FLUIDS & VOLUME EXPANDERS

CHI Formulary Development Project

INDICATION UPDATE

ADDENDUM- November 2023

To the CHI Original Fluids and Volume Expanders Clinical Guidance- Issued May 2020

Table of Contents

Related Documents 4

List of Tables 4

List of Figures 4

Abbreviations 6

Executive Summary 7

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence 13

1.1 Revised Guidelines 13

1.1.1 NICE Guidance: Intravenous Fluid Therapy in Adults in Hospital (Published 2013, Updated 2017) 14

1.1.2 NICE Guidance: Intravenous Fluid Therapy in Children and Young People in Hospital (2020) 14

1.1.3 American Academy of Pediatrics Clinical Practice Guideline: Maintenance Intravenous Fluids in Children (2018) 27

1.1.4 American Academy of Family Physicians (AAFP) Diabetic Ketoacidosis: Evaluation and Treatment (2013) 28

1.1.5 Japan Society of Transfusion Medicine and Cell Therapy Evidence-Based Guidelines for the Use of Albumin Products (2017) 28

1.2 New Guidelines 28

1.2.1 Intravenous fluids - The Royal Children's Hospital (RCH) Melbourne (2020) 28

1.2.2 Society of Critical Care Medicine Surviving Sepsis Campaign (2021) 36

1.2.3 Saudi National Diabetes Center (SNDC) Saudi Diabetes Clinical Practice Guidelines (SDCPG) (2021) 37

1.2.4 The Joint British Diabetes Societies for Inpatient Care: Management of Diabetic Ketoacidosis in Adults (2023) 40

Section 2.0 Drug Therapy in Fluids and Volume Expanders 44

2.1 Additions 44

2.2 Modifications 44

2.3 Delisting 44

Section 3.0 Key Recommendations Synthesis 45

Section 4.0 Conclusion 51

Section 5.0 References.....52
Section 6.0 Appendices.....53
Appendix A. Prescribing Edits Definition.....53
Appendix B. Fluids and Volume Expanders Scope.....55
Appendix C. MeSH Terms PubMed.....56
Appendix D. Treatment Algorithm.....58

Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

List of Tables

Table 1. General Recommendations on Fluids and Volume Expanders 8
Table 2. Clinical Guidelines Requiring Revision 13
Table 3. Grading Scheme for Recommendations 14
Table 4. Clinical Features of Dehydration and Hypovolemic Shock 22
Table 5. Intravenous Fluid Types for Children and Young People 26
Table 6. List of Additional Guidelines 28
Table 7. Calculations of Fluid Requirements and Fluid Deficit 30
Table 8. Calculations of full maintenance fluid rates. Adapted from the 2020 Royal Children's Hospital Guideline. 30
Table 9. Hourly Fluid Rates. Adapted from the 2020 Royal Children's Hospital Guideline. 32
Table 10. Electrolyte Content of Intravenous Fluids. Retrieved from the 2020 Royal Children's Hospital Guideline. 35
Table 11. Grading Scheme for Recommendations 36
Table 12. Conservative total fluid calculation. Adapted from SDCPG 2021 39
Table 13. Fluid Adjustments. Adapted from SDCPG 2021. 39
Table 14. Typical Fluid Replacement Plan for a Previously Healthy 70 kg Adult (Adapted from the JBDS 2023 DKA Guideline) 42

List of Figures

Figure 1. Assessment and Monitoring. Retrieved from the NICE 2020 Guidance. 16
Figure 2. Fluid Resuscitation. Retrieved from the NICE 2020 Guidance. 17
Figure 3. Routine Maintenance. Retrieved from the NICE 2020 Guidance. 18
Figure 4. Replacement and Redistribution. Retrieved from the NICE 2020 Guidance. 19
Figure 5. Managing Hypernatremia (Plasma Sodium More Than 145 mmol/liter) That Develops During IV Fluid Therapy. Retrieved from the NICE 2020 Guidance 19
Figure 6. Managing Hyponatremia (Plasma Sodium Less Than 135 mmol/liter) That Develops During IV Fluid Therapy. Retrieved from the NICE 2020 Guidance 20

Figure 7. Details of Any Ongoing Losses. Retrieved from the NICE 2020 Guidance. ... 21
Figure 8. Approach to IV Fluid Prescription. Retrieved from the 2020 Royal Children's Hospital Guideline. ... 34
Figure 9. Fluid Management in the First Hour. Retrieved from SDCPG 2021. ... 38
Figure 10. Cerebral Edema Management. Retrieved from SDCPG 2021. ... 40

Abbreviations

ADH	Antidiuretic Hormone
CHI	Council of Health Insurance
CPG	Clinical Practice Guideline
D	Dextrose
FDA	Food and Drug Administration
IDF	CHI Drug Formulary
IV	Intravenous
K	Potassium
Na	Sodium
NICE	National Institute for Health and Care Excellence
NS	Normal Saline
SFDA	Saudi Food and Drug Authority

Executive Summary

Fluid resuscitation plays a critical role in maintaining organ perfusion and delivering essential substrates like oxygen and electrolytes. It involves administering fluids and electrolytes, mainly via intravenous (IV) administration. The body's fluids are divided into intracellular and extracellular compartments, and these compartments have distinct electrolyte compositions[1].

Two main types of fluids for resuscitation are colloids and crystalloids[1]. There are certain situations where one specific type of fluid is preferred. Caution should be exercised with 0.9% saline and avoided with colloids in septic shock. Intravenous albumin is contraindicated in patients with traumatic brain injury[1].

