AAFP GLOBAL HEALTH SUMMIT

Primary Health Care and Family Medicine: Health Equity for All

Developing a Contextualized Pediatric Diarrhea Management Protocol for a Tropical LMIC Setting

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Session Objectives

- Describe current diarrhea management guidelines for low-resource settings, based on hydration status, nutrition status, and diarrhea classification.
- Implement an iterative process for developing a contextualized disease management protocol through partnership with an LMIC organization.
- Apply a standard protocol in the management of pediatric diarrhea in resource-limited settings

About Us and Our Context

- UC partnership with Wuqu' Kawoq / Maya Health Alliance
- STEGHs 4 times per year, approximately 3 months apart
- Rural Guatemala sites:
  - 1 Week: Socorro, Suchitepequez: lowland (tropical climate), rural clinic, POC testing only
  - 1 Week: Tecpan region villages: highlands/mountains (subtropical-temperate climate), temporary clinics in community buildings
- Teams:
  - Attendings/GH Fellow (2)
  - Residents (2-3)
  - Medical students (0-4)
  - Pharmacy students (0-4)
  - MPH/nursing students (0-2)

Case: Child in Rural Guatemala with Diarrhea

- CC: A 2 year old boy with diarrhea, brought in by mom, to rural clinic
- HPI: Full-term baby, UTD on immunizations, average health with intermittent URIs and diarrheal illnesses, with "diarrhea" for the past 7 days, approximately 5-6 times daily, not improving, has felt hot to mom and acted more tired. No vomiting, but appetite is decreased, has drunk less fluids than normal, taking in some water and watered-down coffee, urine is dark with below average output. Last bout of diarrhea was around 2 months ago, resolved after 3 days with an unknown antibiotic prescribed from an outside pharmacy.
- ROS: He has not had any rash, or other concerns on ROS.

MOH/UNICEF Immunization Schedule

Immunization schedule

BCG	birth	OPV	2, 4, 6, 18 months; 4 years
DTwP	18 months; 4 years	Pneumo_conj	2, 4 months; 1 year (subnational)
DTwPHibHep	2, 4, 6 months	Rotavirus	2, 4 months
HepB	birth	Td	1st contact; +1, +6 months; +1, +1 year or +10, +10 years
Influenza	high-risk groups	Vitamin A	6-59, 12-59 months
MMR	1 year		
MR	>14 years		

UNICEF: http://www.unicef.org/immunization/files/EN-ImmSumm-2013.pdf

Case: Child in Rural Guatemala with Diarrhea PHYSICAL EXAM

- VS: T 37.5C (99.5F), HR 120, RR 28, Wt 10kg, Weight-for-Age Z-score (WAZ) is -2.1, and Height-for-Age Z-score (HAZ) is -2.3.
- GENERAL: Appears alert but tired and a little fussy.
- HYDRATION: Makes no tears when he cries, eyes are not sunken, radial pulse is palpable, mucous membranes are slightly tacky, and skin has normal turgor
- OTHER: Neck is supple, heart/lungs normal, abdomen is non-tender, no masses, no skin rash.

Case: Child in Rural Guatemala with Diarrhea DISCUSSION/MANAGEMENT

2 yr M w/ 7d diarrhea, afebrile, WAZ -2.1, HAZ -2.3

- How would you classify this child's diarrhea and hydration status?
- What additional problems/findings are concerning in this case?
- How would you manage this case given your setting (rural clinic, intermittent care, limited testing and follow-up options) and the associated problems?

