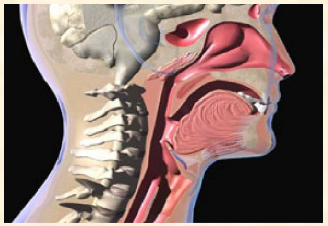
La terapia di supporto in radioterapia oncologica



Distretto testa-collo

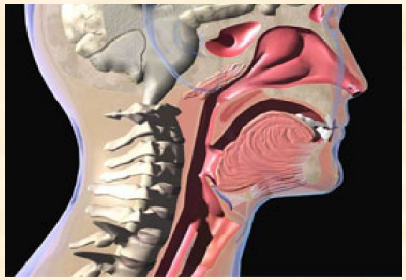
Vitaliana De Sanctis

Radioterapia Oncologica

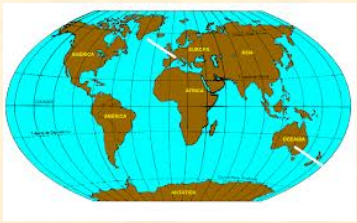
"Sapienza"

Università di Roma

Head and neck cancer

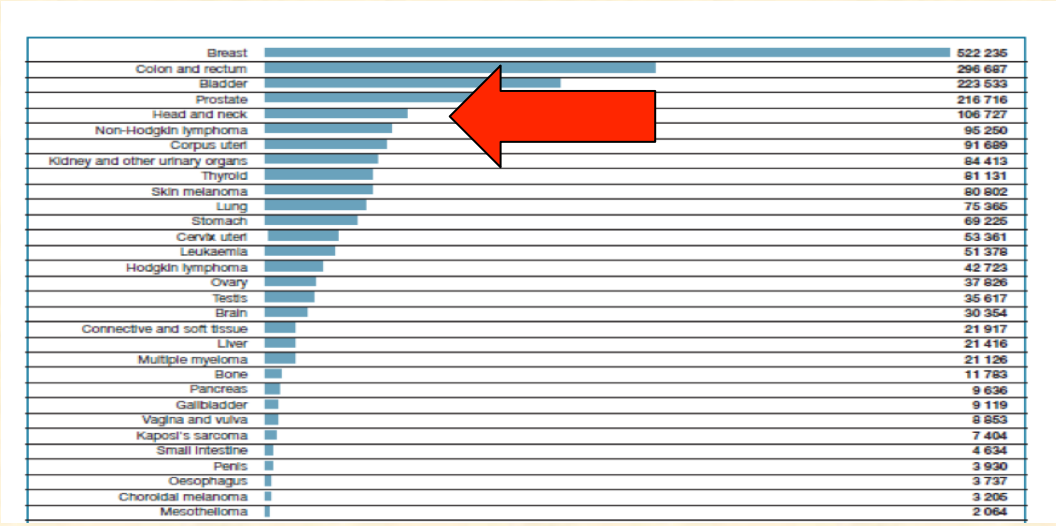


645000 new cases each year worldwide



75% with stages III IV

more than 350000 deaths yearly



Multimodality strategy

Surgery
Brachitherapy
Surgery+radiotherapy (resectable)
Radiotherapy (unresectable and resectable)
Chemoradiotherapy (unresectable and resectable)

IMRT
Unconventional Fractionations

CHART
Accelerated fractionation
Hyperfractionation
SIB

Gain of survival

Increase of toxicity

ACUTE TOXICITY

Severe (grade 3 or higher) adverse effects were more frequent after combined therapy (41 percent) than after radiotherapy (P=0.001);

The incidence of acute adverse effects of grade 3 or greater was 34%
In the radiotherapy group and 77% in the combined-therapy group(P<0.001)

Bernier; Cooper 2004

Accelerated radiotherapy caused a significant (p < 0.05) increase in the peak incidence of: use of analgesics (53% vs. 65%), dysphagia (35% vs. 45%), mucosal oedema (52% vs. 59%), and mucositis (33% vs. 53%).

Mortensen 2012

ACUTE MORTALITY

Retrospective study **7.8%-9%**

Argiris 2004;Mell 2010

Randomized trials **2-10%**

Calais 1999, Brizel1998; Forastiere 2003; Bonner2006;;Bourhis 2012; Rischin 2010

Treatment breaks=worse outcome

Patients with moderate or severe ulcerative mucositis had 15.8% and 46.8% incidences of radiation treatment breaks, respectively.

Russo, 2008;Trotti, 2003;.

An unplanned break of only 1 day resulted in a 0.68% lower 2-year control and therefore several days of breaks resulted in significantly shorter overall survival and relapse-free survival

Schmidt-Ullrich 1999;Robertson, 1998;Suwinski R, 2003;Rosenthal, 2007

depression insomnia

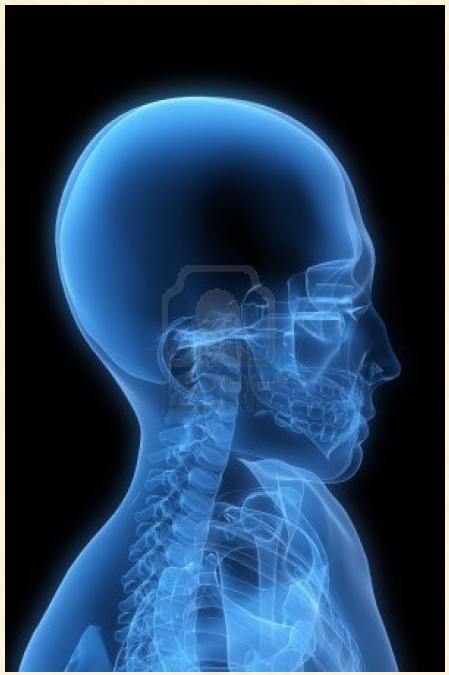
dermatitis mucositis

cachexia

xerostomia

anemia

neutropenia



pain

fever

dysphagia

SIRS

SYMPTOM CLUSTERS

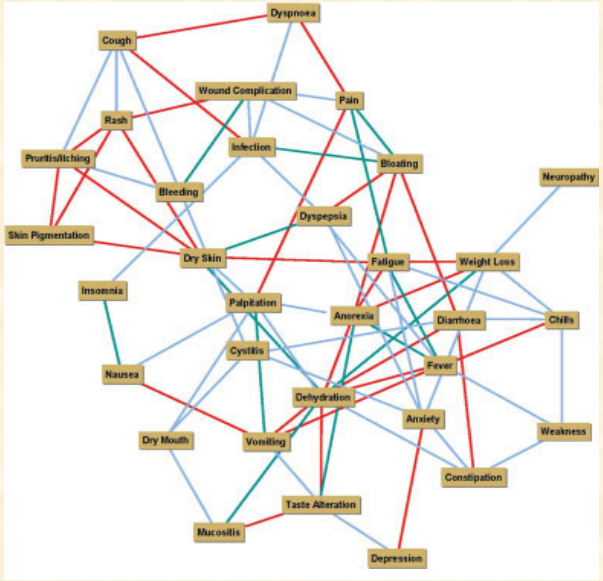
Symptom clusters
represent a clinically important
avenue to identify novel effective
therapeutic strategies
that might target several symptoms
within a cluster simultaneously

Symptom cluster

Application of Distance Matrices to Define Associations Between Acute Toxicities in Colorectal Cancer Patients Receiving Chemotherapy

Giuseppe Aprile, MD[1]

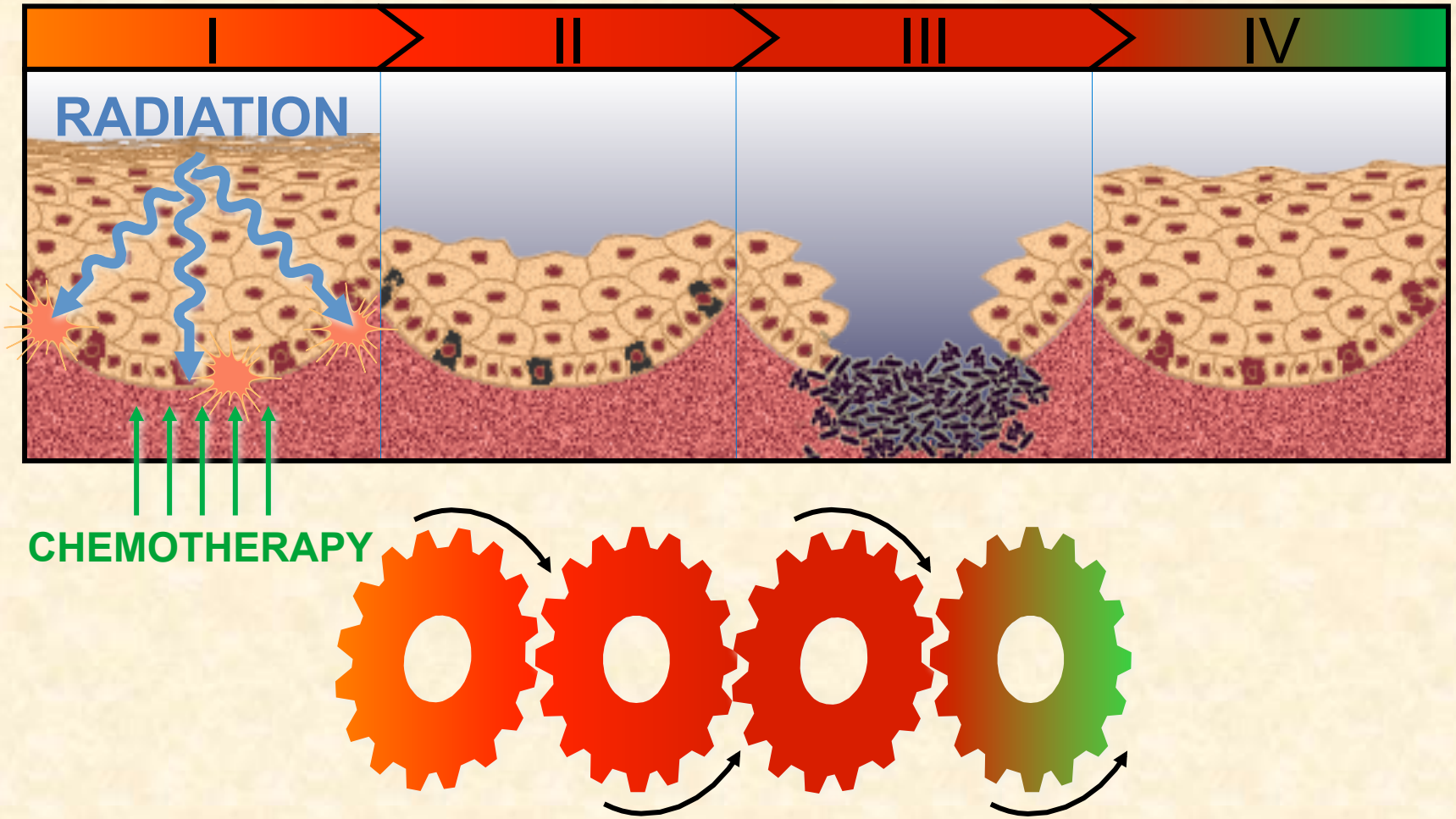
CANCER January 15, 2008 / Volume 112 / Number 2



Local toxicities correlate with distant toxicities

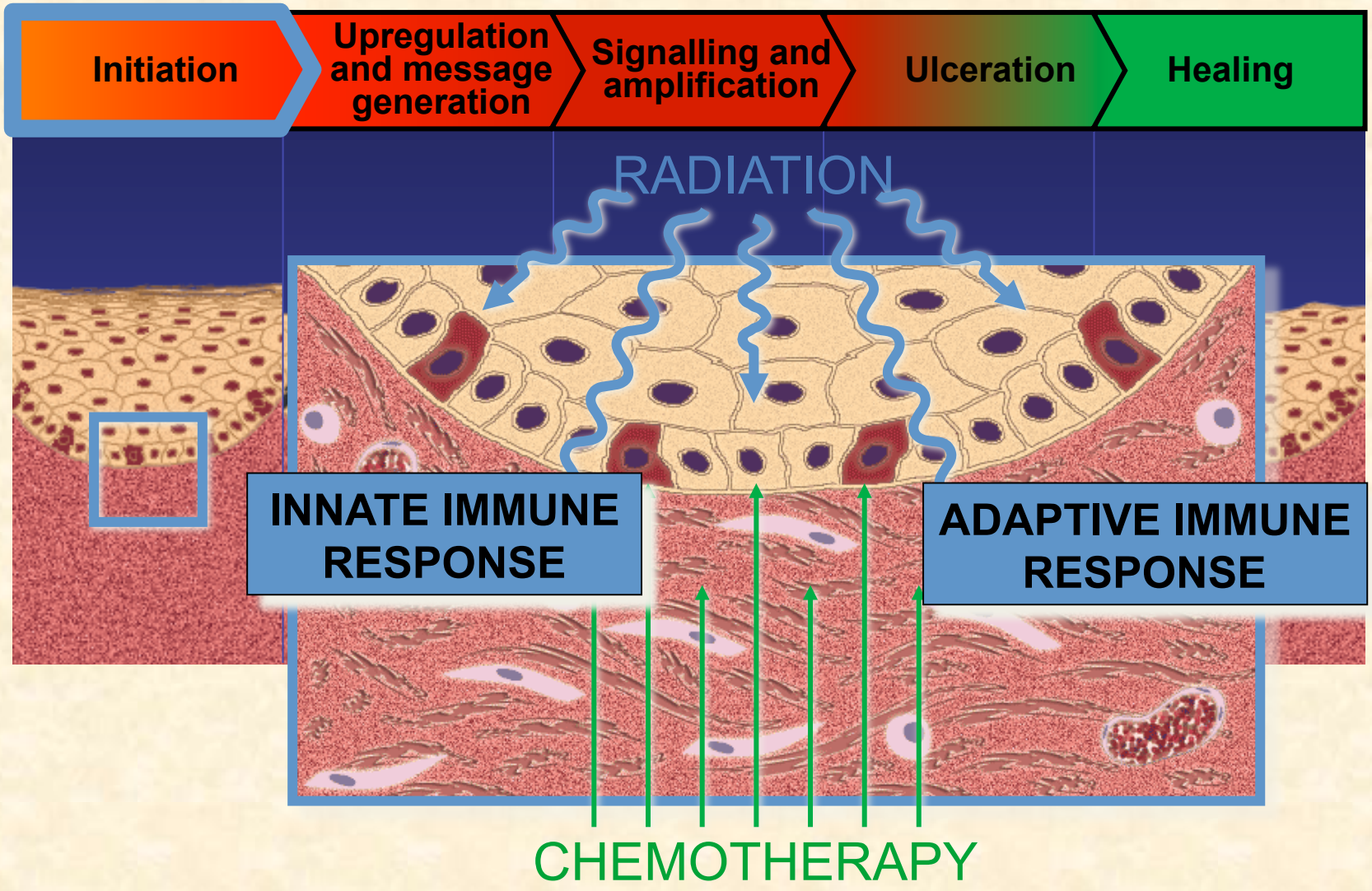
RESULTS. The graphic analysis, in which associations between toxicities were represented as links, identified 6 major hubs (fever, dehydration, fatigue, anorexia, pain, and weight loss), defined as central nodes with more connections than expected by chance. These were highly linked with minor nodes and provided evidence suggesting the existence of symptom clusters associated with CT-induced toxicities.

1998: direct damage to basal clonogenic cells (Lockhart, 1981)



[1]Adapted from Sonis ST, et al. *Cancer*. 2004;100(suppl 10):1995-2025.