Excessive intravenous fluids can lead to hypervolemia, electrolyte imbalances, and complications like pulmonary and subcutaneous edema[1]. These complications can prolong hospital stays, increase the risk of nosocomial issues, as well as increase the risk of mortality[1].

In clinical practice, maintaining fluid balance and electrolyte equilibrium is essential[1]. Maintenance fluids are administered in specific cases, such as prolonged fasting or when oral fluid intake is limited[1]. The fluid requirements are calculated based on body weight[1].

CHI issued Fluids and Volume Expanders clinical guidelines after thorough review of renowned international and national clinical guidelines in May 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI Fluids and Volume Expanders clinical guidance and seeks to offer guidance for the effective management of Fluids and Volume Expanders. It provides an **update on the Fluids and Volume Expanders Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update were summarized, being **the issuance of updated versions of previously reviewed guidelines** namely **Intravenous fluid therapy in children and young people in hospital, Guidance, NICE 2020**. Moreover, **new guidelines are added to the report** such as **Intravenous fluids - The Royal Children's Hospital (RCH) Melbourne**, Surviving Sepsis Campaign by the Society of Critical Care Medicine (2021), the Saudi Diabetes Clinical Practice Guidelines by the Saudi National Diabetes Center (SDCPG, SNDC, 2021), The Management of Diabetic Ketoacidosis in Adults by the Joint British Diabetes Societies for inpatient care (2023)

After carefully examining clinical guidelines and reviewing the SFDA drug list, there are no new drugs to be added to the CHI formulary, and there are no new drugs

approved by the FDA. The following drugs is no longer SFDA-registered, and it is advisable to delist it from CHI formulary: Dextrose 10% w/v in 0.225% w/v Sodium Chloride.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in Fluids and Volume Expanders therapeutic management.

Below is a table summarizing the major changes based on the different Fluids and Volume Expanders guidelines used to issue this report:

Table 1. General Recommendations on Fluids and Volume Expanders

Fluids and Volume Expanders		
General Recommendations	**Level of Evidence/ Grade of Recommendation**	**Reference**
If patients need IV fluid resuscitation, use crystalloids that contain sodium in the range 130–154 mmol/l, with a bolus of 500 ml over less than 15 minutes.	N/A	IV fluid therapy in adults in hospital NICE (2017)[2]
If patients need IV fluids for routine maintenance alone, restrict the initial prescription to 25–30 ml/kg/day of water and approximately 1 mmol/kg/day of potassium, sodium**,** and chloride and 50–100 g/day of glucose to limit starvation ketosis.	N/A	IV fluid therapy in adults in hospital NICE (2017)[2]
For term neonates requiring IV fluid resuscitation, use glucose-free crystalloids containing sodium in the range of 131–154 mmol/liter, administering a bolus of 10-20 ml/kg in less than 10 minutes. Adjust volumes considering pre-existing conditions, such as cardiac or kidney disease.	N/A	IV fluid therapy in children and young people in hospital NICE (2020)[3]
When children and young people require IV fluid resuscitation, use glucose-free crystalloids containing sodium in the range of 131–154 mmol/liter, administering a bolus of 10	N/A	IV fluid therapy in children and young people in hospital NICE (2020)[3]

20 ml/kg in less than 10 minutes. Adjust volumes considering pre-existing conditions, such as cardiac or kidney disease.		
Calculate routine maintenance IV fluid rates for children and young people using the Holliday–Segar. Over a 24-hour period, males generally require up to 2,500 ml, and females up to 2,000 ml of fluids	N/A	IV fluid therapy in children and young people in hospital NICE (2020)[3]
For redistribution, consider isotonic crystalloids with sodium in the range of 131 to 154 mmol/liter. To replace ongoing losses, use 0.9% sodium chloride containing potassium. Base any subsequent fluid prescriptions on the plasma electrolyte concentrations and blood glucose measurements.	N/A	IV fluid therapy in children and young people in hospital NICE (2020)[3]
Patients 28 days to 18 years of age requiring maintenance IVFs should receive isotonic solutions with appropriate potassium chloride (KCl) and dextrose because they significantly decrease the risk of developing hyponatremia.	Evidence quality: A; recommendation strength: strong	IV Fluids in Children by American Academy of Pediatric 2018[4]
In most persons, saline 0.9% is started at 15 to 20 mL per kg per hour, or 1 L per hour initially. As the patient stabilizes, fluids can be lowered to 4 to 14 mL per kg per hour, or 250 to 500 mL per hour. Once the corrected sodium concentration is normal or high (greater than 135 mEq per L [135 mmol per L]), the solution can be changed to saline 0.45%. Dextrose is added when the glucose level decreases to 200 mg per dL (11.10 mmol per L).	N/A	Diabetic Ketoacidosis journal of American family physician 2013[5]
Spontaneous bacterial peritonitis with renal impairment benefits from the treatment with a hypertonic albumin solution at a 1.5 g/kg body weight within 6	1A	Albumin Products; Japan Society (2017)[6]