Case: Child in Rural Guatemala with Diarrhea CONCLUSION

- Acute, new-onset/non-recrudescent, non-bloody diarrhea
- Dehydration: WHO Class B ("Some dehydration") / CDS 3-6% (2 pts)
- Management:
  - Hydration: ORS: How much? How? Clean water?
  - Antibiotics: To give or not to give? Which one? What dose? How long? Is Bactrim okay? HUS?
  - Micronutrient supplementation: Zinc? How much? Are "Chispitas" enough?
  - Macronutrient support: Can we help this chronically malnourished kid?
  - Deworming: MDA dosing (1d) or treat with a higher dose (3d)?
  - Prevention: Promote hygiene – prescribe soap?
  - Follow up: When will we see this child again? Do we need to see them again this week?
- Conclusion: We need a protocol!
  - Standardization to "first do no harm"/maximize patient outcomes and satisfaction, reduce confusion, improve continuity, promote equity, and ensure good antimicrobial stewardship

An Iterative Approach to Protocol Development

1. Define problem and survey team to clarify questions/issues
2. Discuss with host organization leadership/providers
3. Research for contextualized studies/epidemiology
4. Review current guidelines (MOH, WHO/IMCI, CDC, Specialty Boards)
5. Look at best practice guidelines for LRS (MSF, etc)
6. Develop draft protocol
7. Fine-tune with expert input (GI, Peds ID, Trop Med)
8. Pilot/PDSA
9. Finalize standardized protocol and make user-friendly
10. Evaluate/measure, disseminate, and apply continuous QI

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Define problem & survey team

Age	Duration of Diarrhea	Frequency	nonbloody vs Bloody	Toxic vs Nontoxic	Fever vs Afebrile	Dehydrated vs Hydrated	HAZ	WAZ	Additional Desc/Clarification	Assessmt Cat: acute <3d / acute 3-7d / acute 7-14d / persistent 14-28d / persistent >28d
5m	7d	3x/d	nonbloody	nontoxic	afebrile	hydrated			High coffee intake	acute 3-14d
16m	30d	8x/d	nonbloody	nontoxic	afebrile	hydrated				persistent >28d
18m	7d	5x/d	nonbloody	nontoxic	afebrile	dehydrated	<-1	<-1	uncomfortable abd, foul smelling	
3y	7d	3x/d	nonbloody	nontoxic	afebrile	hydrated			present w/ cough	acute 3-14d
15m	7d	3x/d	nonbloody	nontoxic	afebrile	hydrated			present w/ cough	acute 3-14d
12m	15d	4x/d	nonbloody	nontoxic	afebrile	hydrated	nl	nl		persistent 14-28d
13m	60d	5x/d	nonbloody	nontoxic	afebrile	hydrated	nl	nl	foul smelling	persistent >28d
19m	4d	5x/d	nonbloody	nontoxic	afebrile	hydrated	<-2	<-2	foul smelling	acute 3-14d
19m	1y on/off	10x/d	bloody	toxix	febrile	dehydrated	<-2	<-2	intermittent, chronic, dewormed 4m previously, previous metronidazole but lower dose	persistent >28d
2y	15d	5x/d	nonbloody	nontoxic	afebrile	hydrated	<-1	<-1	watery, yellow	persistent 14-28d
3y	6m on/off	4x/d	nonbloody	nontoxic	afebrile	hydrated	<-2	<-2		persistent >28d

Define problem & survey team

- **Hydration**: When and how much ORS? How much to Rx? What options can we suggest for clean water?
- **Antibiotics**: To give or not to give? Which one? What dose? How long? Is Bactrim okay? What about HUS? What if we're running low on azithro? Should we treat for Giardia with Metro? Amoeba dose? What about luminal carriage? Should we test first?
- **Micronutrients**: Zinc? How much? Are "Chispitas" enough? Should we double them for the additional micronutrients?
- **Macronutrients**: Should we prescribe RUTF?
- **Antihelminths**: Can worms be causing this? If I deworm should I use MDA dosing (1d) or treat with a higher dose (3d) to cover whipworm?
- **Prevention**: "WASH"; Can we prescribe soap or do anything else to promote hygiene?; how do ensure vaccination status?
- **Follow up**: When should they come back?