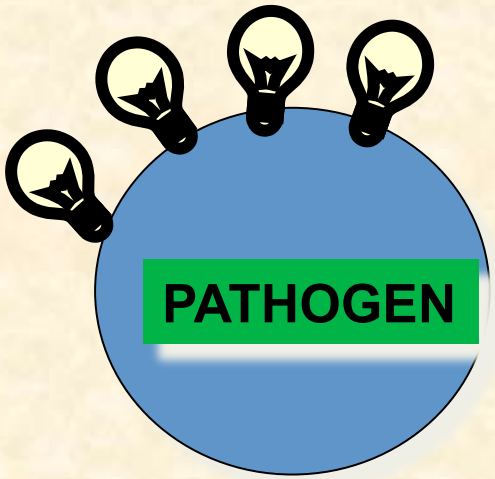
Multistep and multifactorial mechanism



INNATE IMMUNE RESPONSE

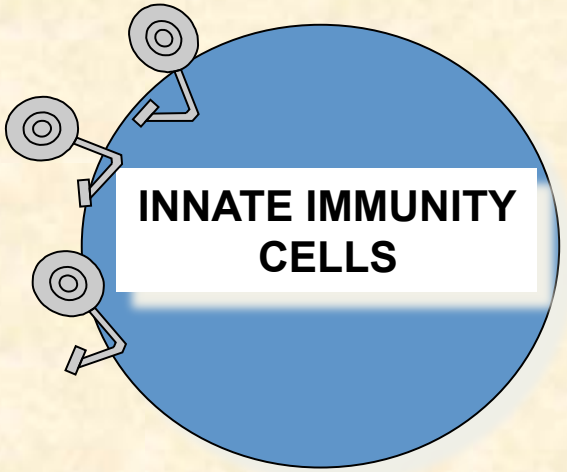
PAMPs

Pathogen Associated Molecular Patterns



PRR

Pattern Recognition Receptors



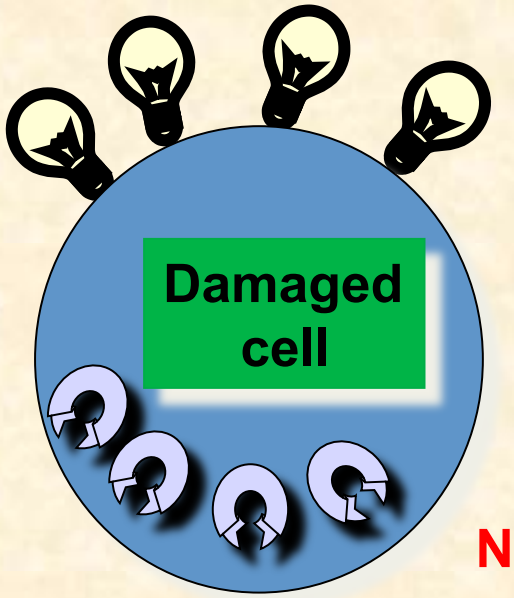
LPS
RNA
Bacterial peptides
Etc, etc

Toll-like
Lectine C
NLR
CARD
RAGE

INNATE IMMUNE RESPONSE

DAMPs
Damage-associated molecular pattern molecules

CRAMPs
Endogenous damage-associated pattern molucules

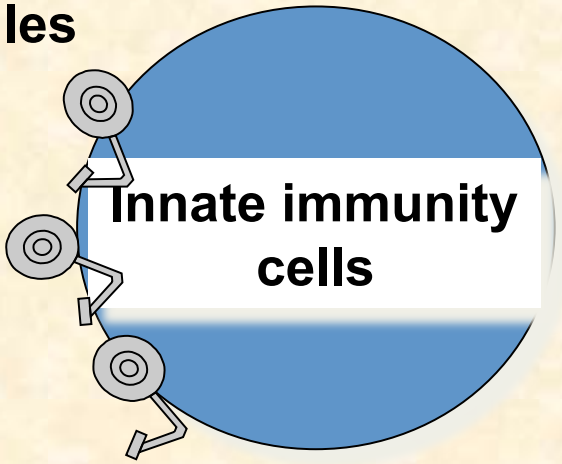


ROS

HMGB1

Nuclear acids

PRR

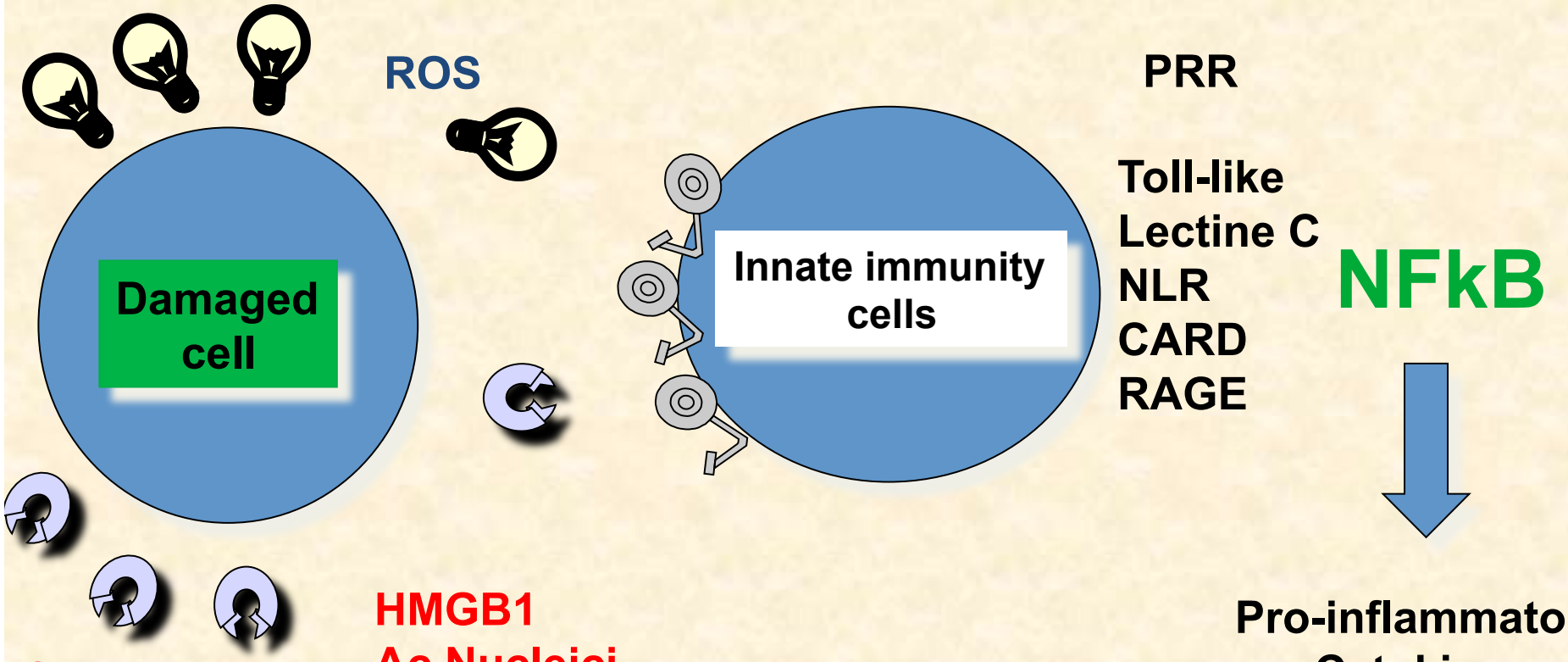


Toll-like
Lectine C
NLR
CARD
RAGE

INNATE IMMUNE RESPONSE

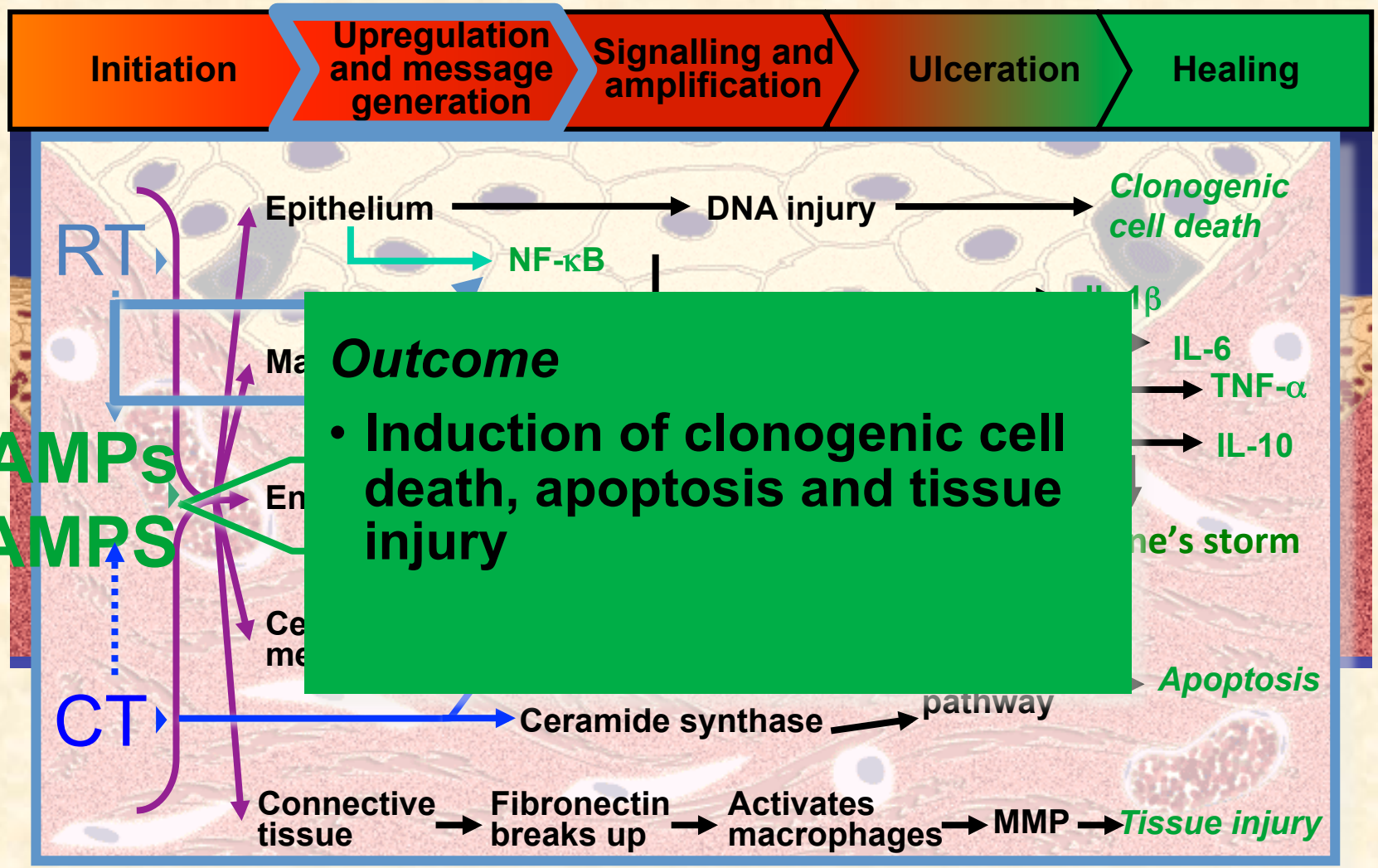
DAMPs

Damage-associated molecular pattern molecules



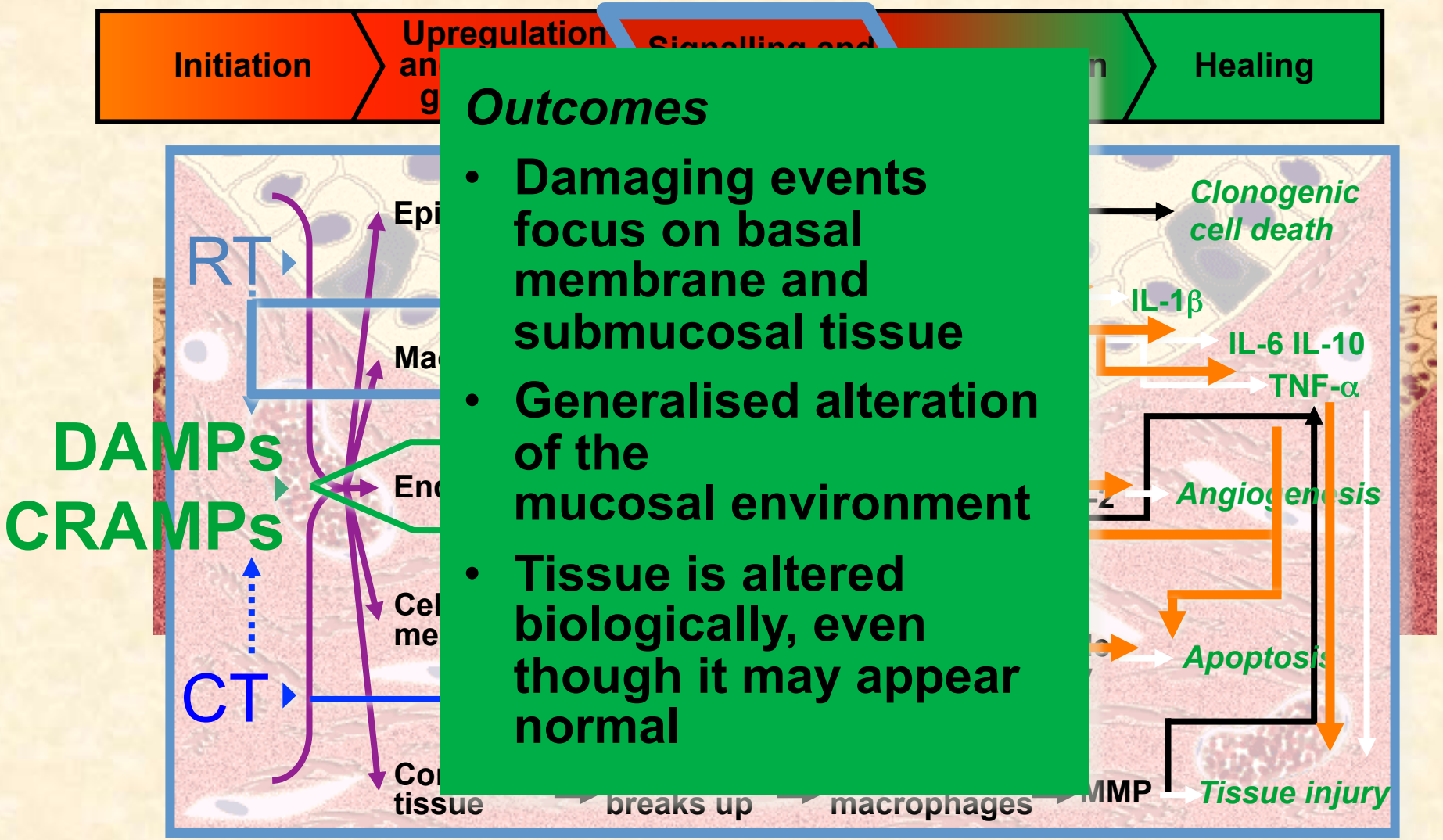
Endogenous damage-associated pattern molucules

Simultaneous biological events in all tissues



MMP = matrix metalloproteinase; COX-2 = cyclo-oxygenase-2

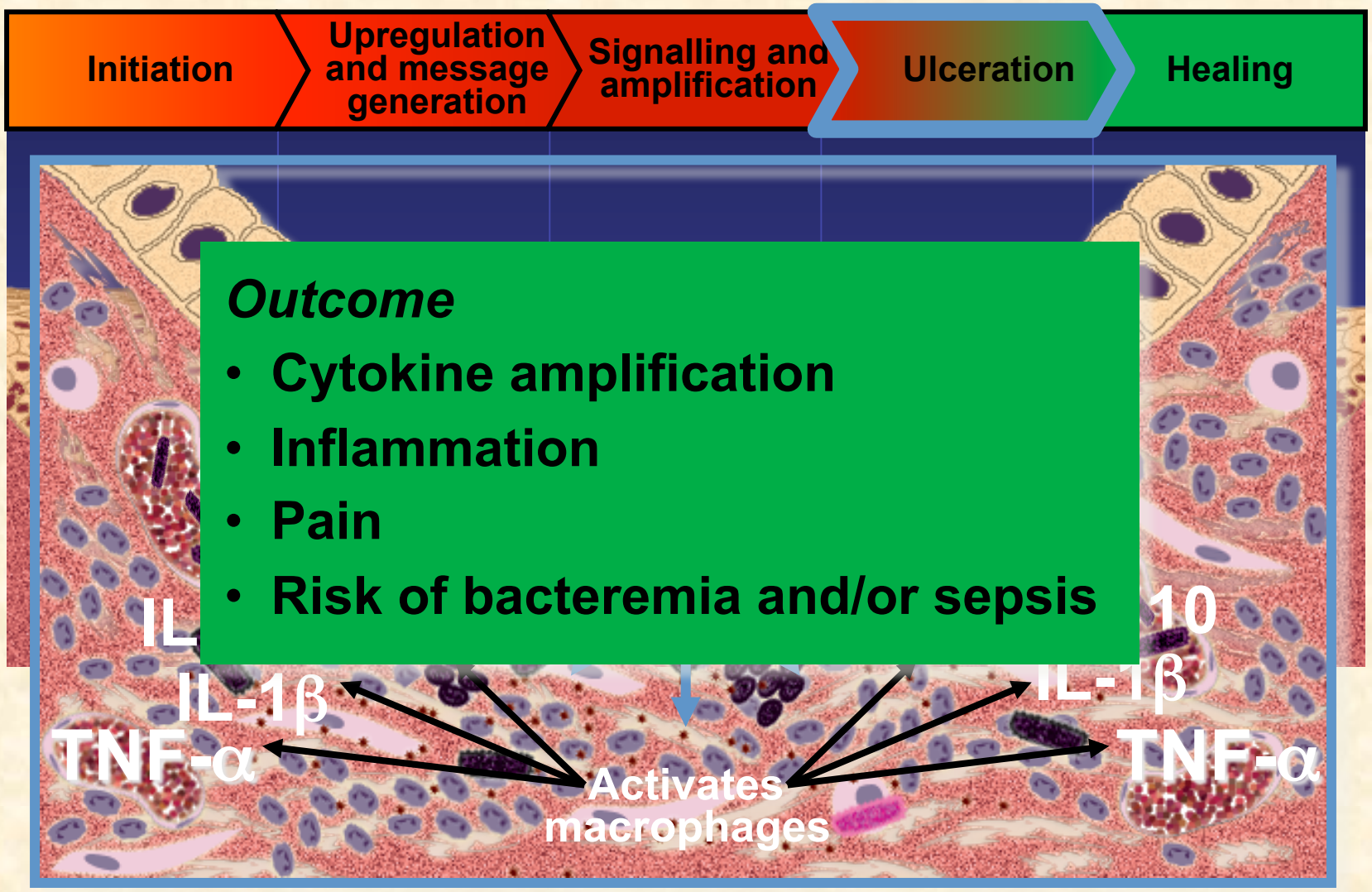
Biological Cross-talk and signal amplification



