

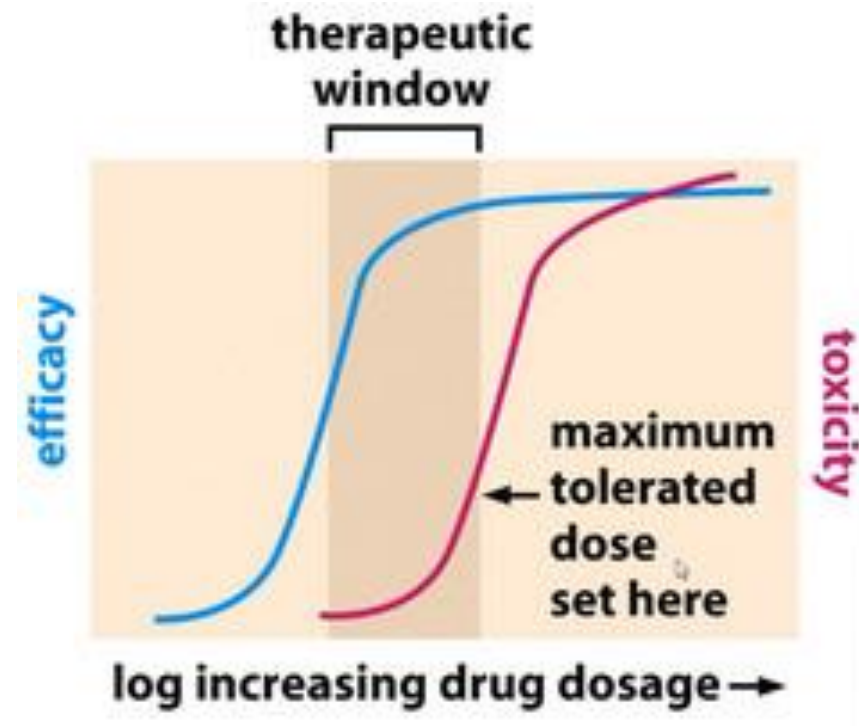
Chemo 101

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Chemotherapy: Titrating Poisons

- Chemotherapy agents are administered classically with the intent of 'curing' cancer.



The 'Usual' Chemotherapy Toxicities

- Myelosuppression
- Nausea and Vomiting
- Hair loss
- Mucositis



Toxicity Reporting

- Some toxicities are managed symptomatically
- Some toxicities require changes to the treatment plan
- Excellent assessment and documentation, and communication of findings to primary team essential

