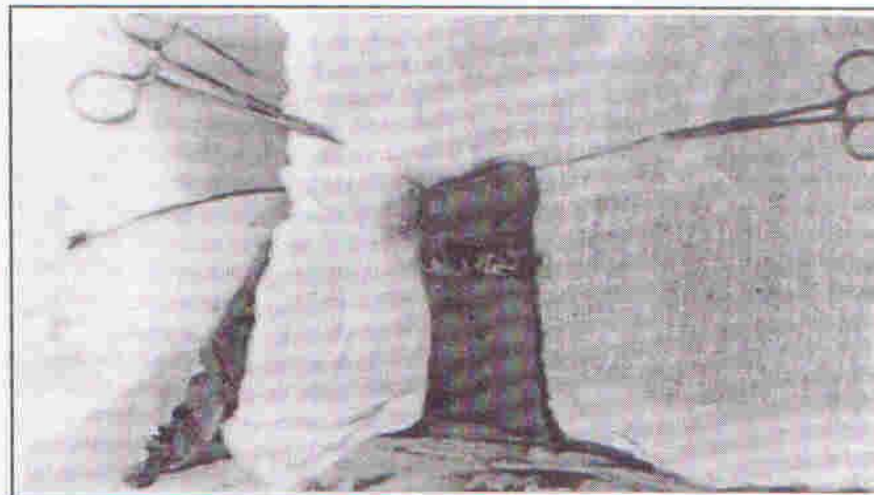


Fig. 1 : Islanding the DP flap by De-epitheliation

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