hours after diagnosis, following by 1 g/kg body weight on day3 of illness.		
Treatment with a hypertonic albumin solution and a vasoconstrictor is effective in improving type-1 hepatorenal syndrome. Albumin should be administered at a dose of 1g/kg body weight on day1 and 20 to 40g/body weight on subsequent days, in combination with terlipressin and other drugs.	1A	Albumin Products; Japan Society (2017)[6]
In burns, Albumin products are indicated in burns involving ≥ 50% of the total body surface area.	2C	Albumin Products; Japan Society (2017)[6]
In patients with treatment-resistant pulmonary edema or marked edema, the use of a hypertonic albumin product is considered only in the case of marked hypoalbuminemia.	2B	Albumin Products; Japan Society (2017)[6]
The use of isotonic albumin should be considered to maintain circulating blood volume in cases of vasospasm after subarachnoid hemorrhages that do not respond to crystalloids.	2C	Albumin Products; Japan Society (2017)[6]
Plasmapheresis: using an isotonic or diluted hypertonic albumin solution as a replacement fluid (1-to1.5-foldplasma volume/ session) is recommended for the treatment of neurological disorders, such as CIDP and GBS.	1A	Albumin Products; Japan Society (2017)[6]
For patients experiencing sepsis-induced hypoperfusion or septic shock, consider administering a minimum of 30 mL/kg of IV crystalloid fluid within the initial 3 hours of resuscitation.	Weak, low quality of evidence	Surviving Sepsis Campaign (2021)[7]
In the case of adults with sepsis or septic shock, our recommendation is to use crystalloids as the primary choice for fluid resuscitation.	Strong, moderate-quality evidence	Surviving Sepsis Campaign (2021)[7]

Use a restrictive transfusion strategy over a liberal one for adults with sepsis or septic shock.	Strong recommendation, moderate quality of evidence	Surviving Sepsis Campaign (2021)[7]
In DKA patients older than 14 years old: **Begin with an initial normal saline bolus, followed by a rapid normal saline infusion**. Initially, use isotonic saline at a rate of 15-20 ml/kg of body weight per hour or 1-1.5 L during the first hour.	N/A	SDCPG, SNDC, 2021[8]
In DKA patients older than 14 years old: **Hypernatremic patients may benefit from 0.45% NaCl at 4-14 ml/kg/hour, while patients with eunatremia or hyponatremia may prefer 0.9% Na Cl at a similar rate.**	N/A	SDCPG, SNDC, 2021[8]
Management of DKA in Emergency room or urgent care area: Start IV 0.9% Saline at: 5 ml/kg/h for mild/moderate DKA 7 ml/kg/h for severe DKA.	N/A	SDCPG, SNDC, 2021[8]
Management plan of DKA after the 1-2 hours: IV maintenance + deficit: Maintenance calculation: 100 ml/kg for the first 10 kg+ 50 ml/kg for the next 10kg + 20 ml/kg for the rest BW. Deficit calculation: 5% for mild/moderate DKA, 10% for severe DKA.	N/A	SDCPG, SNDC, 2021[8]
Common Deficits in DKA for Adults: Water: 100 ml/kg, Sodium: 7-10 mmol/kg, Chloride: 3-5 mmol/kg, Potassium: 3-5 mmol/kg.	N/A	DKA, JBDS, 2023[9]
DKA in First hour: Restoring Circulating Volume: Administer 500 ml of 0.9% sodium chloride solution over 10-15 minutes. If the SBP remains below 90 mmHg, this can be repeated while awaiting input from senior medical staff.	N/A	DKA, JBDS, 2023[9]

At the end of the report, a key recommendation synthesis section is added highlighting the latest updates on **fluids and volume expanders**.

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Fluids and Volume Expanders report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This part contains the updated versions of the guidelines mentioned in the May 2020 CHI Fluids and Volume Expanders report and the corresponding recommendations:

Table 2. Clinical Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated Versions**
Section 1.1 Intravenous fluid therapy in adults in hospital | Guidance | **NICE**. (2013, December 10 last update May **2017**)[2]	N/A*
Section 1.2 Intravenous fluid therapy in children and young people in hospital | Guidance | **NICE**. (**2015**, December 9)	Intravenous fluid therapy in children and young people in hospital | Guidance | **NICE** (**2020**)[3]
Section 1.3 Clinical Practice Guideline: Maintenance Intravenous Fluids in Children by **American Academy of Pediatric 2018**[4]	N/A*
Section 1.4 Diabetic Ketoacidosis: Evaluation and Treatment at journal of **American Family Physician 2013**[5]	N/A*
Section 1.5 Evidence-based Guidelines for the Use of Albumin Products; **Japan Society of Transfusion Medicine and Cell Therapy** (**2017**)[6]	N/A*

*: No updated versions available

1.1.1 NICE Guidance: Intravenous Fluid Therapy in Adults in Hospital (Published 2013, Updated 2017)

*Please refer to **Section 1.1** of CHI Report.*

There are no new updates. The recommendations of this guideline remain unchanged [2].

1.1.2 NICE Guidance: Intravenous Fluid Therapy in Children and Young People in Hospital (2020)

*Please refer to **Section 1.2** of CHI Report.*

Evidence levels and grades of recommendations are outlined below [3]:

Table 3. Grading Scheme for Recommendations

Grading Scheme for Recommendations			
Level	**Type of evidence**	**Grade**	**Evidence**
1	Evidence obtained from a single randomized controlled trial or a meta-analysis of randomized controlled trials	A	At least 1 randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level 1) without extrapolation
2a	Evidence obtained from at least 1 well-designed controlled study without randomization	B	Well conducted clinical studies but no randomized clinical trials on the topic of recommendation (evidence levels 2 or 3); or extrapolated from level 1 evidence
2b	Evidence obtained from at least 1 other well-designed quasi-experimental study	–	–
3	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies	–	–

4	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	C	Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level 4) or extrapolated from level 1 or 2 evidence. This grading indicates that directly applicable clinical studies of good quality are absent or not readily available
4	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	GPP	Recommended good practice based on the clinical experience of the GDG.

