Anti-cancer therapies in resource-restricted settings:
management of chemotherapy toxicity

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Management of Chemo Toxicity

Communication is the golden key

- Alleviates anxieties
- Provides reassurance and support
- Promotes patient safety
- Promotes intelligent decision making
- Dispels myths
- Required for informed consent?
Patient assessment is key to success

- To manage side effects and improve quality of life
- To improve patient safety and morbidity
- To identify serious complications in good time
- To monitor patient response
- To minimise adverse side-effects where possible
- To support patients through chemotherapy
- To assess patient compliance
- To offer an opportunity for patients to ask questions
Pre-Chemotherapy Assessment

- Confirming Patient Details
- Pre-treatment investigations
- Performance Status
- Referral to other Agencies, support
- Venous assessment
- Specific information e.g. car parking
- Home Support
- 24 hour care
- Referral for central venous devices
- Financial advice
- Orientation
- Confirming Prescription Bloods Consent
- Pre chemotherapy issues e.g. fertility, Hair loss
- Information giving
Our Responsibility

To provide information at a level and pace appropriate to patients:

- Emotional state
- Level of understanding
- Culture and background
- Preferred ways of communicating
- Needs
In addition assessment is about:

- Home life
- Social and family support
- Work and finance
- Spirituality
- Psychological and emotional well being
- Body image
Also

- What does the patient know and understand about their illness?
- What have they been told?
- What is their understanding of chemotherapy?
- How are they coping?
- Who supports them and their family at home?
- How is their family coping?
Remember

- It is difficult to predict individual response
- Some patients exhibit anticipatory symptoms
- Many find the waiting and processes involved a struggle
- Patients cope in a number of different ways
What causes some of the chemotherapy side effects?
Chemotherapy attacks fast-growing cells
Fast-growing cells are found in cancer and:

- Bone marrow
- Hair follicles
- GI tract
Affects Bone Marrow

Chemotherapy

Red cells
- Anemia
- fatigue

White cells
- Risk of infection

Platelets
- Easy to get a bruise
- May bleed longer than usual
Advice for Patients?

To avoid bruising or bleeding:

- Use a soft toothbrush that’s easy on your gums.
- Blow nose gently.
- Be careful around the house so that they do not...
  - Nick themselves with scissors, knives, or tools
  - Burn themselves while cooking or ironing
General Advice

To avoid infection:

- Wash hands frequently
- Avoid people who are sick or contagious
- Avoid people who have received certain vaccines
- Avoid crowded places
- In general, do their best to avoid germs??
Fatigue

- One of the most common side effects.
- Move around and exercise when possible
  - BUT rest as well
- Limit activities
  - Delegate, delegate, delegate
- Eat healthfully?? How?
- Drink plenty of fluids
Some chemotherapy causes hair loss

Head
Eyelashes and eyebrows
Arms and legs
Pubis
Everyone reacts differently

- Completely bald or thinning hair
- Within first 2 weeks or after second treatment
  - scalp will start to tingle
- Occurs slowly (hairs on your pillow) or in clumps (handfuls in the shower)
- May grow back totally different or the same
  - Generally, starts growing back 4 weeks after chemotherapy ends
Help patient prepare for changes

- Consider cutting hair very short or shaving off
- ? Wigs availability
- No scalp coolers
Common GI symptoms

- Changes in the taste of foods
- Changes in eating habits
- Nausea and vomiting
- Throat and mouth sores
- Diarrhea
- Constipation
Mouth care during chemotherapy?

- Have teeth cleaned before chemotherapy.
  - Take care of cavities, abscesses, gum disease – How??
  - Brush teeth and gums after every meal.
  - Use an extra-soft toothbrush and a gentle touch.
- Avoid commercial mouthwashes that contain irritants such as alcohol.
If there are taste changes…

- Try bland foods (not too spicy).
- Eat what still tastes good or what is available.
Loss of appetite

- Need nutrients to fight the cancer and help keep strength
  - Nutrients (especially protein) protect muscles and body organs, including skin
- Eat a balanced diet if available?
  - Including protein, fruits, vegetables, starches, dairy
Throat and mouth sores

- **Eat foods cold or at room temperature**
  - Hot foods hurt.