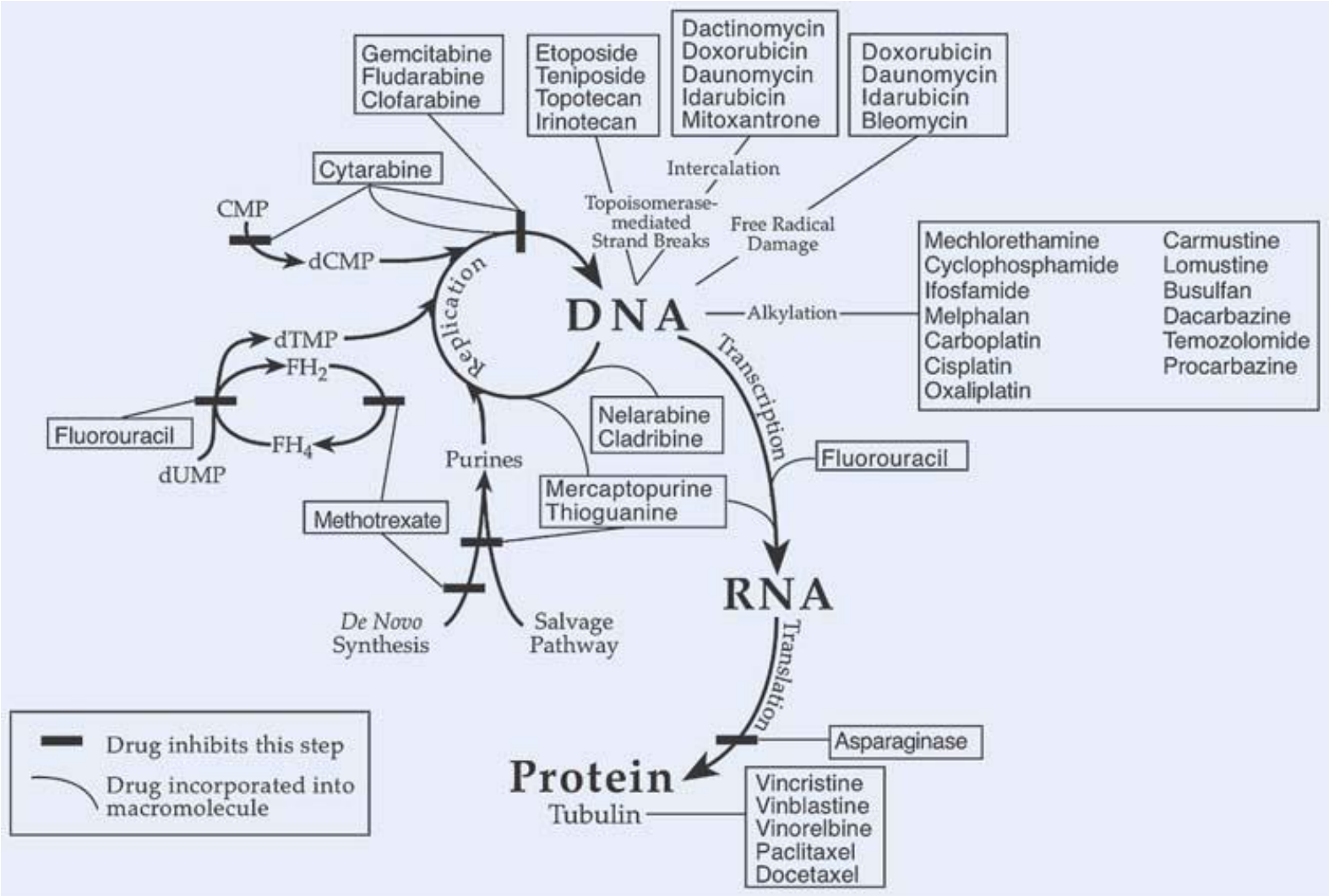


Toxicity Grading

- Adverse Event: unfavourable or unintended symptom, finding, or disease associated with therapy for cancer
- Each adverse event is defined according to the Common Terminology Criteria, and graded on a scale that indicates the severity of the adverse event
- Other grading tools commonly used are the World Health Organization Toxicity Grading Scale, and the Balis Scale for Peripheral Neuropathies



Chemotherapy in 1 Diagram



'Practical' Classification

- Alkylating Agents
- Microtubule Agents
- Antineoplastic Antibiotics
- Antimetabolites
- Topoisomerase Inhibitors
- 'Other Agents'
- Targeted Agents



Reminder: Chemo Safety

Safe Handling

- Chemotherapy Agents are considered Hazardous Drugs
- Hazardous Drugs require special precautions because of their potential health risk
- Primary routes of exposure are skin contact and inhaling aerosolized drug

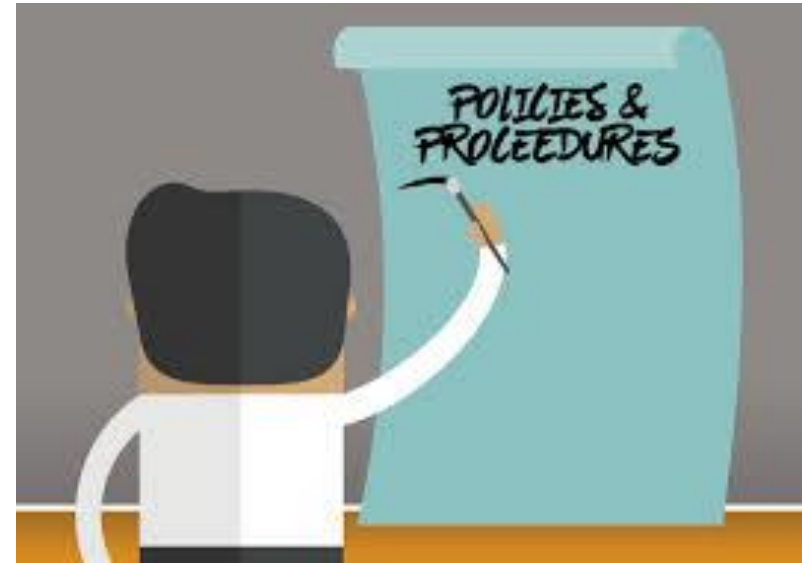
POGO Satellite Manual

Section 3.1 – Safe Handling, Administration and Disposal of Chemotherapeutic Agents