The following recommendations are provided by the NICE on Intravenous fluid therapy in children and young people in hospital [3]:

Principles and Protocols for IV Fluid Therapy

- Offer IV Fluid Therapy as Part of a Protocol:
    - The figures below provide specific algorithms for IV fluid therapy in children and young people, such as assessment and monitoring, fluid resuscitation, routine maintenance, and replacement and redistribution:

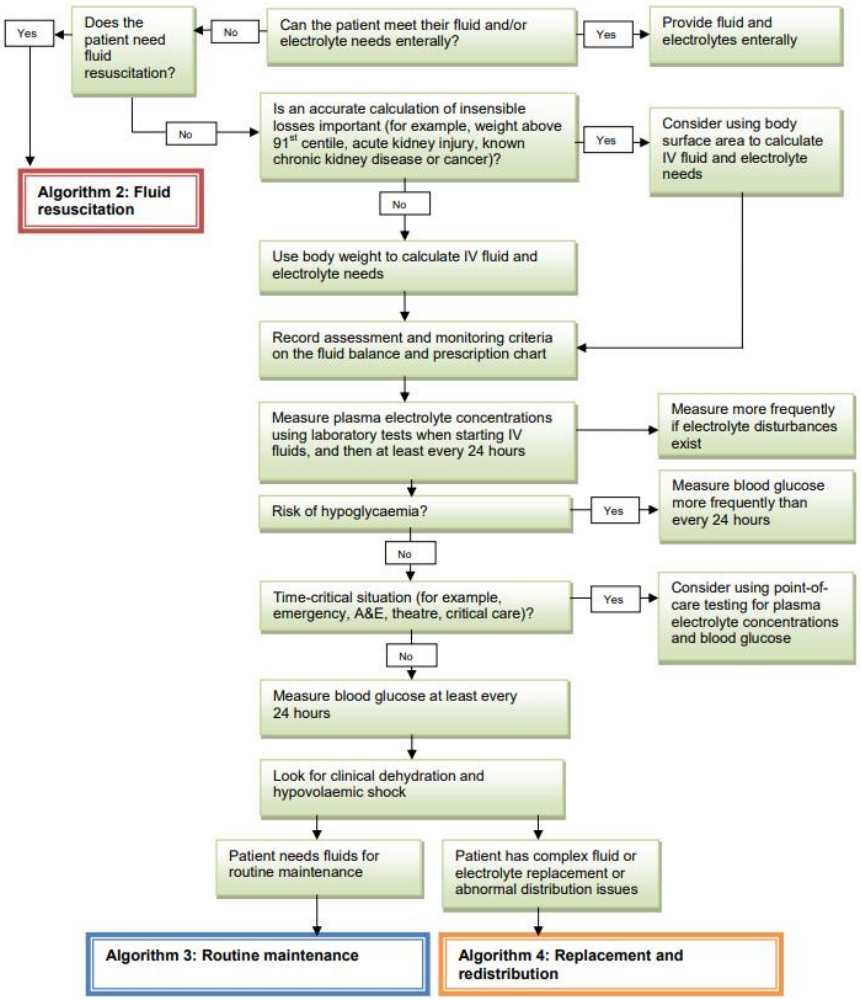

Figure 1. *Assessment and Monitoring. Retrieved from the NICE 2020 Guidance.*