- **Choose soft, soothing foods:**
  - Ice cream, bananas, mashed potatoes, custards

- **Avoid irritating or acidic foods:**
  - Tomatoes
  - Citrus fruit or juice (orange, grapefruit, lemon)
  - Spicy, salty foods
  - Coarse dry foods (toast)
Nausea and vomiting

- Treatment has come a long way – basic, cheap drugs work well

- Risk factors
  - Certain chemotherapies
  - Female sex
  - Younger than age 50
  - History of morning sickness or motion sickness
  - Consume fewer than 7 alcoholic beverages a week
Chemotherapies that can cause nausea and vomiting

**Very likely**
- **AC** (doxorubicin + cyclophosphamide)
- **FAC** (fluorouracil + AC)
- **FEC** (cyclophosphamide + epirubicin + fluorouracil)
- **EC** (epirubicin + cyclophosphamide)
- **ABVD** (doxorubicin + bleomycin + vinblastine + dacarbazine)
- **Regimens with cisplatin**

**Likely**
- **Regimens with carboplatin**
- **TAC/TC/TCH**
- **CMF** (cyclophosphamide + methotrexate + fluorouracil)
- **CHOP, EPOCH**
- **FOLFOX**
- **FOLFIRI**
- **Cetuximab + irinotecan**

TAC = docetaxel + doxorubicin + cyclophosphamide; TC = docetaxel + cyclophosphamide; TCH = docetaxel + carboplatin + trastuzumab; CHOP = cyclophosphamide + doxorubicin + vincristine + prednisone; EPOCH = cyclophosphamide + doxorubicin + etoposide + vincristine + prednisone; FOLFOX = fluorouracil + leucovorin + oxaliplatin; FOLFIRI = fluorouracil + leucovorin + irinotecan.
Nausea and vomiting: what nurses can do?

- Look at chemotherapy and risk factors
- Give antiemetic just before or at the time of treatment to prevent nausea and vomiting
- Give oral antiemetics to take home??
Nausea and vomiting: advice

- Ask about nausea
- Eat small meals every few hours.
- Drink cool, clear liquids, such as apple juice, tea, or ginger ale with no fizz
- Suck on ice cubes, mints if available
- Try to avoid odors such as cooking smells, smoke, and perfume
- Choose cold or room-temperature foods if possible
**Diarrhoea** (different from normal)

**Definition:** 2 or more loose stools in 4 hours?

- Eat small amounts.
- Stay away from spicy, fried, and greasy foods.
- Eat low-fibre foods:
  - White rice, cheese, chicken
- Eat potassium-rich foods:
  - Take advice on bananas, peaches, potatoes
- Drink plenty of clear fluids:
  - Water, apple juice, weak tea, clear broth
Constipation

Definition: No bowel movement in 2 or more days

- Take preventive medicines
- Other advice
  - Fluids and fiber
  - Moving about, even a leisurely walk
Make “advice” consistent

Let’s order Thai food!

A doctor on TV said...

I’m going to send you an article.

Vitamin B

Blueberries

Just tell patients to say:
Thank you
Skin and nail changes

- Temporary color changes, redness, itching, peeling, dryness, rash, or sun sensitivity
  - Gentle soaps, lots of moisturiser if available
  - No perfume or other alcohol products
  - Sun-protective clothing and hats; sunscreen
  - Gloves and moisturising to protect nails
Tingling or numbness in hands or feet

- Can start in any cycle during treatment
- Symptoms may feel like tingling or numbness, or:
  - Loss of balance
  - Clumsiness
  - Vision or hearing changes
- Symptoms most often mild, and may decrease when treatment stops
Targeted Therapies
Common Side Effects and Their Management
Some side effects are similar to those just discussed
- Diarrhoea, nausea, mucosal toxicity, fatigue

Others are specific to targeted therapies
- Infusion/hypersensitivity reactions (MAbs)
- Hypertension (Angiogenic inhibitors - VEGFR, PDGF antagonists)
- Mild skin reactions – dryness redness, pruritis (most kinase inhibitors)
- More intense reactions and acneiform rash (EGFR inhibitors, temsirolimus)
- Hypomagnesemia – EGFR therapies
- Hand foot skin reactions (sorefanib, sunitinib)
- Interstitial lung disease (EGFR inhibitors, temsirolimus)
- Hyperlipidaemia (temsirolimus)
- Hyperglycaemia (temsirolimus)
- Others (Bowel perforation, proteinuria, impaired wound healing, bleedling/bruising)
Diarrhoea with Targeted Therapies