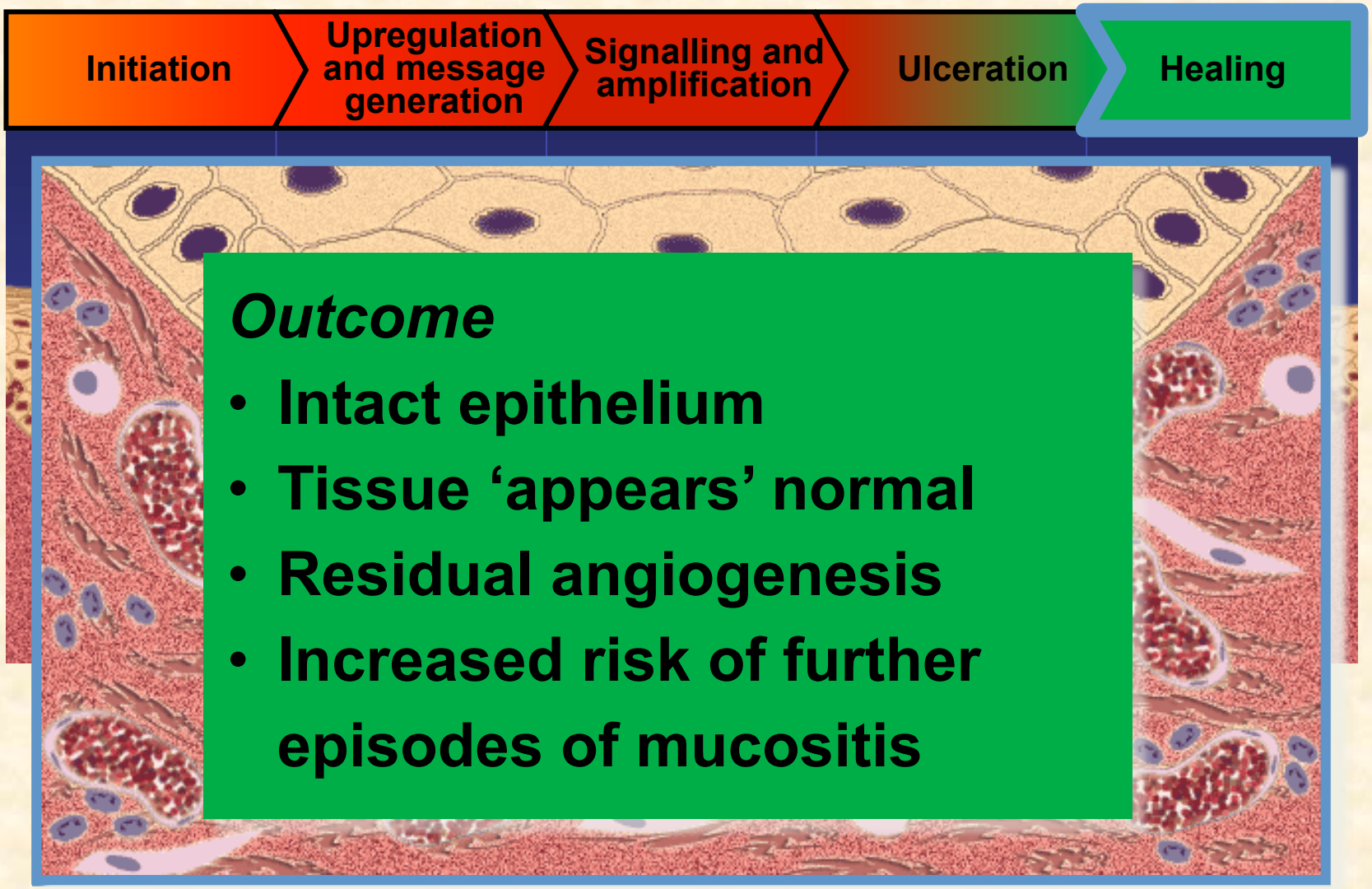
Outcomes

- Damaging events focus on basal membrane and submucosal tissue
- Generalised alteration of the mucosal environment
- Tissue is altered biologically, even though it may appear normal

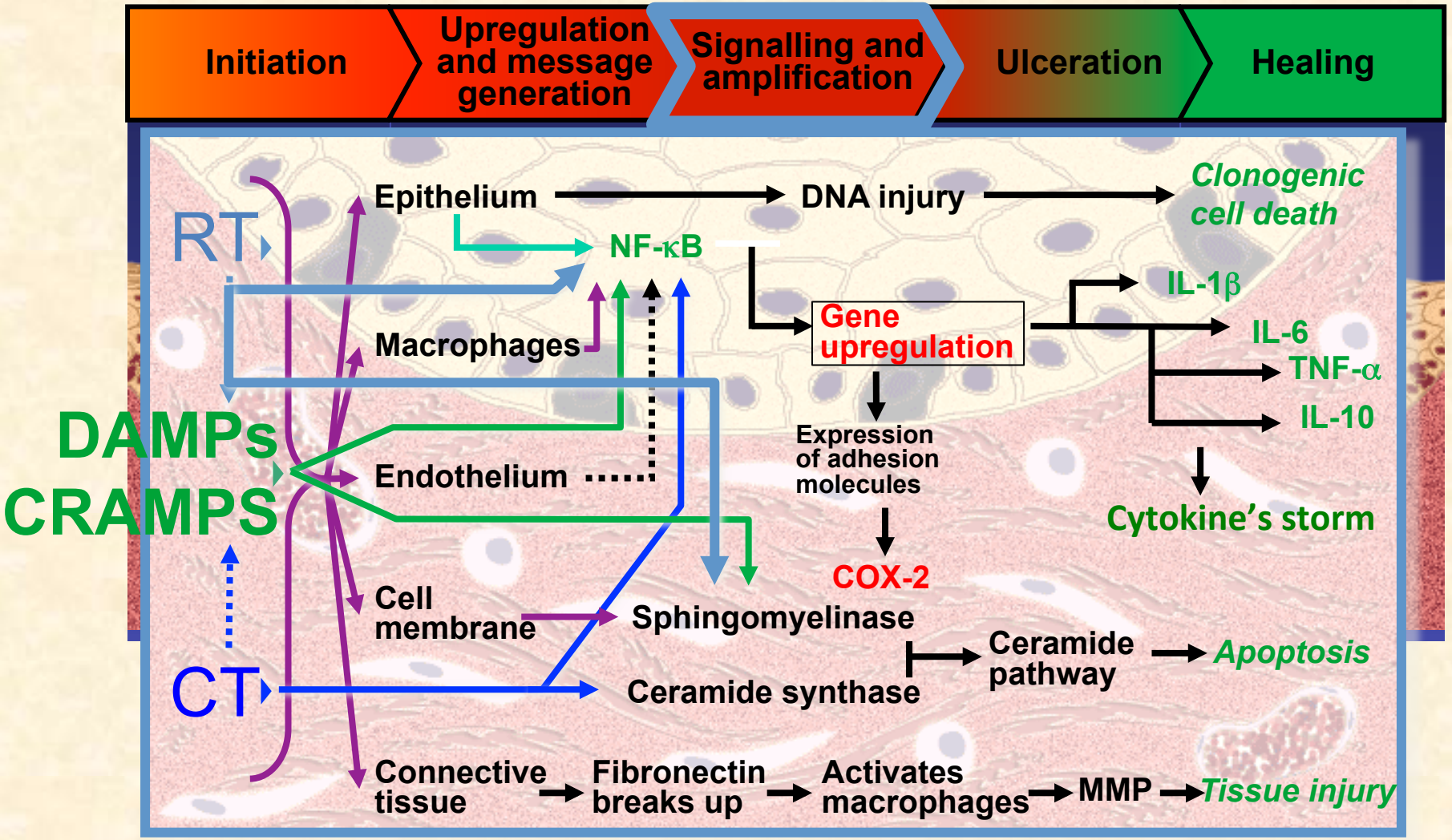
Loss of barrier integrity with sepsis risk and pain



Alterated cellular pattern after the damage

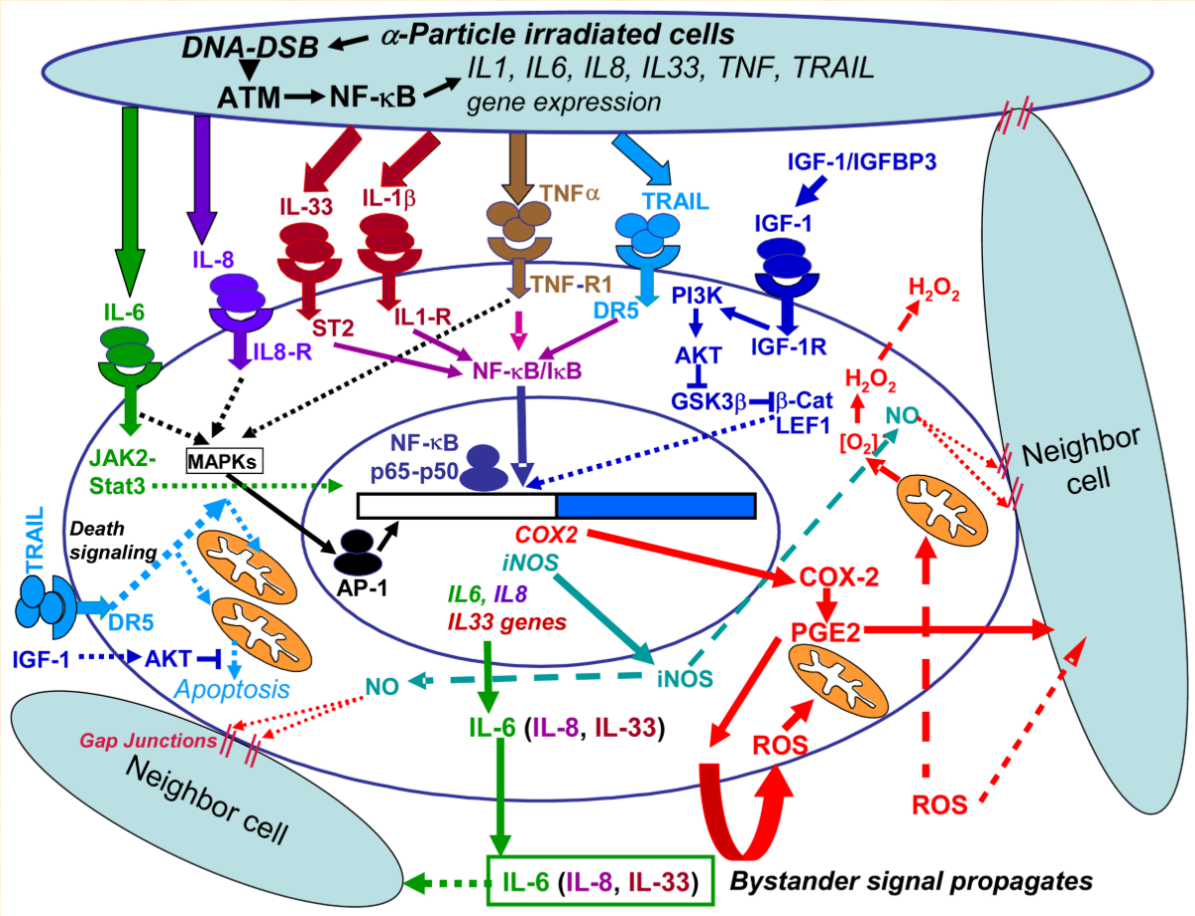


Cytokine’ s storm



MMP = matrix metalloproteinase; COX-2 = cyclo-oxygenase-2

EFFETTO BYSTANDER



Dysphagia
during RT/CRT

Anatomical changes in the pharyngeal constrictors after chemo-irradiation of head and neck cancer and their dose–effect relationships: MRI-based study ☆

Aron Popovtzer, Yue Cao, Felix Y. Feng, Avraham Eisbruch *

Radiotherapy and Oncology 93 (2009) 510–515

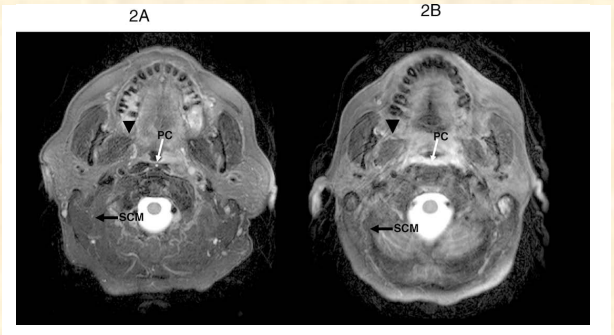
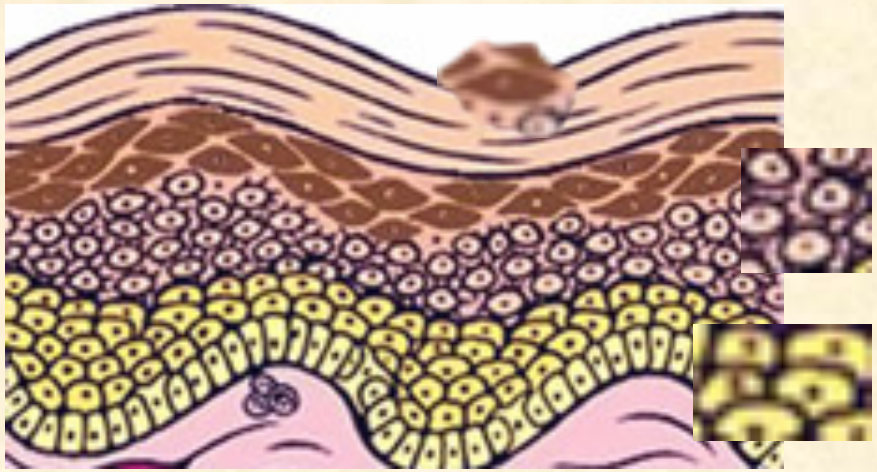


Fig. 2. An MRI cut of a T2-weighted image. (A) Pre-RT and (B) 3 months post-RT. Note the increase in the width and signal of the pharyngeal constrictor (PC) compared to the

As the PCs, GSL lie beneath the mucosa, it is likely that their MRI-observed edema is secondary to acute mucositis

Radiation dermatitis

loss of Langerhans cells.



impair immunologic integrity

activated epithelial cell

IL-1a

mesenchymal cells

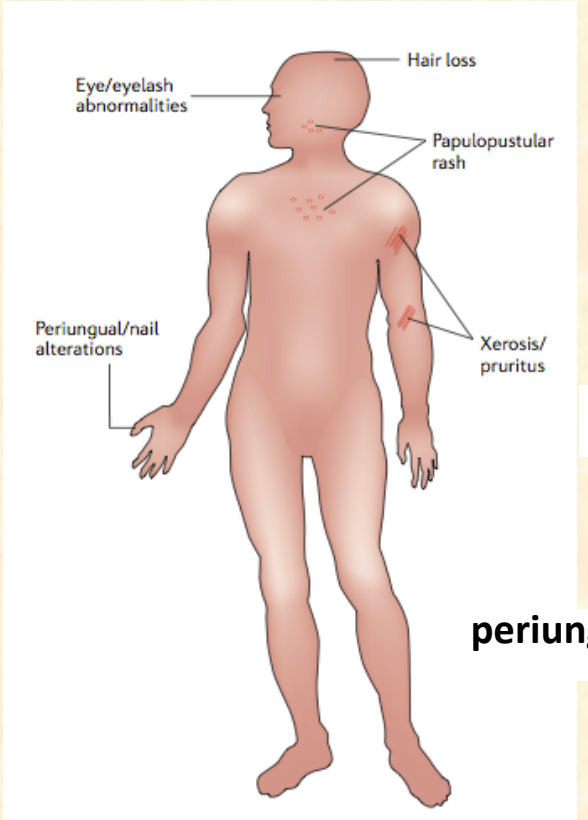
Acute injury

reduction and impairment of
functional stem cells,
endothelial cell changes, inflammation, and
epidermal cell apoptosis and necrosis.