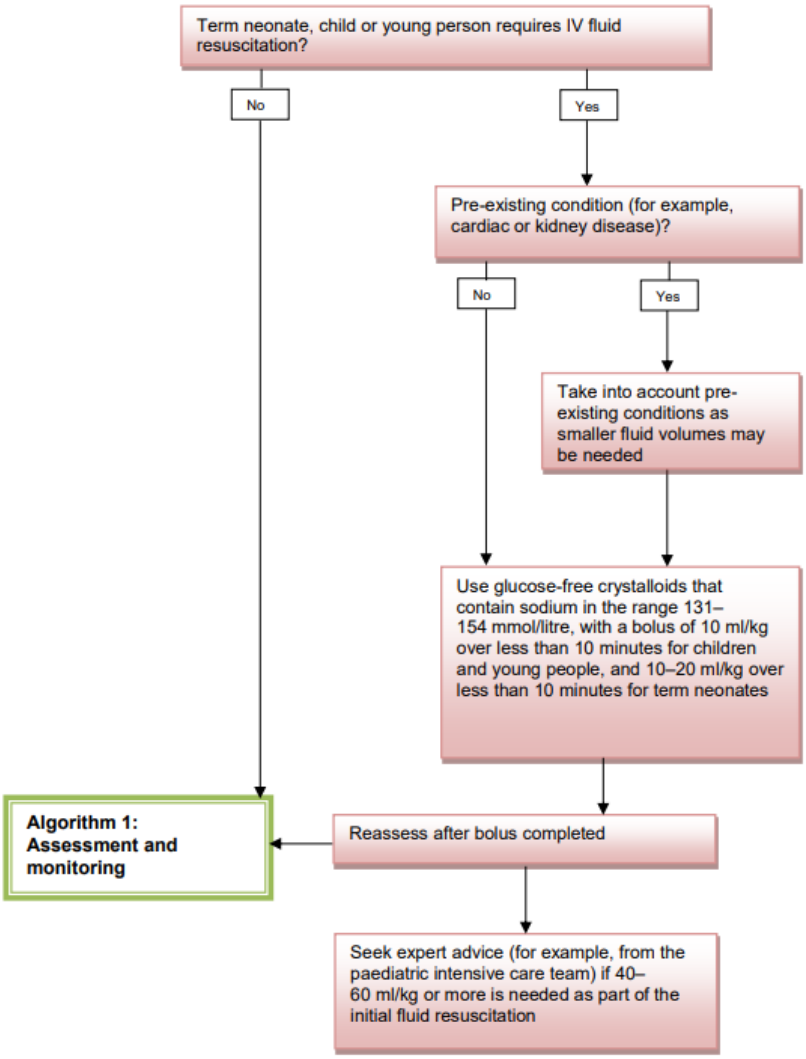

Figure 2. *Fluid Resuscitation. Retrieved from the NICE 2020 Guidance.*

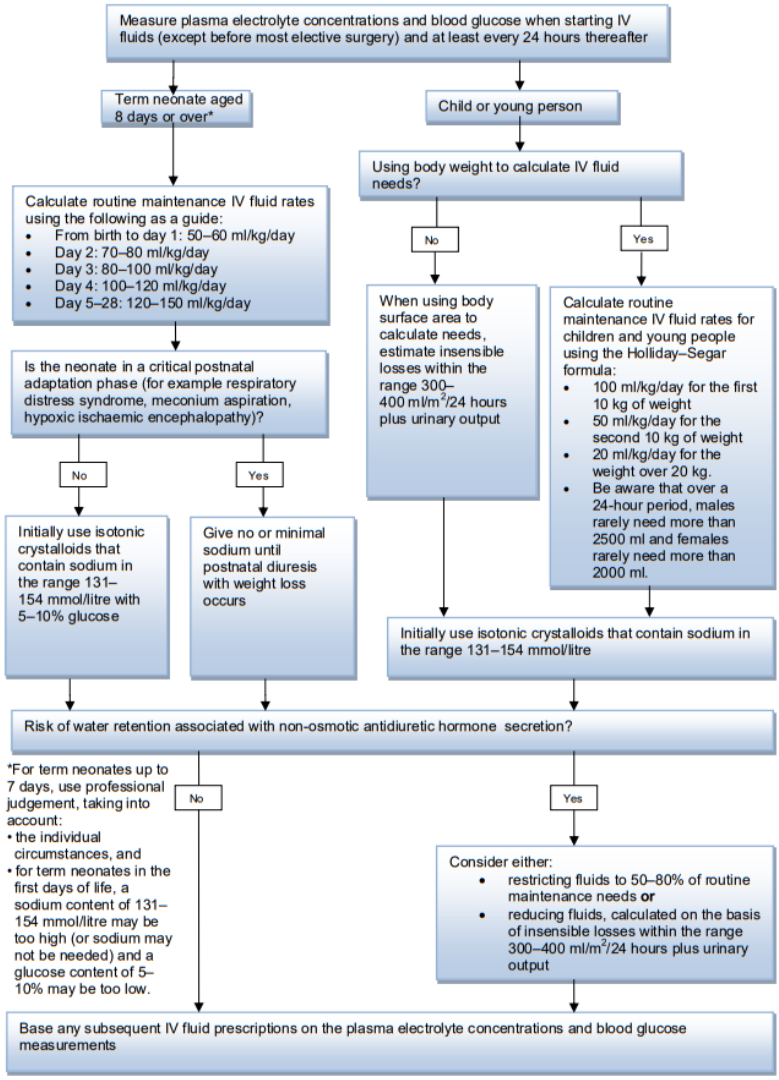

Figure 3. *Routine Maintenance. Retrieved from the NICE 2020 Guidance.*

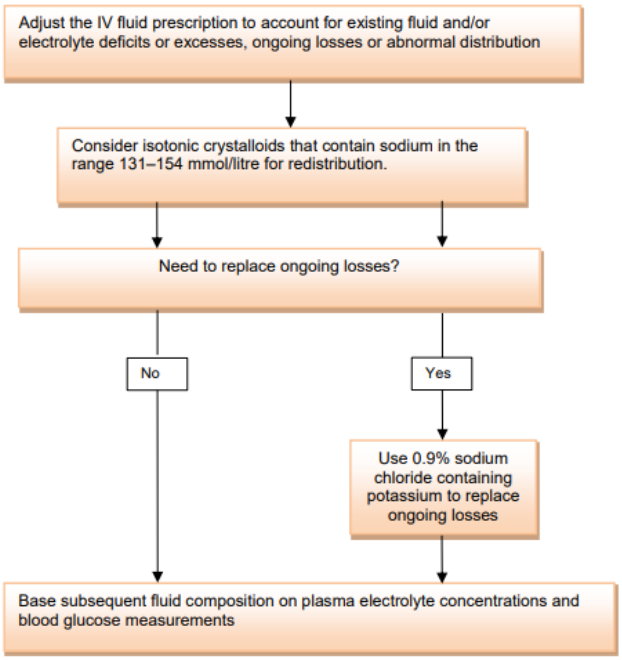

Figure 4. *Replacement and Redistribution. Retrieved from the NICE 2020 Guidance.*

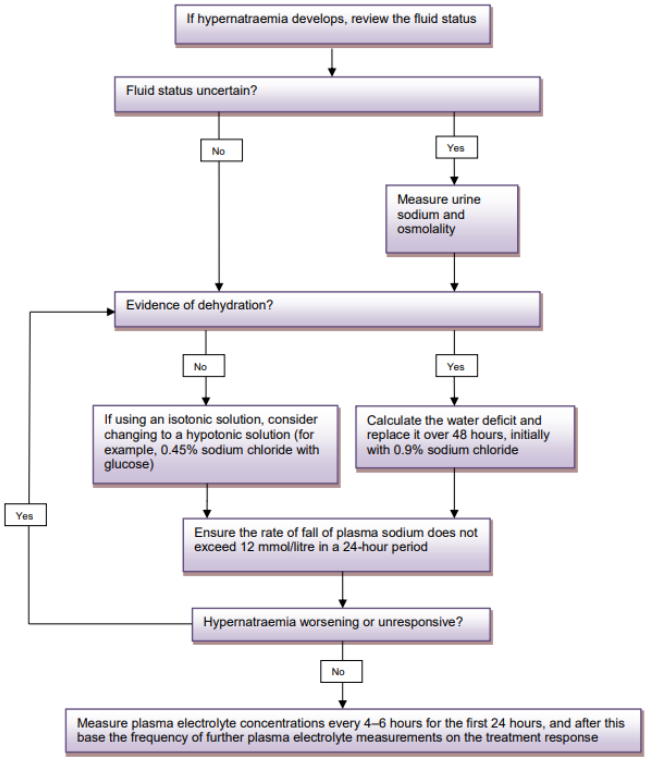

Figure 5*. Managing Hypernatremia (Plasma Sodium More Than 145 mmol/liter) That Develops During IV Fluid Therapy. Retrieved from the NICE 2020 Guidance.*