- Standardized practice guidelines for the safe handling of chemotherapeutic agents across the province

Institutions have Policies and Procedures in place for:

- Receiving and storing agents
- Preparing agents
- Transporting agents and storage after preparation
- Administration of chemotherapy
- Possible spills



Personal Protective Equipment

- Evidence of impermeability to chemotherapeutic agents from manufacturer

PPE Includes:

- Gown - Disposable, impermeable/low permeability fabric, lint-free, with back closure and long cuffed sleeves, which should be tucked into the gloves
- Gloves - tested to protect against permeations by chemotherapy agents
- Goggles/Faceshield - worn wherever chemotherapy agents are being manipulated and administered
- Mask - designated to protect against aerosolized particles, worn throughout the process of chemotherapy drug manipulation and administration

Diapers



- Placed in a biohazard container for up to 7 days after the child received chemotherapy
- “Red bin” in the patient’s washroom

Toilets



- Flushed twice
- Cover with plastic lined absorbent pad, then dispose of in biohazard bin after each use

Linen



- PPE worn when handling soiled linens
- Usually disposed of in regular hospital laundry, in leak-proof plastic bags (Hospital laundry treats all linens as if contaminated)



Body Fluids



- Chemotherapy is excreted in urine, feces, and other body fluids
- Results in a potential risk to health care providers and parents
- Safe Handling practices continue with all body fluids after receiving chemotherapy in the Satellite Clinic, or at the Tertiary Hospital
- PPE should be worn:
 - 48 hours after IV chemo administration
 - Up to 7 days after oral chemo administration

Satellite Administered Chemo Examples

Case 1: Kira

- 5 Year old Girl with Intermediate Risk Rhabdomyosarcoma
- Care shared with Tertiary, but receives majority of therapy at Satellite
- Treatment: Alternating Cycles of VAC (Vincristine, Actinomycin and Cyclophosphamide) and VI (Vincristine and Irinotecan)

Vinca Alkyloids

- Uses
 - Vincristine: 'Salt and Pepper' of chemo
 - Vinblastine: Low Grade Gliomas, NHLs
- Not generally myelosuppressive
- Acute Toxicities?
 - Constipation
 - Pain (Jaw, generalized)
 - SIADH
 - Motor Neuropathy (Foot Drop, Vocal Cord)
 - Extravasation
- Chronic Toxicities?



Dactinomycin

- Uses

- Wilms' Tumour, Rhabdomyosarcoma

- Acute Toxicities

- Veno-occlusive Disease (VOD, aka Sinusoidal Obstruction Syndrome, SOS)
 - Acute hepatic inflammation leading to thrombosis of sinusoids
 - RUQ pain, fluid retention, incr bili
 - Radiation Recall