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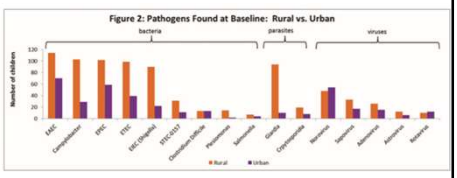
Contextualized Studies

STUDY: Pathogens found on PCR (BioFire) in children 6mos to 3 yrs w/ "acute, moderate severity, non-bloody" diarrhea
CONCLUSION: E.coli species and Giardia common; multiple pathogens common in rural kids (96%+ had multiple – "Pathobiome")



Melgar M. Enteropathogen Identification by Multiplex PCR in Guatemalan Children with Acute, Non-bloody Diarrhea, 2017

Review Guidelines

- Guatemala MOH
- WHO Diarrhea
- IMCI
- EMLc
- CDC
- IDSA
- ACG

WHO/UNICEF 2013

Contextualized Studies

- STUDY: Retrospectively analyzed demographic factors that may affect the prevalence of intestinal parasites among Guatemalan school children.
- DESIGN: Clinical visits performed on 10,586 school children aged 5-15 years over a four-year period (2004-2007) in the Palajunoj Valley of Guatemala (valley near Quetzaltenango), during which 5,705 viable stool samples were screened for infection
- FINDINGS:
  - Risk factors: Young age, wet season, female gender, and severe malnutrition all correlated positively with increased rates of infection.
  - Parasites prevalences: **A. lumbricoides 17.7%**, **E. histolytica 16.1%, G. lamblia 10.9%,** H. nana 5.4%, and B. hominis 2.8%.
  - Higher rates of infection among younger children with G. lamblia and E. histolytica
  - Higher rates during the wet season for E. histolytica and H. nana
  - Higher rates with G. lamblia among malnourished children (OR=1.498) and E. histolytica (OR=1.243)

Cook DM, et al, A Retrospective Analysis of Prevalence of Gastrointestinal Parasites among School Children in the Palajunoj Valley of Guatemala, 2016

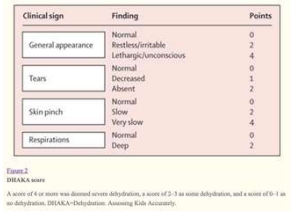
Example 1: Dehydration Assessment **WHO** vs Dhaka vs CDS

Mental status	Normal, awake	Agitated, irritable	Lethargic or unconscious
Radial pulse	Easily palpable	Palpable (possibly rapid)	Difficult to palpate (weak) or absent
Eyes	Normal	Sunken	Sunken
Skin pinch	Disappears rapidly	Disappears slowly (< 2 seconds)	Disappears very slowly (> 2 seconds)
Thirst	Drinks normally	Thirsty, drinks avidly	Incapable or drinks very little
DIAGNOSIS	↓ NO DEHYDRATION	↓ SOME DEHYDRATION	↓ SEVERE DEHYDRATION

Example 1: Dehydration Assessment WHO vs **Dhaka** vs CDS

- DKAHA Scale: Dehydration: Assessing Kids Accurately
- IMCI developed by expert opinion, not validated in LICs
- Evidence of being superior as an estimate of dehydration in LICs

Levine AC, et al. External validation of the DHAKA score and comparison with the current IMCI algorithm for the assessment of dehydration in children with diarrhoea: a prospective cohort study. Lancet Global Health, Oct 4 2016.



Clinical sign	Finding	Points
General appearance	Normal	0
	Restless/irritable	2
	Lethargic/unconscious	4
Tears	Normal	0
	Decreased	1
	Absent	2
Skin pinch	Normal	0
	Slow	2
	Very slow	4
Respirations	Normal	0
	Deep	2

Figure 2
DHAKA score

A score of 4 or more was deemed severe dehydration, a score of 2–3 as some dehydration, and a score of 0–1 as no dehydration. DHAKA=Dehydration: Assessing Kids Accurately.

Example 1: Dehydration Assessment WHO vs Dhaka vs **CDS**

- Clinical Dehydration Score
- Similar to WHO/IMCI but uses a validated point system
- Validated in high and low resource settings

Friedman JN, Goldman RD, Srivastava R, Parkin PC. Development of a clinical dehydration scale for use in children between 1 and 36 months of age. *J Pediatr.* 2004;145(2):201–207).