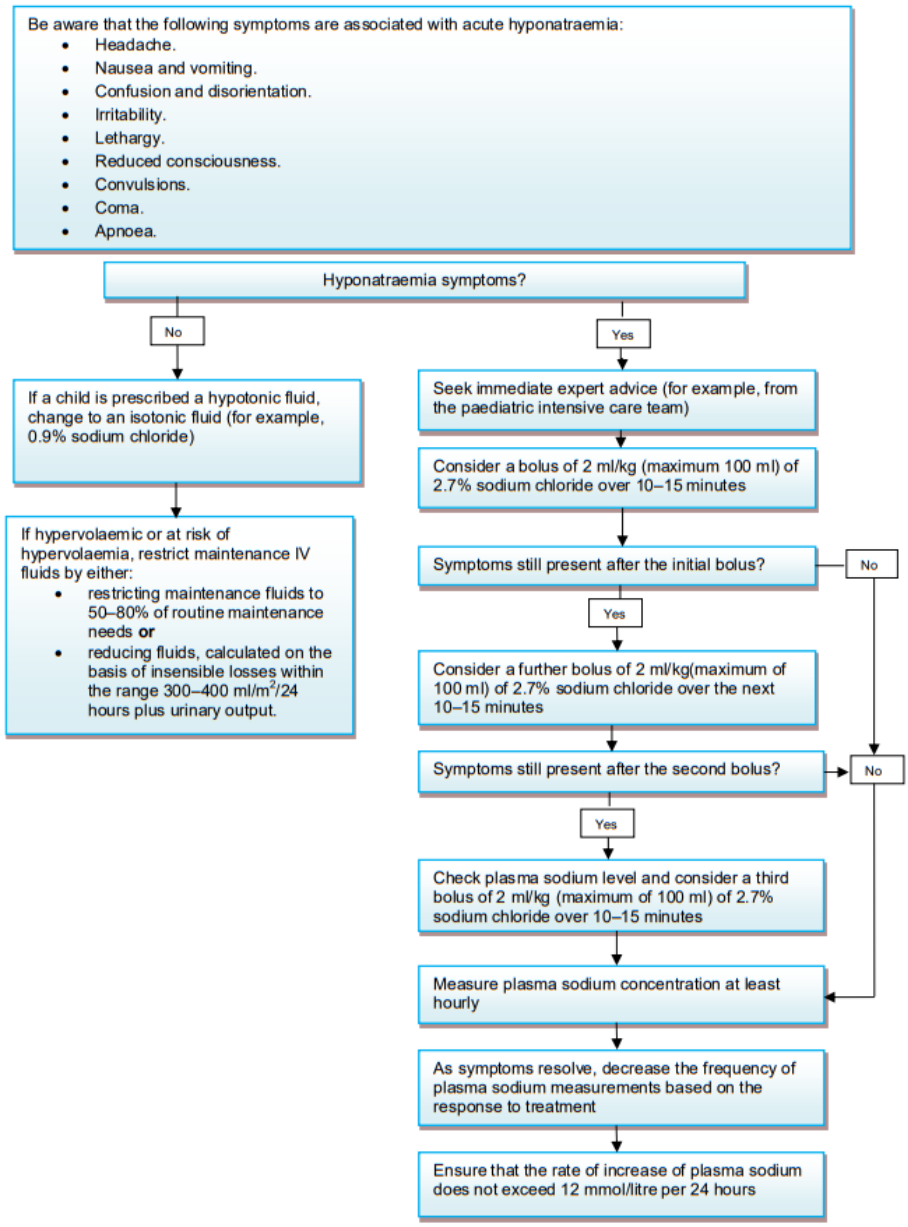

Figure 6. *Managing Hyponatremia (Plasma Sodium Less Than 135 mmol/liter) That Develops During IV Fluid Therapy. Retrieved from the NICE 2020 Guidance.*

- Assessment and Monitoring:
    - Assessment and Documentation of IV Fluid and Electrolyte Needs:
        - Calculate IV fluid and electrolyte needs based on body weight for term neonates, children, and young people.
        - Consider using body surface area for more accurate calculations, especially when weight is above the 91st centile, or in cases of acute kidney injury, known chronic kidney disease, or cancer.