IL-6 production
IL-1a activity
by
keratinocyte-fibroblast interaction.

cutaneous toxicities to EGFR inhibitors

abnormalities in hair growth (21%),

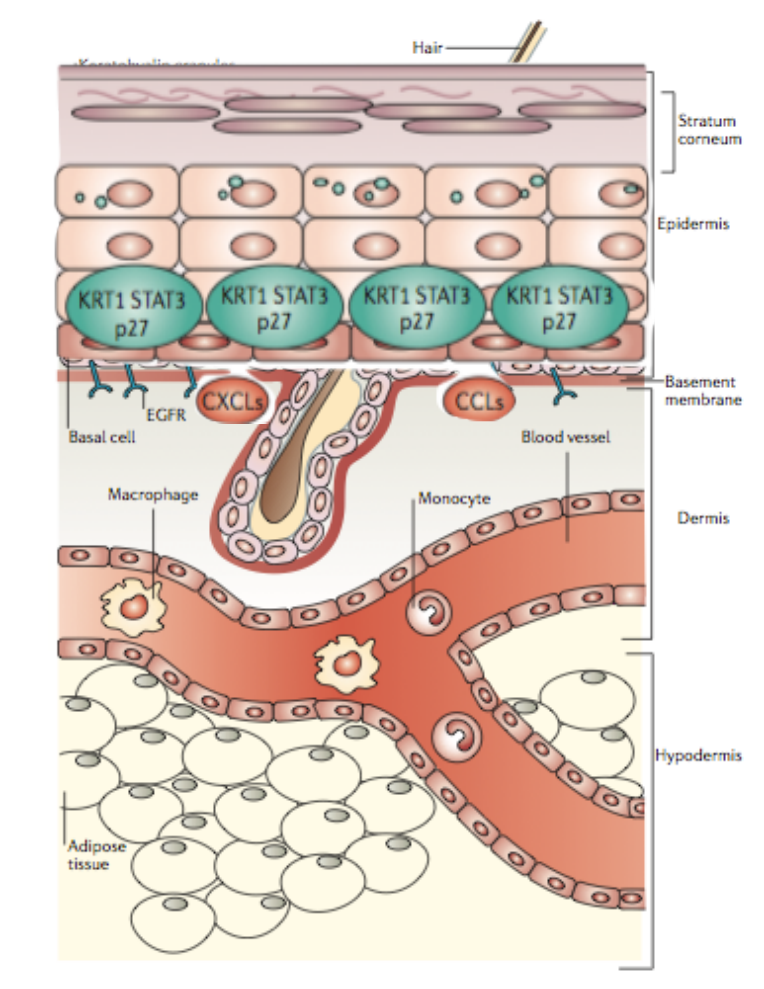


papulopustular rash that affects the face and upper trunk (45–100%)

dry and itchy skin (12–16%);

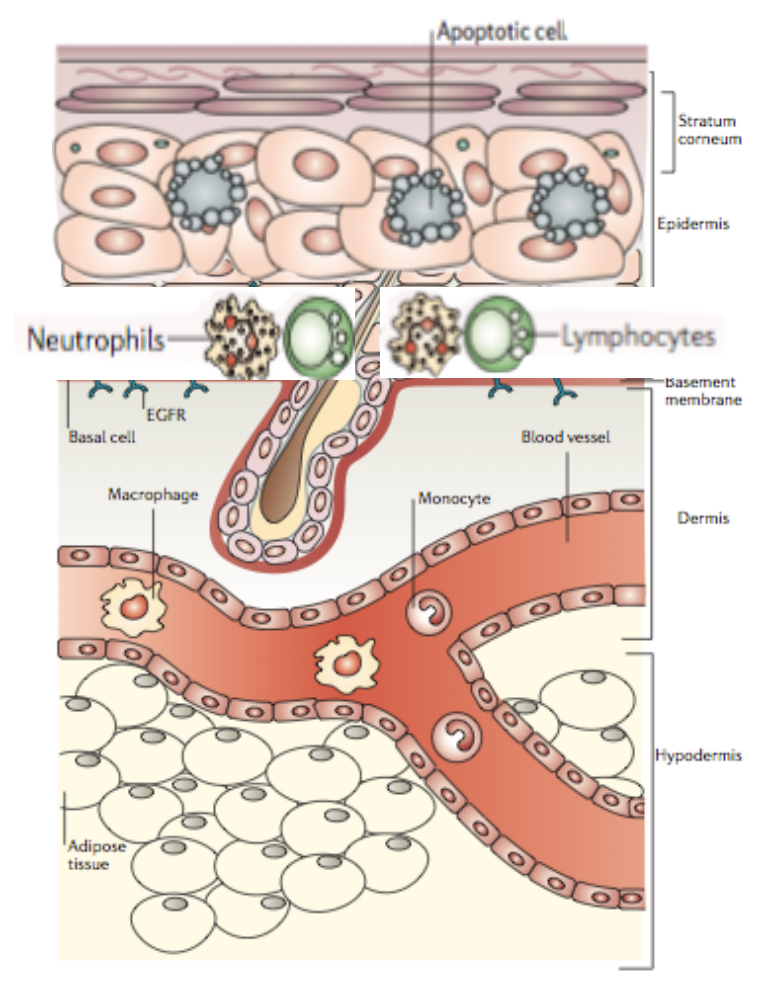
periungual inflammation with tenderness (12–16%)