- The incidence of diarrhoea with kinase inhibitors is
  - Erbitux (varies depending on whether used as monotherapy or in combination with a cytotoxic drug Erbitux plus irinotecan 22%; Erbitux monotherapy 2%)
  - Tarceva (54%)
  - Iressa (40–57%)
  - Lapatinib (42%)
  - Sorafenib (45%)

- Usually mild and transient
Managing Treatment-related Diarrhoea

- **Loperamide is the treatment of choice**
  - Patients should be advised prior to treatment to have tablets available to take should they start to have diarrhoea
  - If diarrhoea occurs (onset usually 10-12 days):
    - Patient should take 2 x 2 mg then 2 mg after every loose bowel movement up to 10 tablets/day for 24–48 hours, until diarrhoea free for 12 hours
  - In the unusual case of Grade 3 (7 or more episodes in 24 hours), doses of EGFR inhibitors should be reduced
  - Dose cessation may be required for severe diarrhoea that is unresponsive
Incidence of Infusion Reactions: First Infusion

Taxanes included for comparison

<table>
<thead>
<tr>
<th>Drug</th>
<th>Severe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>10</td>
<td>77</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>3</td>
<td>15.5</td>
</tr>
<tr>
<td>Panitumumab</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>0.2</td>
<td>2.9</td>
</tr>
<tr>
<td>Taxanes</td>
<td>3</td>
<td>30</td>
</tr>
</tbody>
</table>
Management of Hypersensitivity Reactions

- If mild or moderate infusion reaction (Grade 1/2)
  - Decrease infusion rate and inform physician
  - Give subsequent infusions at this slower rate

- If severe hypersensitivity reaction (Grade 3/4)
  - Stop infusion immediately
  - Inform physician
  - Begin IV fluid – use a separate IV line
  - Obtain vital signs
  - Provide medical management of symptoms
  - Institute emergency interventions
  - Permanent discontinuation of therapy is required
Hypertension (bevacizumab, sarefaniib, sunitinib, vandetanib)

- Monitor blood pressure every 2-3 weeks during therapy (more frequently if hypertension present)
- Refer for oral anti-hypertensive treatment if blood pressure is elevated
- Immediate treatment recommended in patients with grade 3 hypertension ($\geq 180/110$ mmHg) and in those with grade 2 ($>160/100$ mmHg) or 1 ($>140/90$ mmHg) whose blood pressure does not decrease in response to lifestyle modification
Arterial Thromboembolic Events (ATEs) (bevacizumab, sunitinib, vandetanib)

- Educate patients about signs and symptoms
  - Chest pain, Breathlessness
  - Pale, bluish, cool skin
  - Numbness, Tingling
  - Muscular weakness or paralysis
- Patient or nurse should inform physician if any of these symptoms are observed
Mild skin reactions

- Redness
- Dryness
- Itching

Seen with: sorafenib, sunitinib, imatinib

- Rash

Seen with: sorafenib, sunitinib, temsirolimus, dasatinib
Rash
Acne-Like Rash: Side Effect of EGFR Inhibitors

- An acne-like rash appears to be a class effect of all EGFR inhibitors, occurring in 50–100% of patients
  - Appears after a few days to reach maximum at 2–3 weeks
  - Although sometimes called acneiform, it is not acne
  - Appears as erythematous follicular papules – may evolve into pustules
  - Can be itchy
  - Confluent, painful, ulcerating lesions in severe cases
  - Grade 3 in 5–18% of patients
  - Tends to be more severe in patients receiving MAbs
- For some drugs the rash has an “above-the-waist” distribution in the areas rich in sebaceous glands
  - Face, neck, shoulders, behind ears, upper trunk (V-shape), scalp
  - Less often – lower back, abdomen, buttocks and limbs
- For others the rash appears anywhere on the body
Other Side Effects with EGFR Inhibitors

- Patients may experience dry and/or flaky itchy skin
- Fissures may occur on fingers or heels
- Nail lesions can also occur (10–15% of patients on EGFR targeted therapies)
- Late event – usually occurs 4–8 weeks after therapy started
- Nail lesions seen as paronychia with inflammation of the nailfold (mainly in big toe)
- Hair changes - Brittle coarse hair, Excessive eyelash growth, Vellus hairs on face
Timescale of Skin Toxicities