- For individuals receiving IV fluids in this group, assess and document:
    - Actual or estimated daily body weight, including previous-day weight and the difference.
    - Fluid input, output, and balance over the previous 24 hours.
    - Any special instructions for prescribing and relevant medical history.
    - An assessment of fluid status, including the results of laboratory and point-of-care assessments (e.g., full blood count, urea, creatinine, plasma electrolyte concentrations, blood glucose, and urinary electrolyte concentrations).
    - Details of ongoing losses and calculations of fluid needs for routine maintenance, replacement, redistribution, and resuscitation, as shown in the figure below:

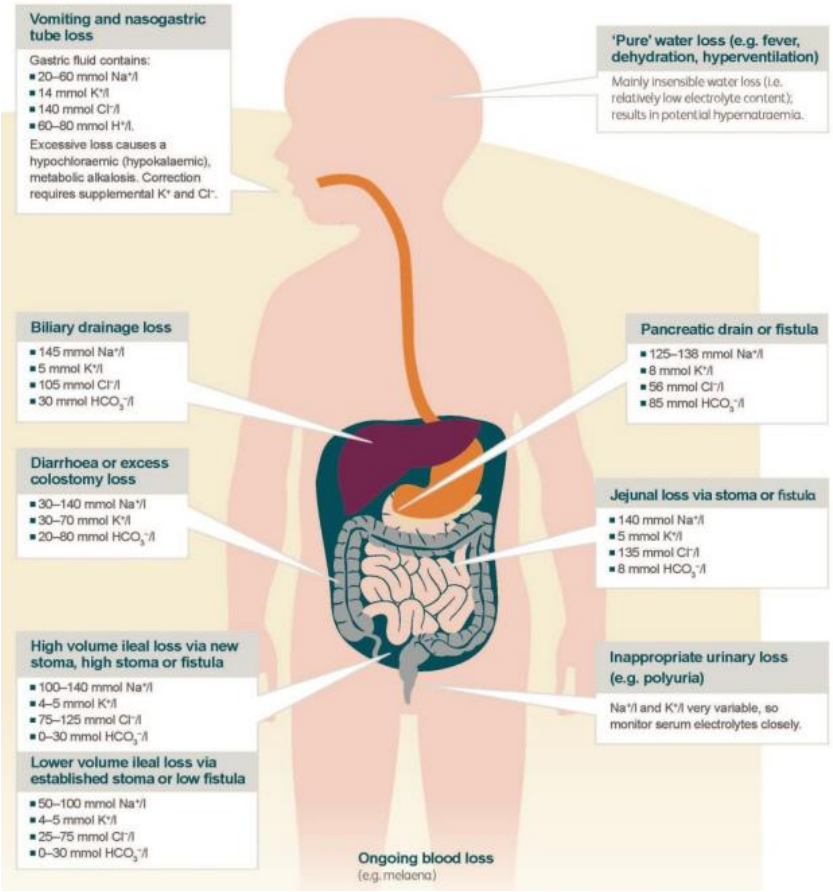

Figure 7. *Details of Any Ongoing Losses. Retrieved from the NICE 2020 Guidance.*

- Fluid and electrolyte prescription in ml per hour with clear signatures, dates, and times.
- Types and volumes of fluid input and output recorded hourly with running totals.
- 12-hourly fluid balance subtotals.
- 24-hourly fluid balance totals.
- 12-hourly reassessments of the fluid prescription, current hydration status, potential initiation of oral fluids, and urine and other outputs.

- Measure plasma electrolyte concentrations using laboratory tests when initiating IV fluids, with subsequent monitoring at least every 24 hours or more frequently if electrolyte disturbances occur.
- Monitor blood glucose when starting IV fluids and continue monitoring at least every 24 hours or more frequently if there's a risk of hypoglycemia.
- Consider point-of-care testing for measuring plasma electrolyte concentrations and blood glucose in time-critical situations when IV fluids are required, such as during emergency situations in the A&E, theatre, and critical care.
- Diagnose clinical dehydration and hypovolemic shock using the clinical features outlined in the table below, with awareness of potential challenges in identifying these features in term neonates. The table is adapted from NICE's guideline on diarrhea and vomiting in children.

Table 4. Clinical Features of Dehydration and Hypovolemic Shock

Clinical features of dehydration and hypovolemic shock		
No clinically detectable dehydration	**Clinical dehydration**	**Hypovolemic shock**
Alert and responsive	**Red flag:** Altered responsiveness (for example, irritable, lethargic)	Decreased level of consciousness
Appears well	**Red flag:** Appears to be unwell or deteriorating	-
Eyes not sunken	**Red flag:** Sunken eyes	-

Moist mucous membranes (except after a drink)	Dry mucous membranes (except for 'mouth breather')	-
Normal blood pressure	Normal blood pressure	Hypotension (decompensated shock)
Normal breathing pattern	**Red flag:** Tachypnoea	Tachypnoea
Normal capillary refill time	Normal capillary refill time	Prolonged capillary refill time
Normal heart rate	**Red flag:** Tachycardia	Tachycardia
Normal peripheral pulses	Normal peripheral pulses	Weak peripheral pulses
Normal skin turgor	**Red flag:** Reduced skin turgor	-
Normal urine output	Decreased urine output	-
Skin color unchanged	Skin color unchanged	Pale or mottled skin
Warm extremities	Warm extremities	Cold extremities

    - Recognize that clinical dehydration encompasses a spectrum of severity, indicated by increasingly numerous and more pronounced clinical features. For hypovolemic shock, one or more of the clinical features listed should be expected. Dashes (–) indicate that these features do not specifically indicate hypovolemic shock.

Fluid resuscitation

- When children and young people require IV fluid resuscitation, use glucose-free crystalloids containing sodium in the range of 131–154 mmol/liter, administering a bolus of 20 ml/kg in less than 10 minutes. Adjust volumes considering pre-existing conditions, such as cardiac or kidney disease.
- For term neonates requiring IV fluid resuscitation, use glucose-free crystalloids with sodium in the range of 131–154 mmol/liter, administering a bolus of 10–20 ml/kg in less than 10 minutes.
- Avoid using tetrastarch for fluid resuscitation.
- After completing the IV fluid bolus, reassess term neonates, children, and young people to determine if they require additional fluids.
- Seek expert advice, such as from the pediatric intensive care team, if the initial fluid resuscitation requires 40–60 ml/kg of IV fluid or more.