cutaneous toxicities to EGFR inhibitors

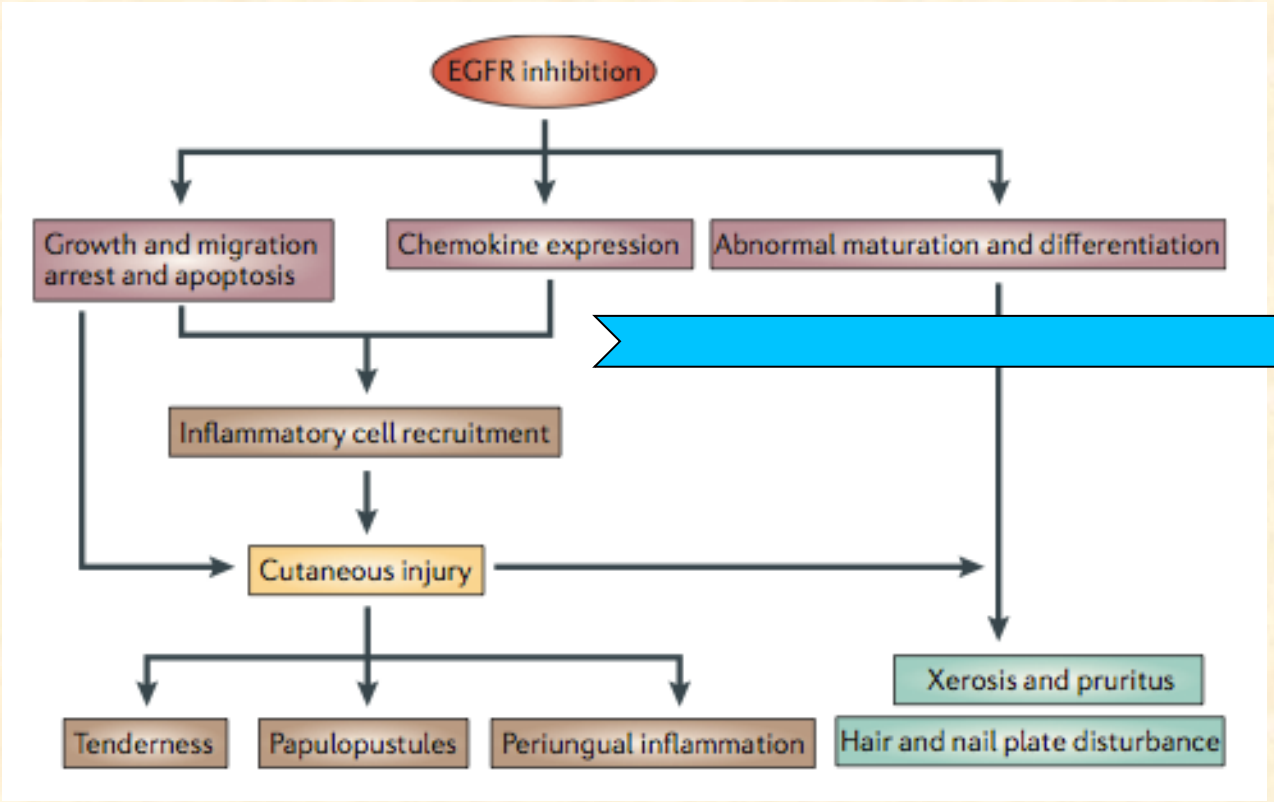


During EGFR inhibitor therapy

cutaneous toxicities to EGFR inhibitors



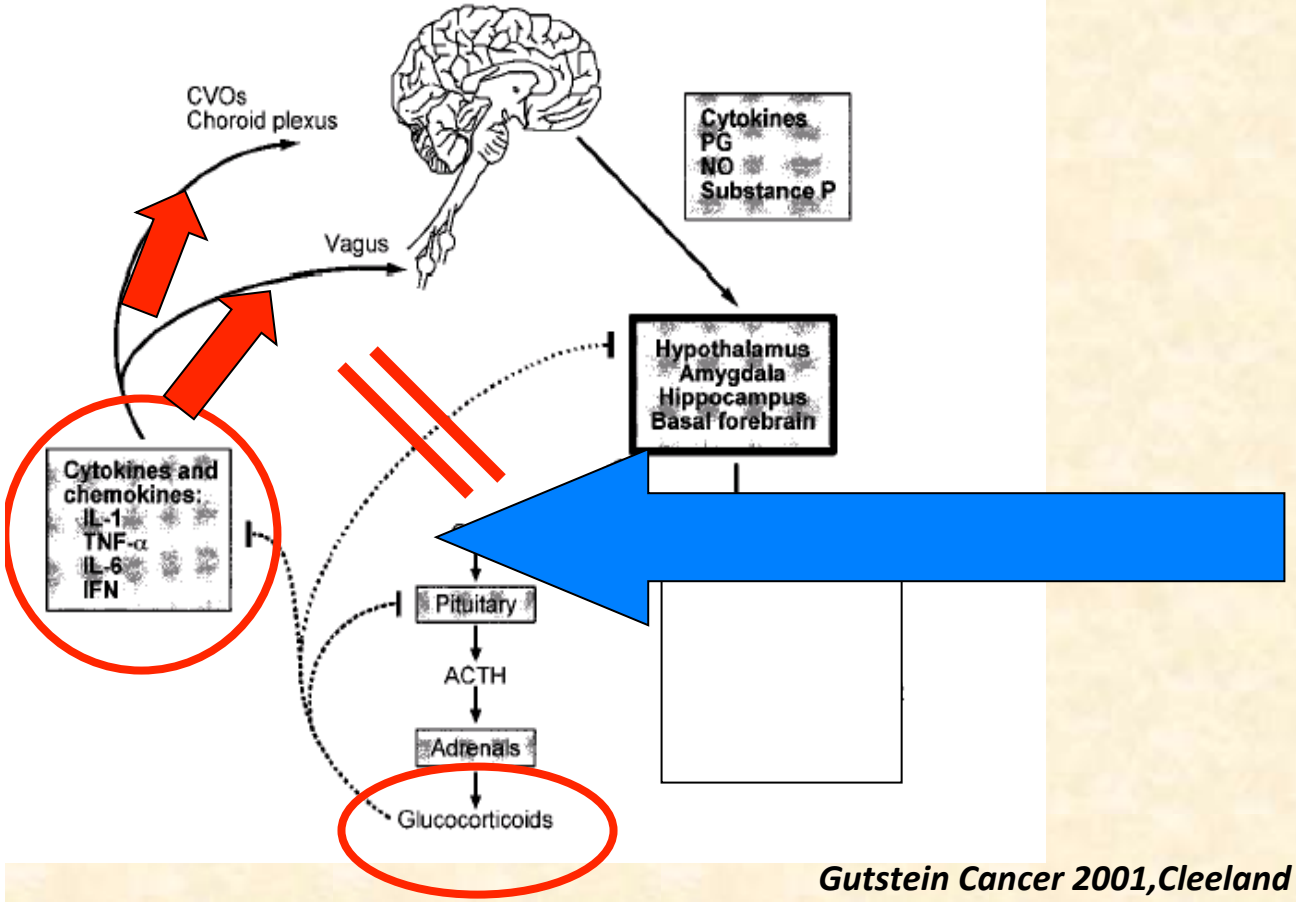
Release of inflammatory cells



MCP1
RANTES
CXCL10
CCL18
XCL1
CXCL9
Fractalkine
CCL3
NFkB

IL6
IL7
IRF5

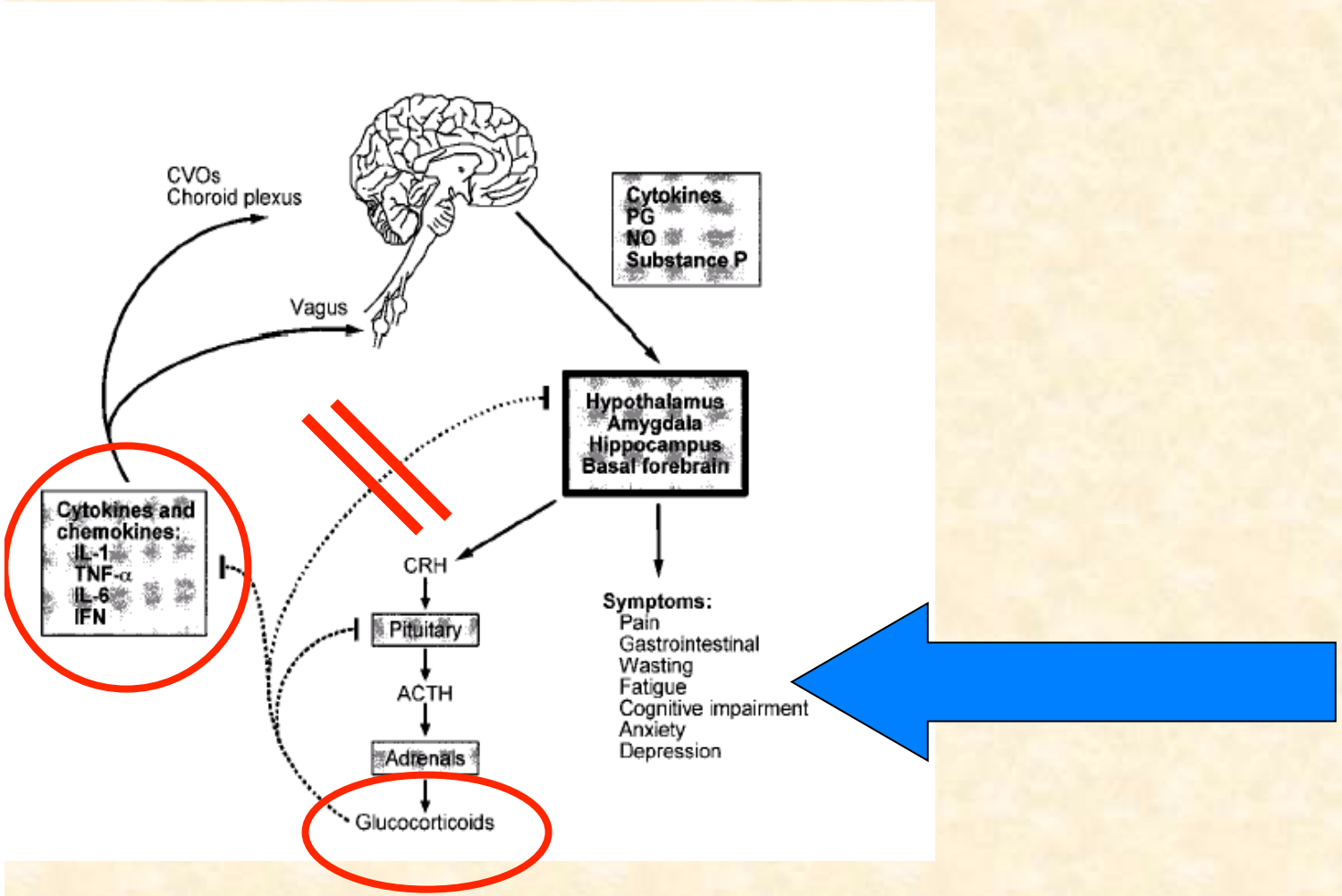
Sistemic symptoms



Tumor chemotherapy radiotherapy,

Gutstein Cancer 2001,Cleeland Cancer 2003

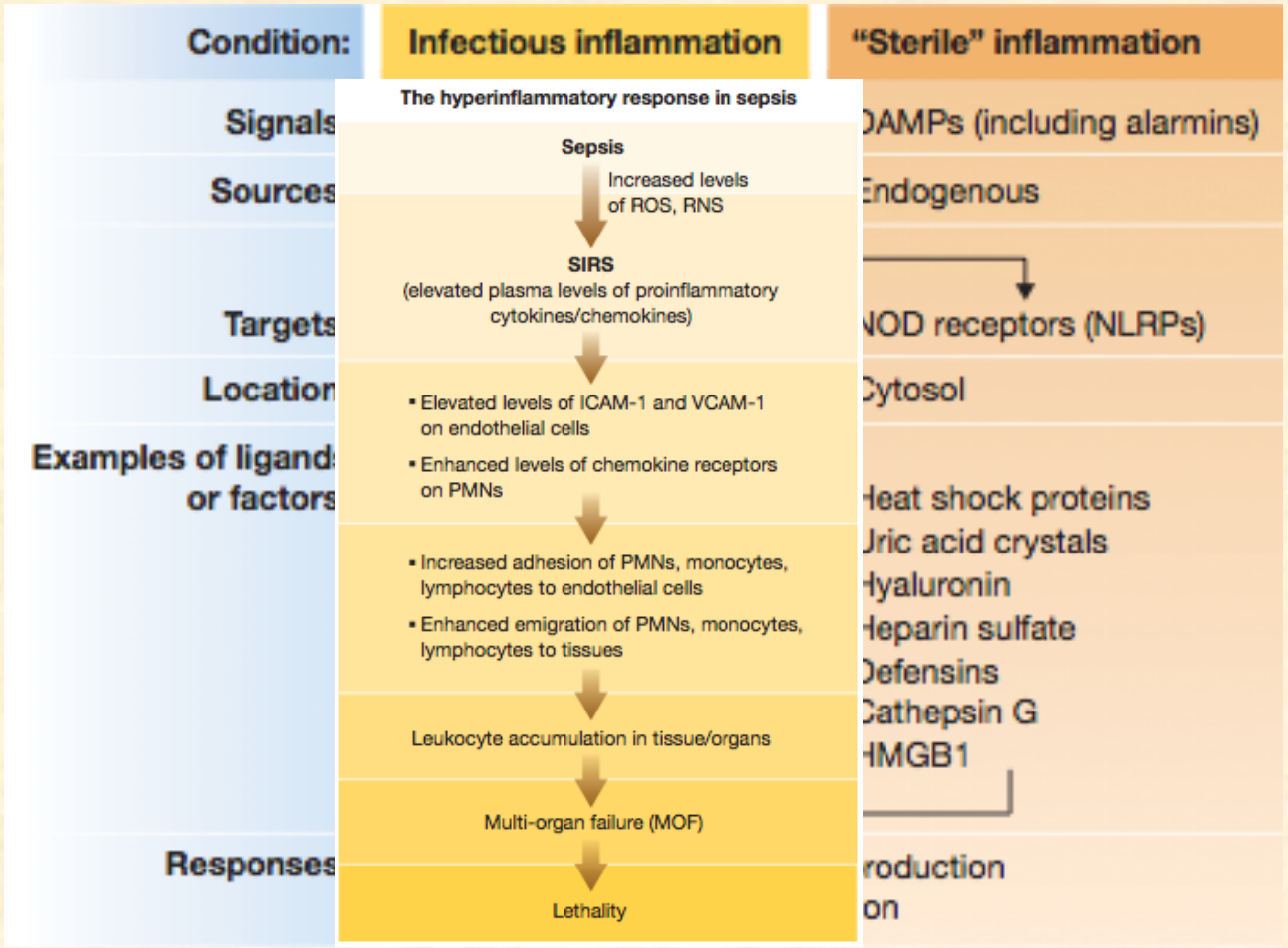
Sistemic symptoms



New approaches to the study of sepsis

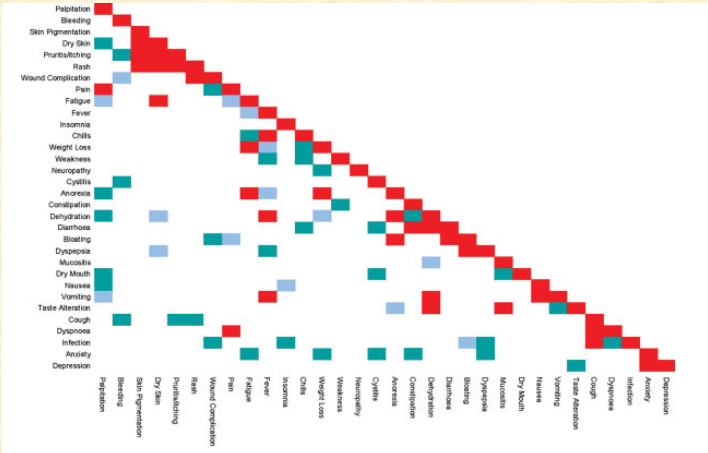
Peter A. Ward

EMBO Mol Med (2012) 4, 1234–1243



Symptom clusters: myth or reality?*

Application of Distance Matrices to Define Associations Between Acute Toxicities in Colorectal Cancer Patients Receiving Chemotherapy



Local toxicities correlate with distant toxicities

TARGET-INFLAMMATION THERAPY

Apoptotic and inflammation markers in oral mucositis in head and Neck cancer patients receiving radiotherapy: preliminary report
Xanthinaki A , Supp Care Cancer 2008

Effect of selective inhibitors of inflammation on oral mucositis: Preclinical studies
Haagen, Rad Oncol 2009

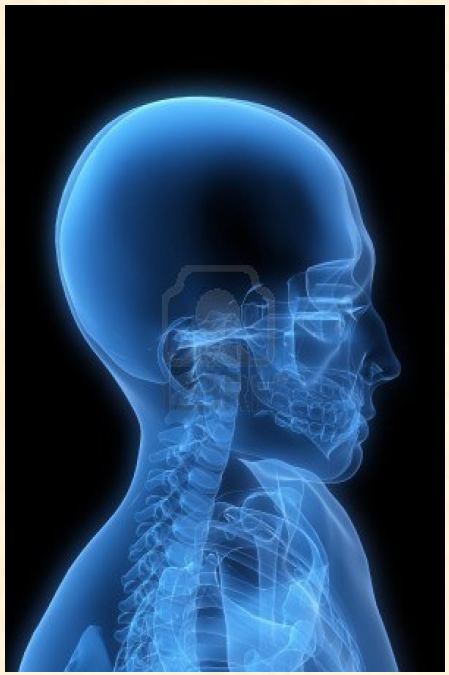
Toll-like Receptor 5 Agonist Protects Mice From Dermatitis and Oral Mucositis Caused by Local Radiation: Implications for Head-and-Neck Cancer Radiotherapy

Lyudmila G. Burdelya, 2012

SYMPTOMS

dermatitis mucositis

xerostomia



pain

dysphagia

depression insomnia

cachexia

anemia

neutropenia

fever

SIRS

Prevalence and correlates of symptoms and uncertainty in illness among head and neck cancer patients receiving definitive radiation with or without chemotherapy

Mary Ellen Haisfield-Wolfe · Deborah B. McGuire ·

Support Care Cancer (2012) 20:1885–1893

Table 2 Memorial symptom assessment scale scores for presence and symptom distress at baseline and weeks 5, 9, and 12

Symptoms	Baseline		Week 5		Week 9		Week 12	
	(*n*=21) *n* (%) Presence Number	(*n*=21) Mean (SD) Symptom distress Range 0–4	(*n*=21) *n* (%) Presence Number	(*n*=21) Mean (SD) Symptom distress Range 0–4	(*n*=21) *n* (%) Presence Number	(*n*=21) Mean (SD) Symptom distress Range 0–4	(*n*=21) *n* (%) Presence Number	(*n*=21) Mean (SD) Symptom distress Range 0–4
Change in the way food tastes	8 (38%)	0.5 (0.9)	18 (86%)	2.1 (1.5)	16 (80%)	2.1 (1.7)	13 (62%)	1.1 (1.5)
Change in skin	8 (38%)	0.8 (1.3)	17 (71%)	0.9 (1.2)	16 (80%)	1.6 (1.6)	9 (43%)	0.5 (0.9)
Dry mouth	17 (71%)	0.6 (0.9)	19 (91%)	1.9 (1.4)	19 (95%)	1.8 (1.3)	19 (91%)	1.6 (1.4)
Difficulty swallowing	8 (38%)	0.6 (1.0)	21 (100%)	2.0 (1.2)	18 (90%)	2.1 (1.2)	10 (48%)	1.7 (1.4)
Feeling irritable	8 (38%)	0.7 (1.2)	12 (57%)	0.9 (1.3)	10 (50%)	0.9 (1.2)	10 (48%)	1.0 (1.4)
Lack of appetite	7 (33%)	0.7 (1.2)	19 (91%)	2.1 (1.1)	16 (80%)	1.7 (1.4)	10 (48%)	1.2 (1.5)
Lack of energy	15 (71%)	1.1 (1.4)	19 (91%)	1.8 (1.3)	19 (95%)	1.6 (1.3)	15 (71%)	1.5 (1.4)
Mouth sores	2 (10%)	0.1 (0.9)	12 (57%)	0.8 (0.9)	14 (70%)	1.5 (1.4)	7 (33%)	0.4 (0.8)
Pain	13 (62%)	1.1 (1.4)	17 (81%)	1.6 (1.1)	17 (85%)	1.9 (1.2)	19 (91%)	1.6 (1.0)
Weight loss	9 (43%)	0.8 (1.3)	19 (91%)	1.3 (1.4)	16 (80%)	1.5 (1.5)	10 (48%)	0.8 (1.3)
Worrying	12 (62%)	1.1 (1.2)	8 (38%)	0.4 (0.8)	6 (30%)	0.4 (0.8)	7 (33%)	0.9 (1.39)

Supportive care needs in newly diagnosed oral cavity cancer patients receiving radiation therapy

Shu-Ching Chen[1,6]

Psycho-Oncology 22: 1220–1228 (2013)

Table 2. Changes of physical symptom severity and supportive care needs ($n = 82$)

Variable	T0[a] $\bar{X}$(SD)	T1 (1 month) $\bar{X}$(SD)	T2 (2 months) $\bar{X}$(SD)	T3 (3 months) $\bar{X}$(SD)	T4 (6 months) $\bar{X}$(SD)	Within subject effect	
Overall physical symptom severity (SSS)	3.2(1.3)	5.0(2.0)	6.1(1.8)	3.0(1.1)	1.8(0.6)	$F_{(4,\ 240.5)} = 173.8,\ p < 0.001$	T2 > T1 > T0 > T3 > T4
Functional status (KPS)	89.4(3.3)	88.3(4.4)	87.8(4.7)	89.5(2.7)	89.8(2.2)	$F_{(4,\ 59.5)} = 7.2,\ p < 0.001$	T4,T3,T0 > T1,T2
Supportive care needs (CNQ-SF-hn)	40.9(12.4)	39.7(13.3)	42.4(12.9)	31.5(11.0)	30.2(9.5)	$F_{(4,\ 2630.6)} = 25.2,\ p < 0.001$	T2,T0,T1 > T3 > T4
Physical/daily living need	30.2(11.0)	34.9(13.6)	37.4(13.4)	28.1(9.1)	26.7(8.3)	$F_{(4,\ 1678.4)} = 13.9,\ p < 0.001$	T2,T1 > T0,T3 > T4
Psychological need	43.2(15.1)	43.0(15.8)	43.9(15.8)	32.4(16.7)	33.7(15.4)	$F_{(4,\ 2659.9)} = 15.2,\ p < 0.001$	T2,T0,T1 > T4,T3
Interpersonal communication need	35.8(18.7)	33.2(16.9)	31.9(17.7)	28.2(14.9)	31.3(13.9)	$F_{(4,\ 638.0)} = 2.8,\ p < 0.05$	T0 > T1,T2,T4 > T3
Patient care/support need	34.8(18.4)	37.2(18.8)	46.2(23.0)	29.4(14.2)	25.7(14.2)	$F_{(4,\ 5096.1)} = 20.6,\ p < 0.001$	T2 > T1,T0 > T3 > T4
Health system/information need	48.9(21.0)	38.5(21.6)	40.0(15.8)	32.4(14.0)	31.3(14.0)	$F_{(4,\ 3812.0)} = 14.7,\ p < 0.001$	T0 > T2,T1 > T3,T4
Head and neck cancer-specific need	48.8(19.5)	46.3(19.4)	49.5(20.6)	37.6(13.6)	38.7(13.4)	$F_{(4,\ 2601.1)} = 10.7,\ p < 0.001$	T2,T0,T1 > T4,T3

SSS, Symptom Severity Scale; KPS, Karnofsky Performance Status; CNQ-SF-hn, Cancer Needs Questionnaire Short Form, head and neck.

[a]Patients were followed up from pretreatment through the first 3 months of receiving radiation treatment (RT; pretreatment and 1, 2, and 3 months from receiving RT). T0 = RT began (reference group), T1 = 1 month after beginning RT, T2 = 2 months after beginning RT, T3 = 3 months after beginning RT, and T4 = 6 months after beginning RT.

Higher educational level
More severe eating difficulty
Worse appetite and fatigue
Higher baseline ansiety

Higher overall supportive care needs

Evidence literature-based

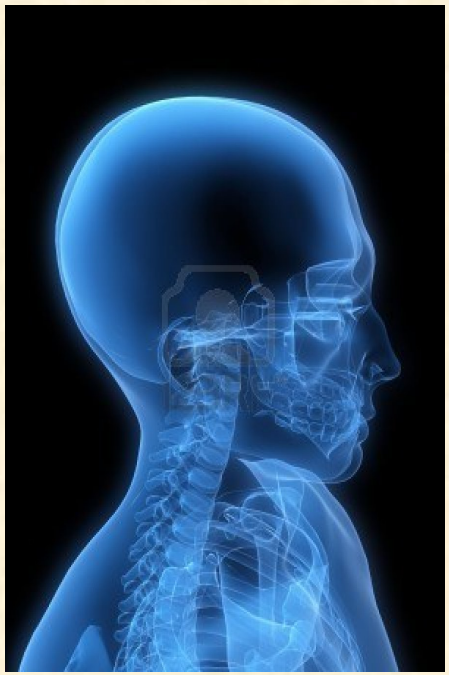
mucositis

dermatitis

xerostomia

pain

dysphagia



depression

insomnia

cachexia

anemia

neutropenia

fever

SIRS

Assessment scales

National Cancer Institute (NCI)-Common Toxicity Criteria (CTC version 4.0)
Toxicity criteria of the Radiation Therapy Oncology Group (RTOG)
European Organization for Research and Treatment of Cancer (EORTC), World Health Organization (WHO)
Oral Mucositis Assessment Scale (OMAS), M. D. Anderson symptom inventory, head and neck module
OMQD scale.

No superiority of one scale over another

adverse events reported by physicians are less accurate
than those reported by patients (patient-reported outcome (PRO))

need to assess mucositis with both modalities.

For the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) 2013

Systematic review of amifostine for the m… …oral mucositis in cancer patients

Systematic review of laser ar… …herapy for the management of ors… … cancer patients

Systematic review … …erapy for management of oral mucositi… …ncer therapy

Syster… … cytokines and growth factors for th… …nt of oral mucositis in cancer patients

Magical mouthwhashes, barrier agents, aloe vera, glutamine, pure natural honey, topical misoprostol

No utility for the prevention of mucositis

Systematic review of anti-inflammatory agents for the management of oral mucositis in cancer patients

Nicolatou-Galitis, MASSC 2013

Prostaglandine,topical misoprostol, Diphenhydramine , Indomethacin PO Betamethasone rinse, Prednisone tablets given orally, Mesalazine topical gel, Flurbiprofen tooth patch, Colchicine mouthwash,

No utility for the prevention of mucositis

New guideline: The panel recommends benzydamine mouthwash for the prevention of oral mucositis in patients with head and neck cancer receiving moderate- dose radiation therapy (up to 50 Gy), without concomitant chemotherapy.

Systemic antibiotics or antiviral agents

No data about their utility in mucositis prophilactic intent in absence of neutropenia

Only in case of overt infection

Table 2. Examples of Mucositis Guidelines

Organization (Alphabetical Order)	URL
ASCO	http://jco.ascopubs.org/content/27/1/127.full
ESMO	http://annonc.oxfordjournals.org/content/22/suppl_6/vi78.full
MASCC/ISOO	http://www.mascc.org/mc/page.do?sitePageId=88037
NCCN	http://www.nccn.org/JNCCN/PDF/mucositis_2008.pdf
ONS	http://www.ons.org/Research/PEP/Mucositis
RTOG	http://www.onlinecancereducationforum.com/OCEF/Oral%20mucositis%20in%20head%20and%20neck%20cancer.pdf
Atlantic Provinces Pediatric Hematology Oncology Network	http://www.apphon-rohppa.com/en/guidelines/mucositis-guidelines
Meta-analysis: Cochrane review (prevention)	http://summaries.cochrane.org/CD000978/interventions-for-preventing-oral-mucositis-for-patients-with-cancer-receiving-treatment
Meta-analysis: Cochrane review (treatment)	http://summaries.cochrane.org/CD001973/interventions-for-treating-oral-mucositis-for-patients-with-cancer-receiving-treatment

Abbreviations: ASCO, American Society of Clinical Oncology; ESMO, European Society for Medical Oncology; MASCC/ISOO, Mucositis Study Group of Multinational Association for Supportive Care in Cancer/International Society of Oral Oncology; NCCN, National Comprehensive Cancer Network; ONS, Oncology Nursing Society; RTOG, Radiation Therapy Oncology Group.

Updated Clinical Practice Guidelines for the Prevention and Treatment of Mucositis

MASCC 2007

Management of oral and gastrointestinal mucositis: ESMO Clinical Practice Guidelines

D. E. Peterson[1], R.-J. Bensadoun[2] & F. Roila[3]
On behalf of the ESMO Guidelines Working Group*

Basic oral care

dental examination and any required treatment (including extraction of diseased teeth) before they start radiotherapy

mouthwashes

Benzidamine
Clorexidine
Na bicarbonate

No alcohol, no perfume

with and after normal daily toothbrushing with a soft brush;

IMRT

IS THERE A "MUCOSA-SPARING" BENEFIT OF IMRT FOR HEAD-AND-NECK CANCER?