Most patients do not experience Grade 3 Acne-like rash.
Assessment of Skin Toxicities

- **Determine**
  - Type
  - Grade
  - Duration
  - Extent of body surface affected
  - Distribution
  - Level of discomfort

- **Impact of skin toxicity on body image**
  - Signs of embarrassment and self-imposed social isolation
  - Depression

- **Impact of toxicity on patient’s daily life**
  - Work, family and social life
# Suggested Treatment Regimens for Acne-like Rash

<table>
<thead>
<tr>
<th>Grade of rash</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>No treatment or Clindamycin gel/lotion Erythromycin gel/lotion Metronidazole gel/cream Salicylic acid in alcohol lotion – back/chest</td>
</tr>
<tr>
<td>Grade 2</td>
<td>As for Grade 1 plus topical menthol cream or oral antihistamine when itch present Plus oral tetracycline</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Consider delaying therapy Treat as for grade 2. Compresses with physiological solutions in cases of acute inflammation Oral antihistamines Oral tetracyclines at higher dose</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Stop therapy. Refer to dermatologist with experience in this type of rash</td>
</tr>
</tbody>
</table>
Prevention and Alleviation of Dry Skin and Rash: Do’s

Advise all patients **to use:**

- Unperfumed moisturisers from the start
- Mild, hydrating, unperfumed shower gels or oils
- Sunscreens
- Skin-friendly liquid cleanser to remove make-up
- Stronger emollients to alleviate over dryness if it develops
Prevention and Alleviation of Dry Skin and Rash: Don’ts

Advise patients to avoid:

- Exposure to **sunlight**, harsh winds, humidity
- Harsh detergents
- Strong perfumes
- Ordinary make-up
- Alcohol-containing skin products
- Wearing clothing that is too tight or rubs
- Self-treatment with over-the-counter acne preparations; advice from the healthcare team
EGFR-inhibitor related skin reactions*

Typical time course of possible skin reactions

Treatment suggestions

<table>
<thead>
<tr>
<th>Topical</th>
<th>Systemic</th>
</tr>
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<tbody>
<tr>
<td>Anti-acne creams</td>
<td>+/- tetracyclines</td>
</tr>
<tr>
<td>Moisturizing creams**</td>
<td>antihistamines in case of pruritus</td>
</tr>
<tr>
<td>+/− topical antibiotics</td>
<td></td>
</tr>
<tr>
<td>Topical antiseptics</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from O. Chosidow, Targeting Cancer Vol2, 2004,
Supporting Patients with Rash

- Provide extra support and encouragement for patients struggling to cope psychologically with rash
  - Help patients understand that the rash is usually a transient and manageable condition that usually disappears without scarring
- Camouflage make-up may be used
  - Dermatologist approved cover-up – not ordinary make-up
- Patients who experiencing more profound emotional problems with the rash should be referred for specialist psychological support
Hand-Foot Skin Reactions

- Tingling or burning
- Redness
- Thickening of skin
- Small tender blisters on the palms of the hands or soles of the feet
- Lesions more prevalent in areas of friction
- Negatively affects quality of life
- Increases in severity with length of treatment
Precautions to Reduce Exposure to Friction and Heat

- Hot water (washing dishes, long showers, hot baths)
- Impact on your feet (jogging, aerobics, walking, jumping)
- Using tools that require you to squeeze your hand on a hard surface (garden tools, household tools, kitchen knives)
- Rubbing (applying lotion, massaging)
Treatment of HFSR

- Tazarotene 0.1% - decreases epidermal proliferation normalizes differentiation, reduces inflammation
- Urea cream 40% - keratolytic, dissolves the intracellular matrix so loosens the horny layer of skin and causes shedding of scaly skin softens hyperkeratotic areas
- Topical fluorouracil 5% - antiproliferative effect on keratinocytes
Conclusions

- Awareness, assessment and prevention
- Lots of Advice that helps patients in low resource settings
- Many cultural specific treatments which need researched
- Much of the symptomatic care e.g. anti-emetics and moisturisers are inexpensive
- Work together to improve symptomatic care