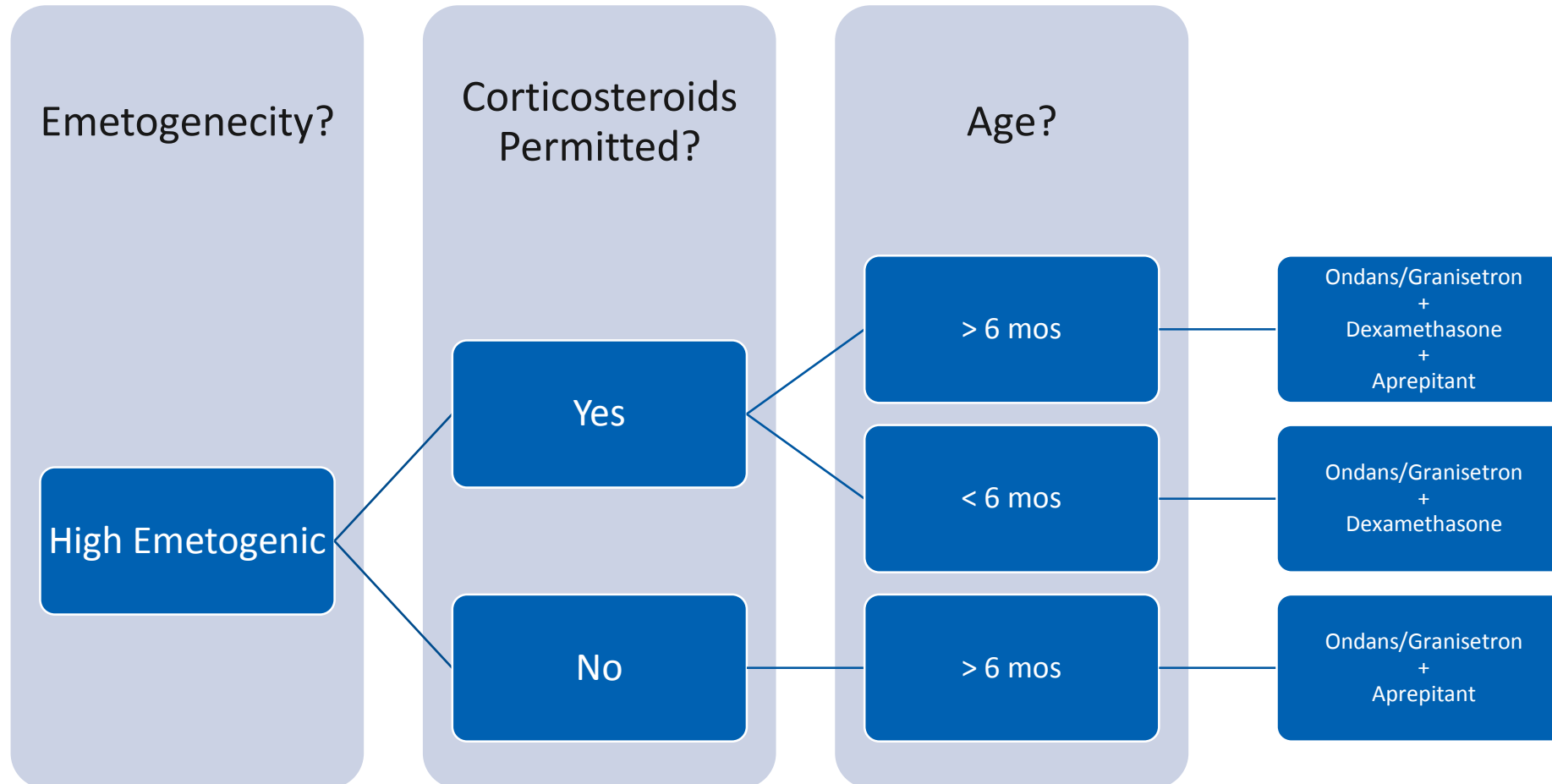
Kira: Continued

- Kira receives her VAC chemotherapy. She's seen in clinic the next day having had a rough night, lots of vomiting, very little sleep. On exam today she's dehydrated
 - Why?
 - Intervention?
 - What about next time?

Emetogenicity: Just HOW Pukey?

High Level of Emetic Risk (> 90% frequency of emesis in absence of prophylaxis)	
<ul style="list-style-type: none"> • Carboplatin • Cyclophosphamide $\geq 1\text{g/m}^2$ • Dacarbazine 	<ul style="list-style-type: none"> • Dactinomycin • Procarbazine (Oral)
Moderate Level of Emetic Risk (30-90% frequency of emesis in absence of prophylaxis)	
<ul style="list-style-type: none"> • Cyclophosphamide $< 1\text{g/m}^2$ • Cyclophosphamide (oral) • Doxorubicin 	<ul style="list-style-type: none"> • Methotrexate $\geq 250\text{ mg}$ to $< 12\text{ g/m}^2$ • Irinotecan • Temozolamide (oral)
Low Level of Emetic Risk (10- < 30% frequency of emesis in absence of prophylaxis)	
<ul style="list-style-type: none"> • Cytarabine $\leq 200\text{ mg/m}^2$ • Etoposide 	<ul style="list-style-type: none"> • Methotrexate $> 50\text{ mg/m}^2$ to $< 250\text{ mg/m}^2$ • Topotecan
Minimal (<10% frequency of emesis in absence of prophylaxis)	
<ul style="list-style-type: none"> • Mercaptopurine (oral) • Methotrexate $\leq 50\text{ mg/m}^2$ • Thioguanine (oral) 	<ul style="list-style-type: none"> • Vinblastine • Vincristine

Choosing Antiemetic Prophylaxis



If At First You Don't Succeed..