Sanguineti, 2006

30 Gy maximum dose objective on the mucosa

20% and 12% mean absolute reduction in % of mucosa volume exposed to a dose equivalent to 30 Gy ($p<0.01$) and 70 Gy ($p<0.01$)
30% reduction in the volume of the mucosa in the high dose region.

No detrimental effect on the coverage of other regions of interest

1) "mucosal" contouring
2)"stress" mucosal avoidance weighted against the potential increase of dose to other OARs.

Evidence literature-based

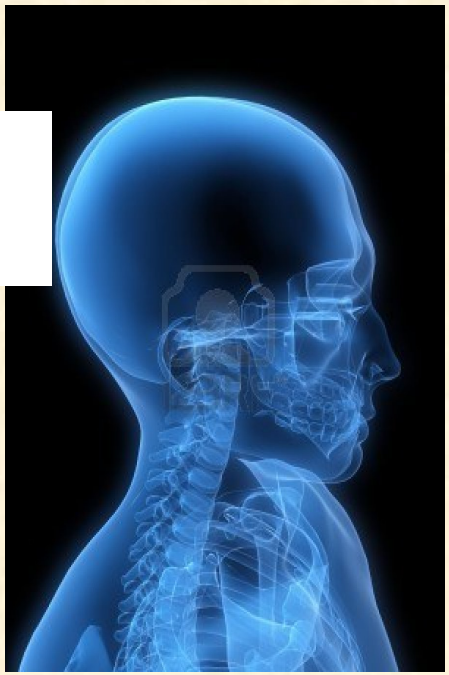
depression

insomnia

mucositis

dermatitis

xerostomia



pain

dysphagia

cachexia

anemia

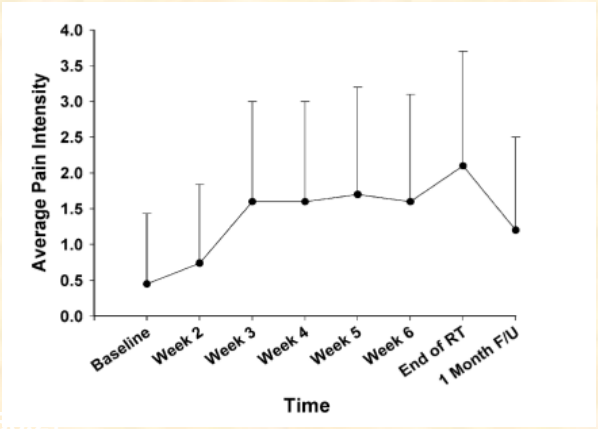
neutropenia

fever

SIRS

pain

Prevalence
pre-tx: 49.5%
during tx: 80.8%;
end of tx: 69.7%
6 months post-tx: 36.2% (0.08) [14.2–58.2]



Epstein, Support Care Cancer (2010)

All patients developed pain due to RT-induced mucositis

Wong, Journal of Pain and Symptom Management, 2006

Updated Clinical Practice Guidelines for the Prevention and Treatment of Mucositis

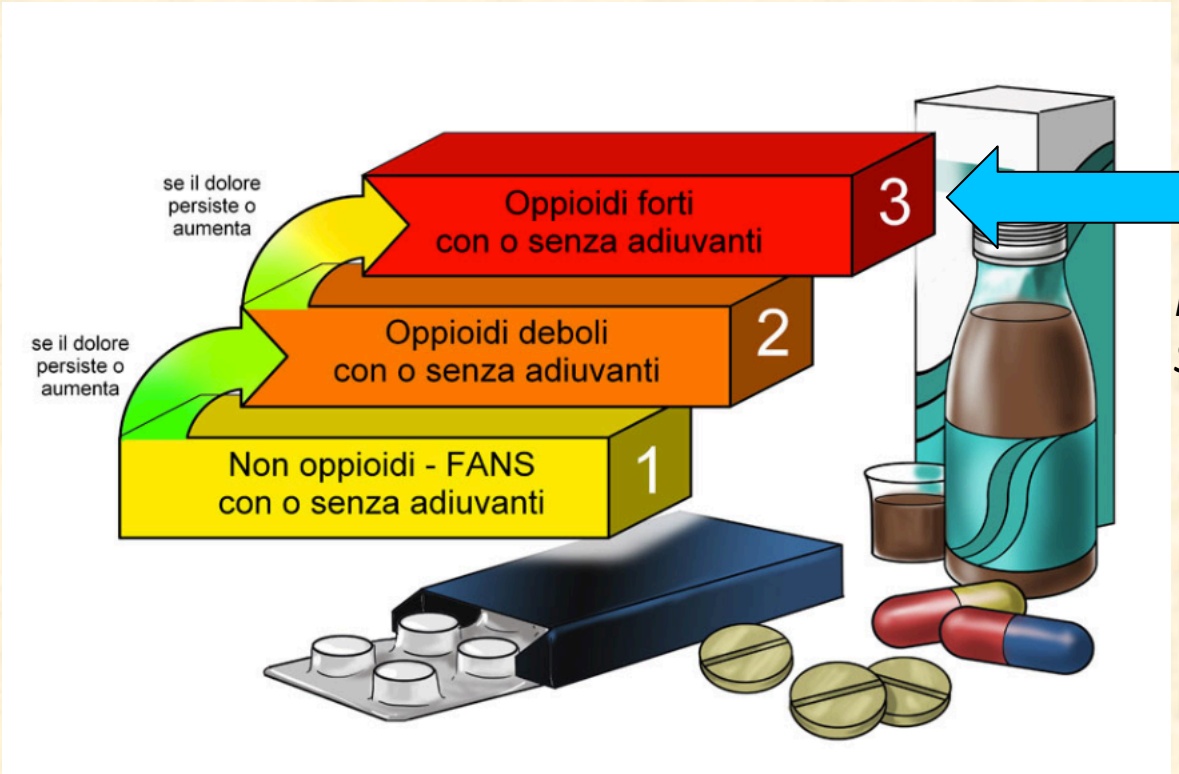
MASCC 2007

2. The panel recommends patient-controlled analgesia with morphine as the treatment of choice for oral mucositis pain in patients undergoing HSCT. Regular oral pain assessment using validated instruments for self-reporting is essential.

Management of oral and gastrointestinal mucositis: ESMO Clinical Practice Guidelines

D. E. Peterson[1], R.-J. Bensadoun[2] & F. Roila[3]
On behalf of the ESMO Guidelines Working Group*

Patient-controlled analgesia with morphine is recommended as the treatment of choice for oral mucositis pain in patients undergoing HSCT [I, A]. Regular oral pain assessment using validated instruments for self-reporting is essential.



Maltoni 2005
Stenstrom 2011

Pain and functional impairment because of mouth and throat soreness increased during the course of therapy despite the use of opioid analgesics in 64 (85%) of the patients.

Murphy, J Pain Symptom Manage 2009

Topical morphine is effective for relieving pain and it's more effective than topical lidocaine

Cerchietti 2002

Transdermal fentanyl has proven to be effective

Sloan 1998; Mystakidou 2002; Menahem 2004

Transmucosal intranasal route administration of fentanyl is a rationale approach to odynophagia treatment.

Grassin-Delyle 2012; Davies A 2011

comprehensive and detailed clinical guidelines concerning pharmacological treatment of OM-induced pain including pain assessment, choice of drugs, administration routes, pharmaceutical forms, and evaluation of effect are lacking.

Evidence literature-based

depression

insomnia

mucositis

dermatitis

xerostomia

pain

dysphagia

cachexia

anemia

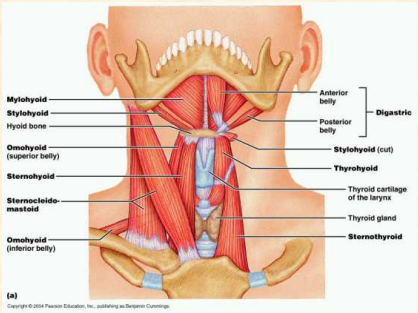
neutropenia

fever

SIRS

dysphagia

Six cranial nerves and over 25 muscles are involved, and any neurological or structural defect affects swallowing. This may result in dysphagia (swallowing dysfunction), a symptom indicating a delay in the passage of solids or liquids from the oral cavity to the stomach.



Pre treatment 4%-40%
During treatment all patients
Post treatment 25-40%

Dysphagia is one of the most important cause of therapy interruption

Approximately, one third of dysphagic patients develop aspiration pneumonia requiring treatment, with mortality rates ranging between 20% and 65%.

Russi 2012

Dysphagia scales

patient- and clinician-rated scales

SWAL-QOL and SWAL-CARE
MD Anderson Dysphagia Inventory (MDADI
OMWQ-HN
EORTC QLQ C-30 (QLQ H&N35)
FACT-H&N)
UW-QOL-R
HNCI

HNQOL
OMWQ-HN
VHNSS
SSQ
CTCAE
EAT-10
RTOG/EORTC

discrepancy
with respect to the correlation
between subjective and objective swallowing evaluation
Combining several subjective and objective evaluation techniques
providing complimentary information
is considered useful.

Dysphagia/swallowing disfunctions pre treatment assessment

All patient

pathologic swallowing: amount and incidence of penetration and aspiration increased risk of aspiration pneumonia or airway obstruction.

Asymptomatic patient

Aspiration may be ‘‘silent’’

.

High-risk patients
Larinx, hypopharynx
Base of tongue
Pharyngeal wall
Elderly patienys
Neck dissection (after CRT)
Advanced T stage

Caudell 2009; Machtay 2008

Total dysphagia risk score
Advanced T
Bilateral neck irradiation
Weight loss
Primary tumor site
Hyperfractionation
Concurrent CRT

Langedjik 2009

Murphy’s Triggers symptoms for dysphagia evaluation.

Inability to control food liquids or saliva within the oral cavity
Pocketing of food in cheek
Excessive chewing
Drooling
Coughing choking or throat clearing before during or after swallowing
Abnormal vocal quality after swallowing; ‘‘wet’’ or ‘‘gurgly’’ voice
Build-up or congestion after a meal
Complaint of difficulty swallowing
Complaint of food ‘‘sticking’’ in throat Nasal regurgitation
Weight loss

Dysphagia/swallowing disfunctions assessment

Diagnostic performance of the screening methods to detect dysphagia.

Bedside test	Endpoint of index text	Endpoint of reference test	Sensitivity (%)	Specificity (%)
Trial swallowing using water test[32–34]	Coughing, choking or voice change, wet voice	Aspiration and penetration	47–85	63–88
Trial swallow using different viscosity[31,35]	Cough and throat clear	Aspiration	78	58
	Gurgly voice		41	76
	Wet voice		50	63
	Reduced laryngeal elevation		66	57
	Multiple swallows		58	57
	Spontaneous cough		68	82
	Subjective estimate of aspiration[32]		78[35]–88[32]	63[35]–30[32]
Oxygen desaturation[33,34,36]	>2% desaturation	Aspiration (or penetration[33,152])	56–87	39–97
Swallow test combining water test with oxygen desaturation[33,34]	Coughing, voice change or >2% desaturation	Aspiration (or penetration)	94 and 98	63–70
Combination of clinical conditions[35]	Spontaneous cough, subjective estimate of aspiration, wet voice	Aspiration	91	47

Low sensibility
Low specificity

Russi, 2012

Dysphagia/swallowing disfunctions assessment

Fiberoptic endoscopic evaluation (FEES)
Videofluoroscopic modified barium swallow (VMBS)

Main parameters of VFSS – MBS.[44]

Acronyms	Index	Definition
OTT	Oral transit time	The time it takes the bolus to move through the oral cavity, measured from the first backward movement of the bolus until the head of the bolus passes the point where the ramus of the mandible crosses the tongue base (Usually < 1 s)
PTT	Pharyngeal transit time	The time required for the bolus to move through the pharynx, measured from the time the head of the bolus passes the ramus of the mandible until the tail of the bolus leaves cricopharyngeal region (Usually < 1 s)
DLC	Duration of laryngeal closure	The length of time the laryngeal between the arytenoid and base of epiglottis is closed during swallow
PDT	Pharyngeal delay time	The time required to trigger the pharyngeal swallow, measured from the time the head of the bolus passes the ramus of the mandible until the onset of laryngeal elevation
DCO	Duration of cricopharyngeal opening	The length of time the cricopharyngeal region is open during the swallow
ORES	Oral residue	Approximate percentage of oral residue after first swallow on a bolus
PRES	Pharyngeal residue	Approximate percentage of pharyngeal residue after first swallow on a bolus
ASP	Percentage of aspirated bolus	Approximate per cent aspirated
OPSE	Oropharyngeal swallow efficiency	The percentage of the bolus swallowed divided by the bolus transit time, from the oral cavity through the cricopharyngeus: [100 – (PRES + ORES + ASP)]/(OTT + PTT) In the calculation of OPSE, the amount aspirated and the amount left unswallowed in the mouth or pharynx is subtracted from the percentage swallowed

standardized protocol for VMBS 'Larynx preservation consensus panel''

"Swallowing Performance Status Scale'' (SPS):
presence and severity of disphagia and aspiration risk

''8-point Penetration–Aspiration Scale'' (8p-PAS):
a penetration-aspiration score >6 is considered suggestive for aspiration.

Russi 2012

A systematic review of interventions for eating and drinking problems following treatment for head and neck cancer suggests a need to look beyond swallowing and trismus

Nadine Cousins [a], Fiona MacAulay [b], Heidi Lang [d], Steve MacGillivray [c], Mary Wells [d,*]

Oral Oncolgy 2013

Exercises directed at swallowing and trismus, with or without additional therapies, are likely to improve functional outcomes in patients with head and neck cancer, particularly if they are introduced before treatment starts

a recent cost- effectiveness analysis suggests that preventative swallowing exercises result in less dependence on tube feeding and fewer hospital admission days than usual care

NUTRITION

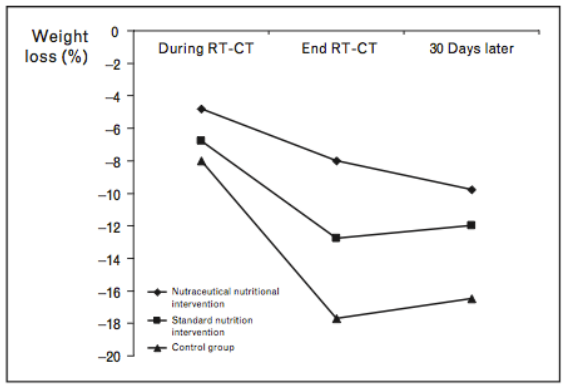
Early nutritional intervention improves treatment tolerance and outcomes in head and neck cancer patients undergoing concurrent chemoradiotherapy

Paccagnella 2006

Malnourished patients

Before RT or CRT 3-52%
During RT and CRT 44-88%.

Figure 2 Percentage weight loss during chemoradiotherapy treatment



Conclusions **Early nutrition intervention in patients with HNC receiving chemoradiotherapy resulted in an improved treatment tolerance and fewer admissions to hospital. This result suggests that nutritional intervention must be initiated before chemoradiotherapy, and it needs to be continued after treatment completion.**

Critical weight loss is a major prognostic indicator for disease-specific survival in patients with head and neck cancer receiving radiotherapy

Langius 2013

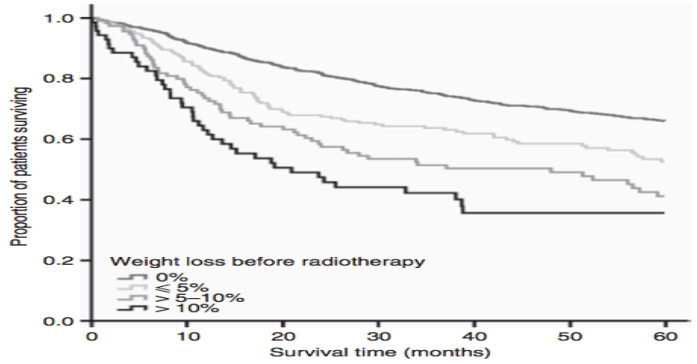


Figure 2. Kaplan–Meier survival plot of overall survival by weight loss category before radiotherapy (log-rank test: $P<0.001$).

Conclusion: Weight loss both before and during radiotherapy are important prognostic indicators for 5-year DSS in HNC patients. Randomised studies into the prognostic effect of nutritional intervention are needed.

NUTRITION

Nutritional Considerations for Head and Neck Cancer Patients: A Review of the Literature

Alshadwi, 2013

Conclusion: Nutritional interventions should be initiated before cancer treatment begins and these interventions need to be ongoing after completion of treatment to ensure optimal outcomes for patients. A nutritional assessment must be part of all comprehensive treatment plans for patients with head and neck cancer. Alternative medical interventions, such as immune-enhancing nutrients or anticytokine pharmaceutical agents, also may be effective as adjuvant therapies, but more research is needed to quantify their clinical effect.