Clinical Dehydration Scale

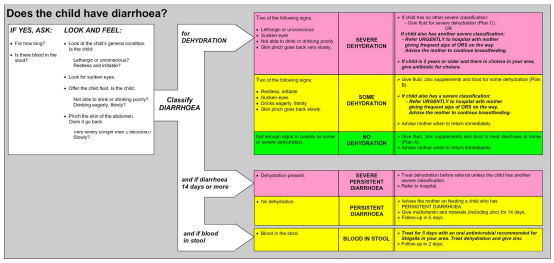
Characteristic	0 points	1 point	2 points
Appearance	Normal	Thirsty, restless, or lethargic but irritable when touched	Drowsy, limp, cold, sweaty, comatose
Eyes	Normal	Slightly sunken	Very sunken
Mucous membranes	Moist	Sticky	Dry
Tears	Tears	Decreased tears	Absent tears

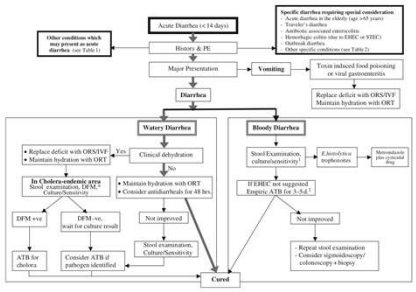
Scoring: 0 points = less than 3% dehydration; 1 to 4 points = mild (3% to 6%) dehydration; 5 to 8 points = moderate to severe (more than 6%) dehydration.

Example 2: Treatment with Antimicrobials WHO vs CDC vs MSF

- Bacterial Enteritis
  - WHO Diarrhea (2005); Ciprofloxacin (Shigella), Tetracycline (Cholera), Acute watery (none)
  - EMLc/AWaRe: Ciprofloxacin "First Choice" (Watch), Azithromycin "Second Choice" (Watch)
  - IDSA/ACG/AAP: Azithromycin (TD)
  - MSF: Acute watery (None); Shigella (Cipro)
  - CDC: Avoid antibiotics in ST-EHEC (STEC)
- Protozoal: Metronidazole
  - Guidelines: WHO 5d vs CDC 5-7d vs MSF 3d
  - Studies: 5-10d yields 90%+ efficacy (Hunter), 3d cures "most" (Beech/Gill TMLN)
  - Giardia vs Amoeba dosing: 15mg/kg/d x5d (Giardia) up to 50mg/kg/d x10d (Amoeba)
  - Eliminating luminal carriage: IDSA Iodoquinol or Paromomycin vs LRS None (Beech/Gill TMLN)

WHO/IMCI Childhood Diarrhoea Protocol





Manatsathitl, et al, Guideline for the Mgmt of Acute Diarrhea in Adults, J Gastroenterology & Hepatology, 2002
Used in Gill/Beeching, Tropical Medicine Lecture Notes, 6th Ed.

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Fine-Tuning Points & Piloting

- Clarified best dosing options in live context ("in vivo vs in vitro")
- Where and when testing is available if needed
- Clarified how our protocol aligned with pre-existing nutritional protocols of host-partner (eg, RUTF, Powder MVT)
- Allowed for adjusting pharmacy medications and supplies amounts
- Expanded to account for exceptions like recurrent diarrhea

Example: Addressing Micronutrient Deficiency

WHO 2005: The Treatment of Diarrhoea

7.5 Give supplementary multivitamins and minerals

All children with persistent diarrhoea should receive supplementary multivitamins and minerals each day for two weeks. Locally available commercial preparations are often suitable; tablets that can be crushed and given with food are least costly. These should provide as broad a range of vitamins and minerals as possible, including *at least* two recommended daily allowances (RDAs) of folate, vitamin A, zinc, magnesium and copper. As a guide, one RDA for a child aged one year is:

- folate 50 ug
- zinc 10 mg
- vitamin A 400 ug
- copper 1 mg
- magnesium 80 mg

Chispita Ingredients:
Ferrous Fumarate (12.5mg iron)
Vitamin C 30mg
Vitamin A 300mcg (IU?)
Folic Acid 160mcg
Zinc Gluconate *5mg*
No Magnesium, No Copper

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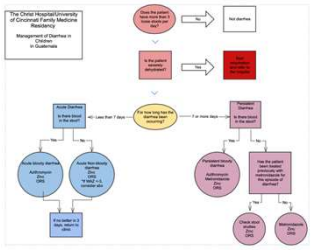
User-Friendly Protocol & Algorithm

MANAGEMENT CHECKLIST:
- ❑Diagnosis: Correctly diagnose and classify diarrhea
- ❑Diagnosis: Rule out other diseases/syndromes that may present with diarrhea
- ❑Triage: Assess vitals and hydration status
- ❑Hydration: Treat dehydration (ORS, IVF, other)
- ❑Antimicrobials: Prescribe antibacterial if appropriate
- ❑Antimicrobials: Prescribe antiprotozoal if appropriate
- ❑Antimicrobials: Prescribe antihelminth if appropriate
- ❑Micronutrient: Prescribe Zinc and Chispitas
- ❑Macronutrient (PEM): Enroll in nutrition program if appropriate (eggs, RUTF, other)
- ❑Deworming: Ensure up-to-date with deworming
- ❑Prevention: WASH: Ensure clean water access; Promote hygiene (Rx Soap if available, etc); Immunizations
- ❑Other Factors: Dietary (coffee/soda/juice)

User-Friendly Protocol & Algorithm



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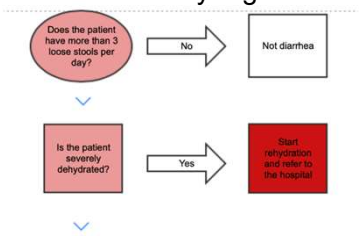

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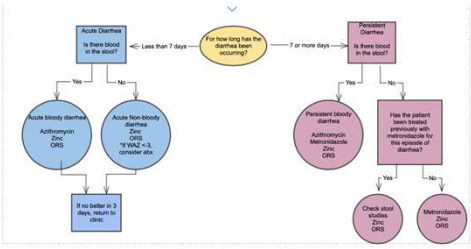

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Continuous QI: Next Steps

- Cross-pollinate/present (here!) to get more ideas
- Stool study (MPH student) – NAAT/PCR
- Household surveys to follow up patients identified with diarrhea

Case: Child in Rural Guatemala with Diarrhea APPLYING OUR PROTOCOL

2 yr M w/ 7d diarrhea, afebrile, WAZ -2.1, HAZ -2.3

Diagnose & Classify:
- Acute, new-onset/non-recrudescent, non-bloody diarrhea
- WHO Class B dehydration (CDS 3-6%)
- Acute malnutrition and stunting

Case: Child in Rural Guatemala with Diarrhea APPLYING OUR PROTOCOL

MANAGEMENT:
- ❑ Hydration: ORS 1200ml / 300ml/hr in first 4 hours
- ❑ Antibiotics: Azithromycin 10mg/kg/d x 3 days
- ❑ Antiprotozoal: None
- ❑ Micronutrient supplementation: Zinc sulfate 20mg daily x10 days (12m-5y); double Chispitas x2wks
- ❑ Macronutrient support: Enroll in nutrition program
- ❑ Deworming: Not UTD on MDA deworming, not chronic/recurrent or abdominal symptoms, so 1d Albendazole 400mg
- ❑ Prevention (WASH): Water filter, Coloring book on hand-washing, Bar of soap
- ❑ Follow up: Only as needed since reassessed same-day at 4 hours
- ❑ Discontinue coffee and soda if able

References/Links

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- Armon, et al. An evidence and consensus based guideline for acute diarrhoea management, *Arch Dis Child* 2001;**85**:132–142; https://adc.bmj.com/content/archdischild/85/2/132.full.pdf (Example of HIC algorithm: 40 steps)