- Consider increasing level of emetogenic prophylaxis next cycle
- Consider addition of Olanzapine
- Consider Palonosetron (\$\$\$)

Kira: Continued

- Kira returns to clinic 3 days later with a complaint of abdominal pain
 - History?
 - Questions?
 - Exam?

Kira: Continued

- 6 weeks later returns for Days 2-5 of 'VI'
- On day 3, mom reports Kira was up all night with Diarrhea
- What's next?

Irinotecan Diarrhea

- Early Diarrhea (rare)
 - Often associated with infusion or within a few hours
 - Cholinergic manifestations: Sweaty, flushed, cramping
 - Tx: Atropine
- Late Diarrhea (common)
 - Hours after 1st dose
 - Parents should be educated on use of loperamide
 - Loperamide non-responsive: Consider transfer for octreotide infusion

<https://www.pogo.ca/satellite-manual/3-0-chemotherapy-administration/3-7-chemotherapy-quick-reference/3-7-2-provider-guide-prevention-and-management-or-irinotecan-induced-diarrhea/>

Case 2: Mohammed

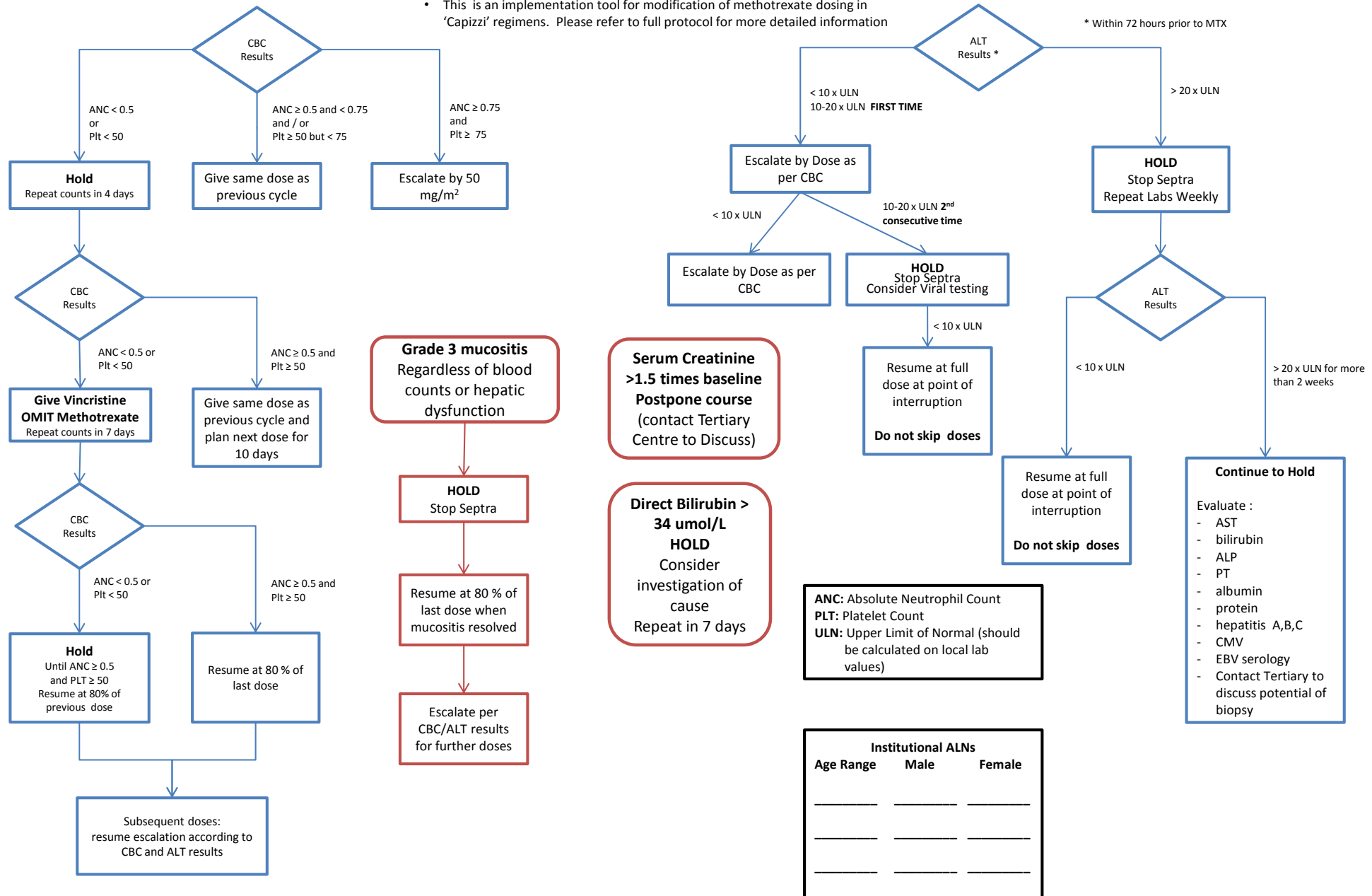
- Mohammed is an 8 year old with Standard Risk ALL
- Arrives to Clinic for Interim Maintenance 1, Day 11
- Chemo to be given today:
 - ✓ IV vincristine and IV Methotrexate
- Bloodwork:
 - ✓ CBC, ALT, Bilis and creatinine prior to determining dose for escalating (Capizzi) doses