Table 1. MALNUTRITION CLASSIFICATION BASED ON WEIGHT MEASUREMENTS

Index	Mild	Moderate	Severe	Appropriate Weight
Weight loss (% IBW)*	<10	10-20	>20	>10
BMI (kg/m^2)	17-18.5	16-16.9	<16	18.5-25

Abbreviations: BMI, body mass index; IBW, ideal body weight.
* Patient's weight loss as a percentage (% IBW).

Table 2. BIOMARKERS USED TO ASSESS PATIENT'S NUTRITIONAL STATUS

Index	Mild	Moderate	Severe
Albumin (g/dL)	3.5-2.8	2.7-2.1	<2.1
Transferrin (mg/dL)	200-151	150-100	<100
Prealbumin (mg/dL)	15-10	9.9-5	<5
Total lymphocyte count (per mm^3)	1,800-1,500	1,499-900	<900

Nutritional intervention for improving treatment tolerance in cancer patients

Agostino Paccagnella[a], Ildamaria Morassutti[a] and Giovanni Rosti[b]

Current Opinion in Oncology 2011,

Oral Nutrition Supplements

Risk of malnutrition

1) Anorexia and/or mild dysphagia not resolvable within 10-15 days
Calorie intake <50% of requiremets

2) Malnourished patients (BMI<18 Kg/m2)
with anorexia and/or mild dysphagia,
loss of 5% of their normal weight
in the previuos 6 months
calorie Intake <50% of requirements

20% protein (1.2 – 2 g/kg/day)
20% fats
50 – 60% carbohydrates.

Arends,2006;Barak 2002

Enteral nutrition treatment

Ability to take food

1)Normally nourished patients or those at risk of malnutrition with anorexia and/or severe dysphagia or with severe o moderate hypercatabolism calorie intake <50% of requiremets for at least 10-15 days

Rate of weight loss

1) Malnourished patients (BMI<18)
weight loss of 10% in the previuos 6 months
calorie Intake <50% of requirements for at least 5-10 days

NGT/PEG

Parenteral nutrition treatment

Only in specific situation
Malnourished patients
Severe mucositis
Severe enteritiis

PN is ineffective and probably harmful in patients in whom there is no gastrointestinal reason for intestinal failure (Grade A).
PN is recommended in patients with severe mucositis or severe radiation enteritis (Grade C).

Bozzetti 2009

The choice of Feeding Tubes

NGT vs PEG

the timing of their use

Prophylactic vs Reactive Use

their effect on

weight loss,
hospitalizations,
quality of life (QOL)
long-term functional outcomes

the timing of the NGT/PEG

Prophylactic vs Reactive Use

Preventing weight loss,
reducing rates of dehydration
and hospitalizations,
avoiding treatment breaks
perhaps improving overall
disease response

VS

Early oral nutritional supplements

Close monitoring

NGT or PEG limited to
those patients who are
unable to maintain their
nutritional requirements.

Conflicting results

FOR
Better weight preservation
Less hospitalization
Improved QOL

AGAINST
longer FT dependence,(>1 year)
increase the risk of late esophageal strictures

AGAINST
FT rates >70%
FT rates 40%50%

FOR
Spare patients who do not need
enteral feeding tubes
Lower late dysphagia
Shorter duration of tube dependence

The choice of Feeding Tubes

NGT vs PEG

Enteral feeding methods for nutritior ment in patients with head and neck cancer ated with radiotherapy and/or chemot view)

Nugent B, Lewis S,

The Cochrane Library

NO DIFFERENCES

OCHRANE LABORATION®

Randomized study ous endoscopic gastrostomy versus nasogastric tubes for enteral feed id neck cancer patients treated with (chemo)radiation.

Corry, 2008

33 pts

Dysphagia/swallowing disfunctions nutrition

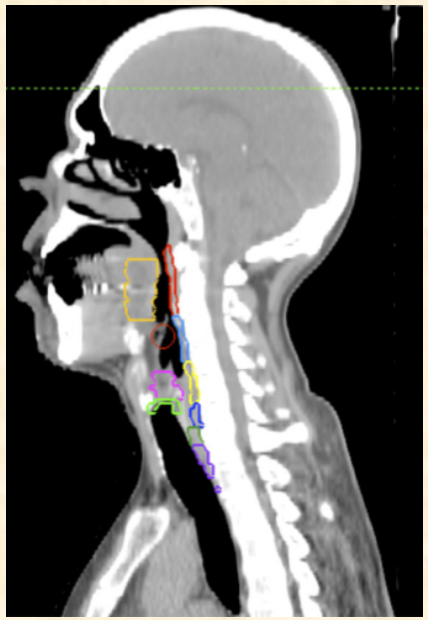
No data about the otimal timing and method of artificial Nutrition (NSG vs PEG)

Patients should be encouraged to continue to swallow

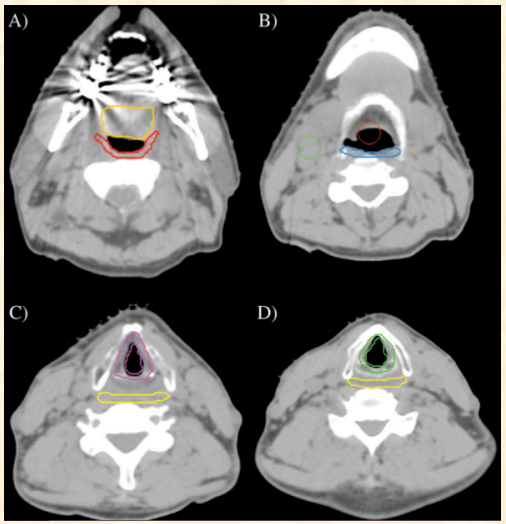
Stop the artificial nutrition as soon as possible

Dysphagia-Aspiration Related Structures Radiation-induced Swallowing Dysfunction (SWOARs).

Red, superior pharyngeal constrictor; light blue, middle pharyngeal constrictor; yellow, inferior pharyngeal constrictor; dark blue, cricopharyngeus; dark green, esophageal inlet; purple, cervical esophagus; orange, base of tongue; pink, supraglottic larynx; and light green, glottic larynx



A) the base of tongue and superior pharyngeal constrictor,
(B) middle pharyngeal constrictor,
(C) supraglottic larynx and inferior pharyngeal constrictor, and
(D) glottic larynx and inferior pharyngeal constrictor delineated



Christianen, 2011

mean dose constraints or treatment planning goals of <40 Gy for the glottic/supraglottic larynx and 55 Gy for the pharyngeal constrictors seem reasonable and should be effective at reducing the risk of long-term dysphagia.

IMRT

WEEKLY DOSE–VOLUME PARAMETERS OF MUCOSA AND CONSTRICTOR MUSCLES PREDICT THE USE OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY DURING EXCLUSIVE INTENSITY-MODULATED RADIOTHERAPY FOR OROPHARYNGEAL CANCER

Sanguineti, 2011

Conclusions: The risk of PEG use is drastically reduced when OM V9.5–V10 Gy/week is <50–60 cm3. These data warrant prospective validation.

Predictors of PEG dependence after IMRT ± chemotherapy for oropharyngeal cancer

Sanguineti, 2013

Conclusions: OM V9.5 Gy/week and CHT/PEG_policy modulate the risk of early PEG dependence. For longer PEG dependence, larynx V50 (or D_mean) and SC D_mean are highly predictive, suggesting that the fibrosis of constrictors and larynx is the main cause.

Evidence literature-based

depression insomnia

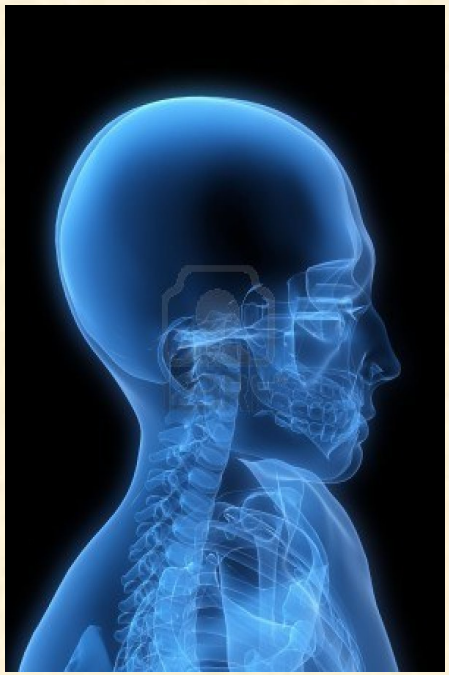
mucositis

dermatitis

cachexia

anemia

xerostomia



neutropenia

pain

fever

dysphagia

SIRS

Clinical practice guidelines for the prevention and treatment of acute and late radiation reactions from the MASCC Skin Toxicity Study Group

Wong, 2013

Dermatitis scales

Table 1 Frequently used grading of acute radiation dermatitis

	RTOG	LENT/SOMA	CTCAE 4.0
0	No change from baseline/no symptoms	No change from baseline/no symptoms	Non change over baseline/no symptoms
1	Follicular, faint or dull erythema, epilation, dry desquamation, decreased sweating	Minor symptoms present that require no treatment	Faint erythema or dry desquamation
2	Tender or bright erythema, patchy moist desquamation, moderate edema	Moderate symptoms present that require conservative treatment	Moderate to brisk erythema, patchy moist desquamation, mostly confined to skin folds and creases, moderate edema
3	Confluent moist desquamation other than skin folds, pitting edema	severe symptoms, which have a significant negative impact on daily activities, and which require more aggressive treatment	Moist desquamation other than skin folds and creases, bleeding induced by minor trauma or abrasion
4	Ulceration, hemorrhage necrosis	Irreversible functional damage, necessitating major therapeutic intervention	Life-threatening consequences, skin necrosis or ulceration of full thickness dermis, spontaneous bleeding from involved site, skin graft indicated
5	Death related to treatment effects	Death or loss of organ	Death

limited evidence to support any of these scales, use of more than one scale should be considered

Clinical practice guidelines for the prevention and treatment of acute and late radiation reactions from the MASCC Skin Toxicity Study Group

PREVENTION

STRONG RECOMMENDATION FOR

the prophylactic use of gentle washing with water, with or without mild soap/shampoo to reduce the worse toxicity grade experienced

STRONG RECOMMENDATION AGAINST

the prophylactic use of aloe vera or trolamine

NO RECOMMENDATION POSSIBLE

Topical sulcrate and its derivatives, hyaluronic acid, ascorbic acid, silver leaf dressing, LED, Theta-Cream, dexpanthenol, and calendula; oral proteolytic enzymes, sucralfate, zinc, and pentoxifylline

Clinical practice guidelines for the prevention and treatment of acute and late radiation reactions from the MASCC Skin Toxicity Study Group

TREATMENT

NO RECOMMENDATION POSSIBLE

hydro- colloid dressing
vapor permeable dressing (TegadermTM)
Gentian violet
sucralfate cream,
hydrocortisone 1 %,
honey,
trolamine

in reducing time to recovery.

Level of evidence II, Recommendation Grade C

IN-FIELD BIO-RADIATION SKIN TOXICITY

Management of radiation dermatitis in patients receiving cetuximab and radiotherapy for locally advanced squamous cell carcinoma of the head and neck: proposals for a revised grading system and consensus management guidelines

Bernier, 2011

increase of 5% in the incidence of grade > 3 radiation dermatitis in the cetuximab arm

Bonner 2006

A single-center non randomized comparison

incidence of grade 3/4 dermatitis

radiotherapy plus cetuximab versus CRT
(18.0% versus 2.1%; P = 0.014)

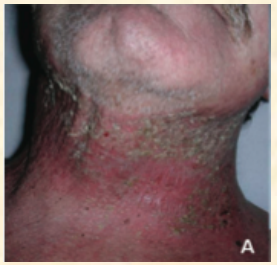
treatment compliance

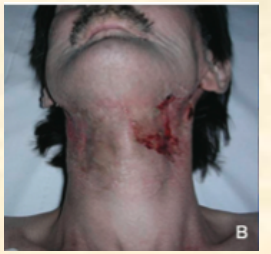
radiotherapy plus cetuximab versus CRT
(noncompliance 12.0% versus 37.5%, P = 0.003)

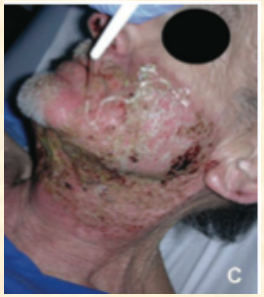
IN-FIELD BIO-RADIATION SKIN TOXICITY

Management of radiation dermatitis in patients receiving cetuximab and radiotherapy for locally advanced squamous cell carcinoma of the head and neck: proposals for a revised grading system and consensus management guidelines

	Grade of dermatitis associated with radiation-based therapy			
	Grade 1	Grade 2[a]	Grade 3[a]	Grade 4[a]
Definition: NCI–CTCAE, v4.03 dermatitis radiation	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	Life-threatening consequences; skin necrosis or ulceration of full-thickness dermis; spontaneous bleeding from involved site; skin graft indicated
Definition: Proposed modification of NCI–CTCAE, v4.03	Faint erythema or dry desquamation	Moderate to brisk erythema and/or dry desquamation; patchy moist desquamation, or non-hemorrhagic crusts mostly confined to skin folds and creases	Moist desquamation or hemorrhagic crusts; non-hemorrhagic crusts other than in skin folds and mostly confined to skin folds and creases; bleeding induced by minor trauma or abrasion; superinfection requiring oral antibiotics	Life-threatening consequences; extensive confluent hemorrhagic crusts or ulceration (>50% of involved field); extensive spontaneous bleeding from involved site (>40% of the involved site); skin necrosis or ulceration of full-thickness dermis or any size ulcer with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures with or without full-thickness skin loss[b]; skin graft indicated; ulceration associated with extensive superinfection with i.v. antibiotics







Impact of AEs on patient's activity daily living
AEs seriouness (level of treatment or necessity of hospitalization

IN-FIELD BIO-RADIATION SKIN TOXICITY

Management of dermatitis in patients with locally advanced squamous cell carcinoma of the head and neck receiving cetuximab and radiotherapy

Gutierrez 2012

	Grade of radiation dermatitis			
	Grade 1	Grade 2	Grade 3	Grade 4
Follow-up	Weekly	Consider twice-weekly	Consider daily	Daily
Management	General measures: • Skin hygiene twice a day, using pH 5 (pH neutral) soaps and/or showering oils for sensitive skin. • Topical moisturizers (Ureadin®, Avéne Trixéra®, Radiocare®).	(1) *Dry desquamation without crust*: • Topical antiseptic (chlorhexidine 0.5–1%, polyhexanide solution or sodium hypochlorite 1–3%) and antibiotics (erythromycin, clindamycin or mupirocin) at any sign of superinfection. They are used for the prevention of more severe reactions. • Consider glucocorticosteroid cream (betamethasone 0.1%) (Celestoderm®), methylprednisolone aceponate cream 0.1% (Adventan®), etc. for a limited period. (2) *Moist desquamation in skin folds*: • Topical antiseptic and consider adding topical glucocorticosteroid. • Topical antibiotics active against *Staphylococcus aureus* at any sign of superinfection. • Consider systemic antibiotics if superinfection becomes more severe (clindamycin, doxycycline, ciprofloxacin, etc.). • Topical eosin or soft zinc preparations in the skin folds (should be removed before treatment with radiotherapy). (3) *Dry desquamation with isolated non-hemorrhagic crust* • Like section 2 by adding the following: • Hydrogels can be used to keep crusts flexible. • Consider debridement using hydrogels.	(1) *Confluent moist desquamation without crust*: • Topical antiseptic and consider adding topical glucocorticosteroid. • Topical antibiotics active against *Staphylococcus aureus* at any sign of superinfection. • Consider systemic antibiotics if superinfection becomes more severe (i.v. if unresponsive to oral antibiotics). • Topical eosin or soft zinc preparations in the skin folds (should be removed before treatment with radiotherapy). (2) *Confluent moist desquamation with crust*: • Topical antiseptic. • If superinfection becomes more severe, consider the use of i.v. antibiotics if unresponsive to o.v.) • Consider debridement using hydrogels. • Skin trauma should by avoided to prevent superinfection.	• Hospitalized the patient. • In the case of severe superinfection, consider the use of i.v. antibiotics.

Evidence literature-based

mucositis

depression insomnia

dermatitis

anemia

xerostomia

cachexia

neutropenia

pain

fever

dysphagia

SIRS

A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life

MASCC 2010

Type of cancer therapy	Pre-tx	During RT	1-3 months post-RT	3-6 months post-RT	6-12 months post-RT	1–2 years post-RT	>2 years post-RT
3D conformal RT							
Prevalence	0%	NR	46.7%	74.5%	90.3%	75.4%	69.4%
Std. err.	NA		NA	NA	NA	0.05	NA
95% CI	NA		NA	NA	NA	10.1–100	NA
IMRT							
Prevalence	11.8%	100%	89.4%	72.7%	90.1%	66.0%	68.1%
Std. err.	NA	0.04	0.10	0.10	0.04	0.11	0.06
95% CI	NA	90–100	61.0–100	39.5–100	81.0–99.2	34.3–97.7	40.4–95.7

Assessments were carried out at a wide range of different time points during and after cancer treatment and, in some cases, ranger from a few months to several years after cancer therapy.

saliva collection procedures
whole saliva
selective parotid saliva (single or both glands pooled)
submandibular/sublingual saliva
all major glands pooled after collection

stimulatory state of the glands
unstimulated, stimulated by chewing paraffin wax, parafilm, rubber, rubber ring, surgical latex tube, vitamin C tablets, corn chips, chewing gum, sucking on lemon candy, or oral application of 1%, 2%, or 5% citric acid)

flow rate units, i.e., ml/min, ml/2 min, ml/5 min, ml/10 min,

g (no time unit), g/2 min, g/5 min, g/10 min,

and percent change with/without reporting of baseline values.