Methotrexate

- There are clear instructions in the protocol for how to dose the methotrexate for this cycle.
 - Ideally, the dose is escalated each time, according to the roadmap
 - BUT: The dose may remain the same as previously given, or held altogether, depending on the bloodwork results
 - Consult the protocol each time Capizzi methotrexate is administered, to ensure the correct dose is given
 - Consult the primary team at the tertiary hospital if needed
- Administer antiemetics prior to IV methotrexate

Capizzi Methotrexate Escalation Algorithm

- This is an implementation tool for modification of methotrexate dosing in 'Capizzi' regimens. Please refer to full protocol for more detailed information



Methotrexate

Considerations for Inpatient Unit:

- Potential to present to the inpatient unit with the following concerns:
 - Mucositis – could be admitted for pain management, fluid and nutrition management
 - Abdominal pain- Transaminitis, Hyperbilirubinemia
 - Renal impairment – elevated creatinine/decreased urine output
 - Red/peeling skin, especially soles and palms
 - Hand-Foot Syndrome (AKA Acral Erythema, Palmar-Plantar Erythrodysesthesia)

Mohammed: Cont

- Mohammed returns 6 days later to clinic with mouth sores
- Worse past 2 days
- Now unable to eat or drink
 - Steps to manage?

Tertiary Administered Chemo Examples

Case 3: JD

- 5 year old boy with High Risk Neuroblastoma
 - Admitted to tertiary hospital for Cycle 5 of induction chemotherapy (Cisplatin and Etoposide)
 - Discharged yesterday, presents today to clinic with having vomited all night
 - On exam, Dehydrated and looks unwell
 - Labs
 - Urea: 9.6
 - Creatinine 58 (21 last week)
 - Mg 0.39
 - P04 0.93
 - What's the cause?

Platinum Agents

- Attach platinum molecule to DNA in similar mechanism to Alkylating Agents
- Uses
 - Neuroblastoma, Medulloblastoma, Osteosarcoma, Germ Cell Tumours
- Special Toxicities
 - Acute/Delayed Nausea and Vomiting
 - Renal Toxicity
 - High Frequency Hearing Loss
 - Radiation
 - Aminoglycosides
 - Age

Topoisomerase Inhibitors

- Interfere with DNA uncoiling and recoiling during replication
- Toxicities
 - Topoisomerase I Inhibitors (Irinotecan/ Topotecan)
 - Severe Secretory Diarrhea (Acute)
 - Tx: Atropine, loperamide, Cefixime
 - Topoisomerase II Inhibitors (Etoposide)
 - Acute Toxicity: Infusional Allergy/Allergy-Like Reaction
 - Late Effect: Secondary Malignancy (AML, *MLL* (11q23) rearrangement)

JD: Management

- Outpatient vs Inpatient
- Escalate Antimetotics
- IV Fluids
- Electrolyte Replacement (IV vs. PO)

Outpatient Management

- Nausea/vomiting under control, and able to continue regimen orally at home?
- Fluid bolus, able to maintain PO intake?
- Oral supplements, able to take PO?
- If not – then Inpatient Management

Case 4: SD

- 13 yo with T-Cell ALL
- Comes to Satellite for assessment Day 19 of consolidation complaining of nausea, vomiting and severe abdominal pain
- O/E: Looks unwell, not toxic, abdomen diffusely tender, no clear rebound
- CBC
 - WBC <0.5
 - Hgb 87
 - Plt 35
- Chemistry: Ur 5.6, Creatinine 65, Na 131, Cl 101, K 3.1
- What's next?

SD: Continued

- Abdominal Pain settles with 5mg of IV morphine
- Abdominal X-ray: No obstruction, ? Small pleural effusions
- Ultrasound Pending
- Amylase: 785, Lipase > 1000

What's going on?

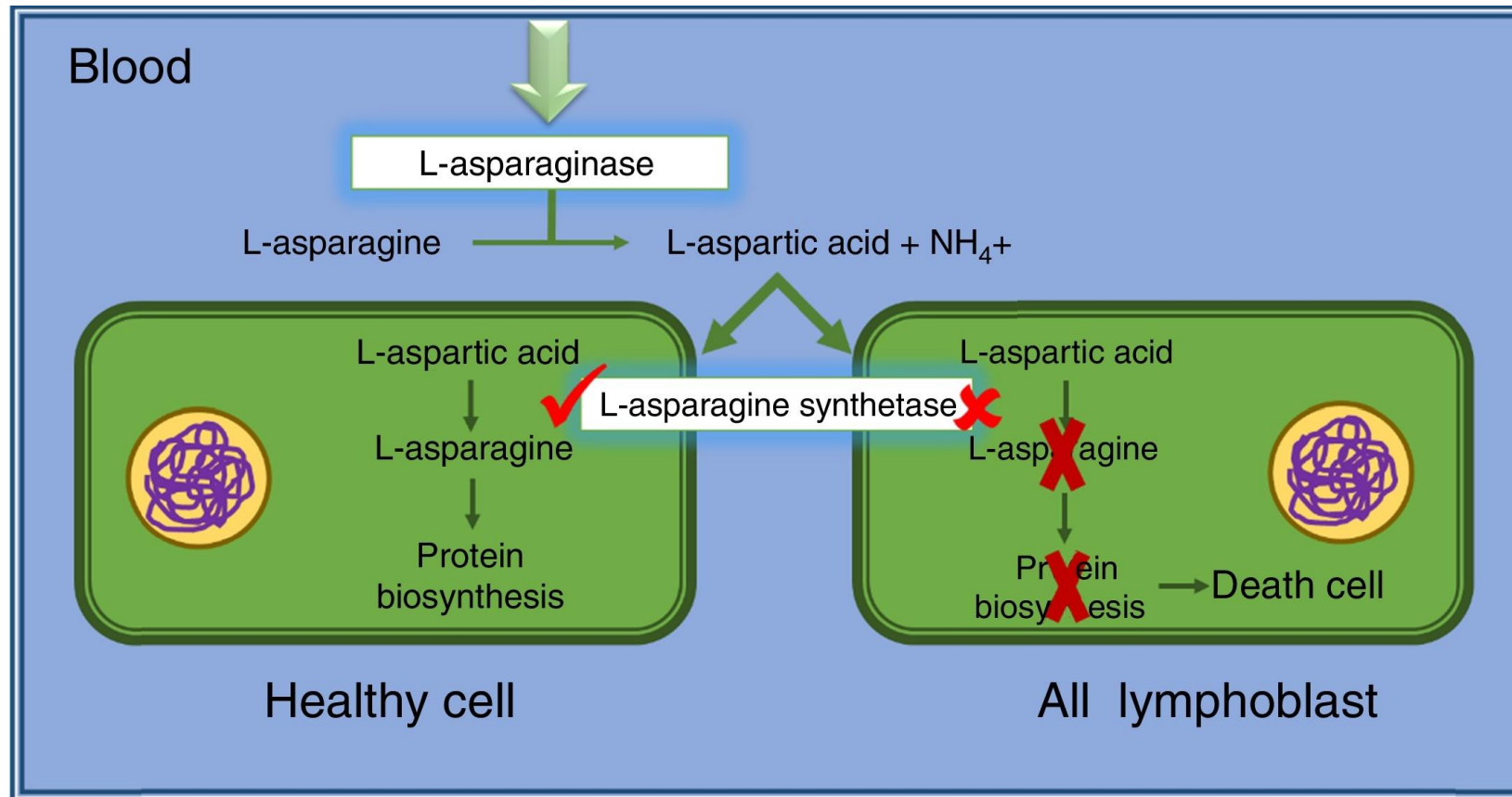
4.3.1 CONSOLIDATION (56 days) – HR B-ALL Patients enrolled prior to March 19, 2018	Patient name or initials	DOB
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Start Consolidation on Day 36 (7 days following Day 29 LP) or when peripheral counts recover with ANC $\geq 750/\mu\text{L}$ & platelets $\geq 75,000/\mu\text{L}$ (whichever occurs later). This Therapy Delivery Map is on **one (1)** page.