IMRT

Nutting CM, et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol 2011;12:127–136.

Kam MK, et al. Prospective randomized study of intensity-modulated radiotherapy on salivary gland function in early-stage nasopharyngeal carcinoma patients. J Clin Oncol 2007;25:4873–4879

QUANTEC Group concluded that severe xerostomia, defined as long-term stimulated salivary flow <25% of baseline, can be reduced if at least one parotid gland is spared with a mean dose of less than 20 Gy or if both glands are spared with a mean dose of less than <25 Gy

IMRT

The QUANTEC criteria for parotid gland dose and their efficacy to prevent moderate to severe patient-rated xerostomia

Beetz 2013

Significantly lower rates of radiation-induced patient-rated xerostomia were found among patients treated according to the QUANTEC criteria,
but these criteria do not completely protect against xerostomia.

Older age, xerostomia pre-RT, oropharyngeal, nasopharyngeal carcinoma bilateral irradiation ,lymph node metastases.

major overlap of the PTV with larger parts of the parotid glands.

AMIFOSTINE

VOLUME 27 · NUMBER 1 · JANUARY 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

American Society of Clinical Oncology 2008 Clinical Practice Guideline Update: Use of Chemotherapy and Radiation Therapy Protectants

Martee L. Hensley, Karen L. Hagerty, Tarun Kewalramani, Daniel M. Green, Neal J. Meropol, Todd H. Wasserman, Gary I. Cohen, Bahman Emami, William J. Gradishar, R. Brian Mitchell, J. Tate Thigpen, Andy Trotti III, Daniel von Hoff, and Lynn M. Schuchter

Amifostine Use in Radiation Therapy-Associated Toxicities

Xerostomia: 2008 recommendation. The use of amifostine may be considered to decrease the incidence of acute and late xerostomia in patients undergoing fractionated radiation therapy alone for head and neck cancer. Current data do not support the routine use of amifostine with concurrent platinum-based chemoradiotherapy for head and neck cancer. [This represents a change from the 2002 recommendation.]

Evidence literature-based

mucositis

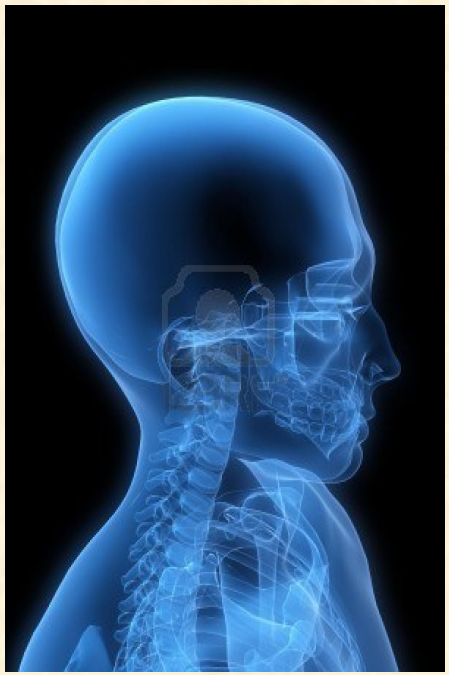
depression insomnia

dermatitis

anemia

xerostomia

cachexia



neutropenia

pain

fever

dysphagia

SIRS

Infections

a) Oropharyngeal candidiasis

b) Skin-soft Tissue infection
in site of gastrostomy or tracheostomy

c) CVC infections

d) Systemic Infections

A systematic review of oral fungal infections in patients receiving cancer therapy

V. Lalla MASCC 2010

Prevalence **7.5% pre- treatment,**
39.1% during treatment,
32.6% after the end of cancer therapy.

Pseudomembranous candidiasis (thrush)
Chronic hyperplastic candidiasis:
Erythematous candidiasis:
Angular cheilitis:

Italy

42.4% of people >70years and in 58.2% of younger individuals
Mucositis and dysphagia were higher and salivation reduced among people with OPM (p<0.0000).
Patients with OPM had longer hospitalization (p=0.0002) and longer (>12days) treatment interruptions (p=0.0288).

Busetto Rad Onc 2013

Table 3 Weighted prevalence of colonization by candida species

Candida species	Number of studies [references]	Total number of subjects	Prevalence: mean (SE) [95% CI]
Candida albicans	Five [33, 37, 40, 41, 43]	174	46.2% (0.13) [9.8–82.5]
Candida tropicalis	Three [33, 40, 43]	122	16.6% (0.07) [0–48.4]
Candida glabrata	Three [33, 41, 43]	120	5.5% (0.02) [0–12.8]
Candida krusei	Three [33, 41, 43]	120	3.0% (0.02) [0–9.8]

SE standard error, *CI* confidence interval

Candida tropicalis, are more likely to spread into the systemic circulation.

A systematic review of oral fungal infections in patients receiving cancer therapy

PROPHYLAXIS

Table 4 Weighted prevalence of clinical oral fungal infection during cancer therapy by preventive treatment regimen

Treatment	Number of studies [references]	Total number of subjects	Weighted prevalence	Standard error	95% Confidence interval
Fluconazole	Seventeen [4, 5, 11, 13–16, 19–23, 26–29, 32]	1,642	1.9%	0.006	0.1–3.1
Amphotericin	Three [21, 22, 28]	454	2.3%	0.01	0–7.0
Itraconazole	Four [11, 12, 25, 31]	452	1.5%	0.17	0–5.2
Amifostine	One [24]	38	28.9%	NA	NA
Clotrimazole and nystatin	Two [15, 16]	96	14.6%	NA	NA
Nystatin alone	One [13]	53	6%	NA	NA
Placebo/ No treatment	Twelve [4, 5, 12, 19, 20, 23–25, 27, 29, 31, 32]	989	20.3%	0.54	8.4–32.1

NA not available

Systemic fuconazole, effective in the prevention of clinical oral fungal infection and in reducing oral fungal colonization
(level of evidence I, recommendation grade A)

A systematic review of oral fungal infections in patients receiving cancer therapy

PROPHYLAXIS

Their use for prophylaxis in certain oncology settings (e.g., patients receiving head and neck radiation therapy over 6–7 weeks) can be problematic.

The emergence of resistant species is one important concern with such prophylactic use.

Effects of fluc
candidiasis in
and neck tum
placebo-contr

Fluconazole or

Higher rate of

h placebo (P = 0.008)

PATIENTS AT RISK

Busetto 2013

IMMUNOCOMPROMIZED PATIENTS

DIABETIC

STEROID THERAPY

A systematic review of oral fungal infections in patients receiving cancer therapy

Lalla 2010

TREATMENT

(IDSA) guidelines recommend the use of clotrimazole troches or nystatin suspension/ pastilles as first-line therapy for the management of mild oropharyngeal candidiasis

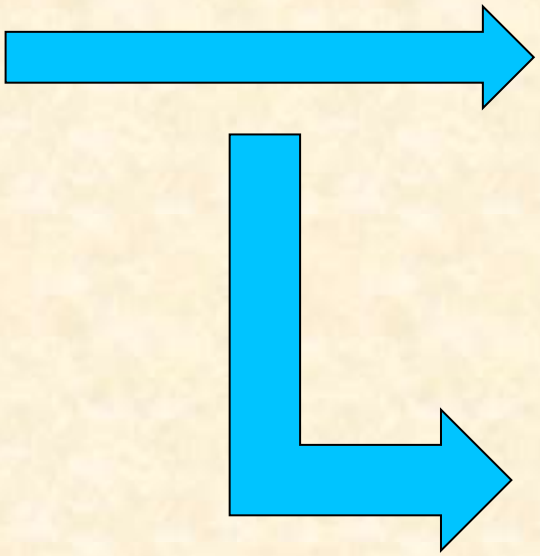
Pappas 2009

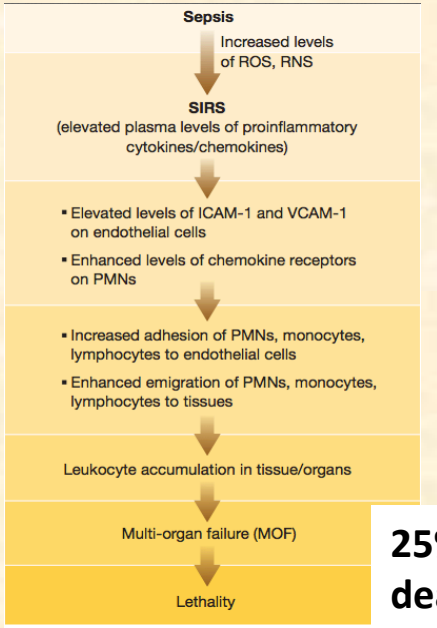
Nongenital mucocutaneous candidiasis			
Oropharyngeal	Clotrimazole troches 10 mg 5 times daily; nystatin suspension or pastilles qid (B-II); or fluconazole 100–200 mg daily (A-I)	Itraconazole solution 200 mg daily; or posaconazole 400 mg qd (A-II); or voriconazole 200 mg bid; or AmB oral suspension (B-II); IV echinocandin[a] or AmB-d 0.3 mg/kg daily (B-II)	Fluconazole is recommended for moderate-to-severe disease, and topical therapy with clotrimazole or nystatin is recommended for mild disease. Treat uncomplicated disease for 7–14 days. For refractory disease, itraconazole, voriconazole, posaconazole, or AmB suspension is recommended.

inconsistent picture of the efficacy of topical agents in patients receiving cancer therapy (level of evidence II, recommendation grade C).

Sistemic Inflammatory Response Syndrome
SIRS

Mucositis
Dermatitis
Oropharyngeal candidiasis
Skin-soft Tissue infection
in site of
gastrostomy or tracheostomy
CVC infections
Systemic Infections





25%-70% death

fever with a core temperature >38°C or <36°C
heart rate >90 beats per min,
respiratory rate >20 breaths per min, leukocytosis (>12 · 109/l)
or leukopenia (<4 · 109/l).

Longitudinal oncology registry of head and neck carcinoma (LORHAN®): initial supportive care findings

Barbara A. Murphy · Amy Chen · Walter J. Curran Jr. · Adam S. Garden · Paul M. Harari · Stuart J. Wong · K. Kian Ang

Support Care Cancer (2009) 17:1393–1401

Table 4 Use of supportive care measures

	Intergroup comparisons			
	ALL (%)	Academic (%)	Community (%)	*p* Value
Feeding tube placed	55	59	48	0.001
Tracheotomy tube placed	13	16	9	0.002
Opioid analgesics prescribed	79	89	59	<0.0001
Anti-emetics prescribed	78	83	68	<0.0001
Amifostine prescribed	15	17	11	0.02

Academic centres received more supportive interventions

lower rates of toxicity requiring less supportive care,

less stringent documentation,

less aggressive use of supportive care measures.

MUCOSITIS PREVENTION AND TREATMENT IN HEAD AND NECK CANCER PATIENTS TREATED WITH (CHEMO)RADIATION: REPORT OF AN ITALIAN SURVEY

courtesy of Bossi 2013

September 2012 to November 2012.
Results
CTCAE scale is employed by 55% of the physicians in assessing mucosal toxicity. Gastrostomy is placed with prophylactic intent in less than 10% of the patients, mainly due to weight loss before treatment.
Preventive antibiotic or antimycotic are prescribed by 46% of the responders (mainly local or systemic antimycotic drugs).
Alkalinizing mouthwashes or coating agents are frequently adopted (70% of the cases).
Among therapeutic intervention, systemic fluconazole is administered by 80% of the physicians, while the antibiotics chosen are penicillins, cephalosporins or fluoroquinolones (20% each).
Mucositis induced pain is mainly treated by weak followed by strong opioids. Pain during swallowing is considered as breakthrough pain by 69% of the responders.

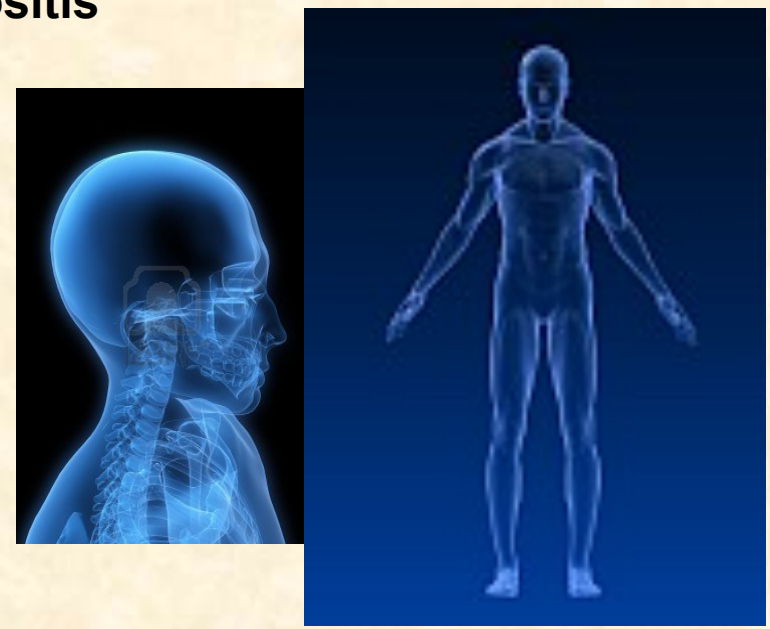
Conclusions

Pattern of mucositis prevention and treatment varies among Italian Centers, with some uniform conducts in nutrition, use of antimycotic and painkillers. There is a strong need for well conducted clinical trials in assessing best choices regarding mucositis prevention and treatment in HNC.

MULTIDISCIPLINARY APPROACH

depression

mucositis



dermatitis

xerostomia

pain

dysphagia

insomnia

cachexia

anemia

neutropenia

fever

SIRS

ONCOLOGIST

RADIOTHERAPIST

ENG SURGEON

SPECIALIST
OF SWALLOWING ASSESSEMENT

NUTRITIONIST

DENTISTS

PSYCO ONCOLOGY

AIRO-AIOM

Consensus on supportive therapy in patients with head and neck cancer receiving integrated chemo-radiotherapy treatments

VOLUME 30 · NUMBER 25 · SEPTEMBER 1 2012

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Clinical Practice Guidelines: Formal Systematic Review–Based Consensus Methodology

D. Andrew Loblaw, Ann Alexis Prestrud, Mark R. Somerfield, Thomas K. Oliver, Melissa C. Brouwers, Robert K. Nam, Gary H. Lyman, and Ethan Basch

Table 1. Consensus-Based Guidance Process Based on Modified Delphi Approach[7]

Step	Description
Generate draft recommendations	Define clinical questions, comparisons of interest—SC
	Conduct systematic review of the literature—ASCO
	Draft consensus recommendations and clinical rationale—SC
Panel meeting	Review literature and consensus recommendations—GP
	Revise consensus recommendations—GP
Consensus round one: ratings	Obtain anonymous ratings, written feedback—CG*
	Compile ratings and comments—ASCO
Consensus round one: review results	Ratings that meet predefined threshold for consensus are accepted—SC†
	Minimum of 75% is required for consensus; higher threshold may be determined, a priori, by the SC or GP
	If consensus is not achieved, recommendations are drafted again with particular attention to comments from CG—SC
	Only changes made to recommendation content are returned to CG for additional rating rounds
	GP may be consulted when rewriting recommendations
Consensus round two: ratings	Consensus recommendations are sent to CG—ASCO
	Both new and previous iterations of recommendations are presented
	Recommendations with style or wording modifications may be sent for rating; re-rating not required
	Ratings and comments are compiled—ASCO
Evaluation of consensus	Ratings are accepted if consensus is achieved
	Revisions to style or wording are accepted based on simple majority
	If consensus has still not been achieved, recommendations can again be rewritten, or left unanswered as "consensus could not be achieved"

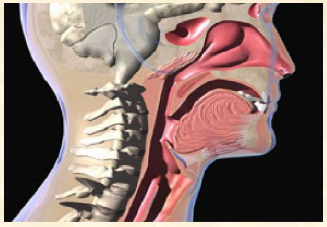
Maggio – Novembre 2013

MUCOSITE
DISFAGIA
TOSSICITA' CUTANEA
TOSSICITA' EMATOLOGICA
NUTRIZIONE-IDRATAZIONE
INFEZIONI
DOLORE
PROBLEMATICHE ODONTOIATRICHE

La terapia di supporto in radioterapia oncologica

GRAZIE PER L'ATTENZIONE

Distretto testa-collo



Vitaliana De Sanctis

Radioterapia Oncologica

"Sapienza"

Università di Roma