DRUG	ROUTE	DOSAGE	DAYS	IMPORTANT NOTES	OBSERVATIONS										
Cyclophosphamide (CPM)	IV over 30-60 min	1000 mg/m ² /dose	Days 1 & 29	See Section 4.3 for admin guidelines	a. Hx, PE, Wt., Ht. b. CBC/diff/platelets c. CSF cell count, cytospin ¹ d. Bilirubin ALT, & Creatinine e. BM Evaluation f. Osteonecrosis study (optional) g. Neurocognitive study (optional)										
Cytarabine (ARAC)	IV over 1-30 mins or SubQ	75 mg/m ² /dose	Days 1-4, 8-11, 29-32 & 36-39												
Mercaptopurine (MP)	PO	60 mg/m ² /dose*	Days 1-14 & 29-42	*See Section 5.9 for suggested starting dose based on TPMT and NUDT15 status See Section 4.3 for admin guidelines											
Intrathecal Methotrexate (IT MTX)	IT	<table><tr><td>Age (yrs)</td><td>Dose</td></tr><tr><td>1-1.99</td><td>8 mg</td></tr><tr><td>2-2.99</td><td>10 mg</td></tr><tr><td>3-8.99</td><td>12 mg</td></tr><tr><td>≥ 9</td><td>15 mg</td></tr></table>	Age (yrs)	Dose		1-1.99	8 mg	2-2.99	10 mg	3-8.99	12 mg	≥ 9	15 mg	Days 1, 8, 15 & 22	See Section 4.3 for admin guidelines Note age-based dosing
Age (yrs)	Dose														
1-1.99	8 mg														
2-2.99	10 mg														
3-8.99	12 mg														
≥ 9	15 mg														
VinCRISTine (VCR)	IV push over 1 minute ⁺	1.5 mg/m ² /dose	Days 15, 22, 43 & 50	+ Or infusion via minibag as per institutional policy Maximum dose: 2 mg	OBTAIN OTHER STUDIES AS REQUIRED FOR GOOD PATIENT CARE										
Pegaspargase (PEG-ASP)	IV over 1-2 hours	2500 International Units/m ² /dose	Days 15 & 43	Administer through the tubing of a freely infusing solution of D ₅ W or 0.9% NaCl											

¹ Patients with testicular disease at diagnosis & continued clinical evidence of testicular disease at end-Induction will receive testicular YRT. See [Section 4.3](#) &

Asparaginase: A 'smartish' drug



Asparaginase

- Indication: Acute Lymphoblastic Leukemia and Lymphoblastic Lymphoma (Also AML...)
- Common Toxicities
 - Hypersensitivity
 - Hyperglycemia
 - Pancreatitis
 - Thrombosis/bleeding
 - Nausea and Vomiting
 - Pain/Bruising at injection site (When Given IM)
 - Hepatotoxicity (Much more in Adults)

SD Management

- Pancreatitis Management
 - RECOGNIZE IT!
 - Requires aggressive pain control
 - Avoid feeding stomach (TPN, ?NJ feeding)
 - Careful Fluid Management
 - +++ Third spacing
 - Early transfer to Tertiary

Chemotherapy

- Each patient reacts to chemotherapy differently – some may experience more significant side effects than others
- Side effects may be immediate, or days, weeks or years after treatment
- May involve any body system
- May be transient or permanent
- Satellite Team role:
 - to recognize side effects, report as necessary, and provide appropriate symptom management
- And Now....