Routine maintenance

- Calculate routine maintenance IV fluid rates for children and young people using the Holliday–Segar formula (100 ml/kg/day for the first 10 kg of weight, 50 ml/kg/day for the next 10 kg and 20 ml/kg/day for the weight over 20 kg). Over a 24-hour period, males generally require up to 2,500 ml, and females up to 2,000 ml of fluids.
- Calculate routine maintenance IV fluid rates for term neonates based on their age:
    - From birth to day 1: 50 to 60 ml/kg/day.
    - Day 2: 70 to 80 ml/kg/day.
    - Day 3: 80 to 100 ml/kg/day.
    - Day 4: 100 to 120 ml/kg/day.
    - Days 5 to 28: 120 to 150 ml/kg/day.
- When children and young people require IV fluids for routine maintenance, initially use isotonic crystalloids with sodium in the range of 131 to 154 mmol/liter.
- Measure plasma electrolyte concentrations and blood glucose when initiating IV fluids for routine maintenance, except before most elective surgeries, and continue monitoring at least every 24 hours.
- Understand that routine measurement of plasma electrolyte concentrations and blood glucose before elective surgery is based on the child's medical condition or surgery type.
- Base subsequent IV fluid prescriptions on plasma electrolyte concentrations and blood glucose measurements.
- For term neonates aged 8 days or over, use isotonic crystalloids with sodium in the range of 131–154 mmol/liter and 5–10% glucose for routine maintenance. For term neonates aged up to 7 days, use professional judgment, considering individual circumstances, and for term neonates in the first days of life, a sodium content of 131 to 154 mmol/ liter may be too high (or sodium may not be needed) and a glucose content of 5% to 10% may be too low.
- In term neonates in critical postnatal adaptation phases, withhold or provide minimal sodium until postnatal diuresis with weight loss occurs.
- If there is a risk of water retention due to non-osmotic ADH secretion, consider either restricting fluids to 50% to 80% of routine maintenance needs or reducing fluids calculated on the basis of insensible losses within the range 300–400 ml/m2 /24 hours plus urinary output.

- When calculating IV fluid needs for routine maintenance using body surface area, estimate insensible losses within the range of 300–400 ml/m2/24 hours plus urinary output.

Replacement and redistribution

- When IV fluids are needed for replacement or redistribution in term neonates, children, and young people, adjust the IV fluid prescription to consider existing fluid and electrolyte imbalances, ongoing losses, and abnormal distribution (e.g., tissue edema in sepsis).
- For redistribution, consider isotonic crystalloids with sodium in the range of 131 to 154 mmol/liter.
- To replace ongoing losses, use 0.9% sodium chloride containing potassium.
- Base any subsequent fluid prescriptions on plasma electrolyte concentrations and blood glucose measurements.

Managing hypernatremia that develops during intravenous fluid therapy

- If hypernatremia occurs in term neonates, children, and young people, assess fluid status:
    - Consider switching from isotonic to hypotonic fluids (e.g., 0.45% sodium chloride with glucose) if no dehydration is evident.
    - If dehydration is diagnosed, calculate, and replace the water deficit over 48 hours, starting with 0.9% sodium chloride.
    - In case of uncertain fluid status, measure urine sodium and osmolality.
    - If hypernatremia persists or worsens after replacing the deficit, consider shifting to a hypotonic solution (e.g., 0.45% sodium chloride with glucose).
- When correcting hypernatremia, ensure that the rate of plasma sodium decrease does not exceed 12 mmol/liter within a 24-hour period.
- Measure plasma electrolyte concentrations every 4 to 6 hours in the first 24 hours and adjust the frequency based on the response to treatment.

Managing hyponatremia that develops during intravenous fluid therapy

- If asymptomatic hyponatremia develops in term neonates, children, and young people, assess fluid status:
    - Transition from hypotonic to isotonic fluids (e.g., 0.9% sodium chloride).

- Restrict maintenance IV fluids in individuals at risk of hypervolemia by either reducing to 50-80% of routine maintenance or calculating based on insensible losses within the range 300–400 ml/m2 /24 hours plus urinary output.

- Recognize symptoms associated with acute hyponatremia during IV fluid therapy: Headache, Nausea and vomiting, Confusion and disorientation, Irritability, Lethargy, Reduced consciousness, Convulsions, Coma, Apnoea.
- If acute symptomatic hyponatremia occurs in term neonates, children and young people, review the fluid status, seek immediate expert advice (for example, from the pediatric intensive care team) and consider taking action as follows:
    - Administer a bolus of 2 ml/kg (maximum 100 ml) of 2.7% sodium chloride over 10–15 minutes.
    - Consider a further bolus of 2 ml/kg (maximum 100 ml) of 2.7% sodium chloride over the next 10 to 15 minutes if symptoms persist.
    - If symptoms are still present after the second bolus, check the plasma sodium level and consider a third bolus of 2 ml/kg (maximum 100 ml) of 2.7% sodium chloride over 10 to 15 minutes.
    - Measure plasma sodium concentration at least hourly.
    - Adjust the frequency of plasma sodium measurements as symptoms resolve.
- Do not rely on fluid restriction alone to manage acute hyponatremic encephalopathy.
- After resolving hyponatremia symptoms, ensure that the rate of plasma sodium increase does not exceed 12 mmol/liter in a 24-hour period.

The following table provides the intravenous fluid types for children and young people:

Table 5. Intravenous Fluid Types for Children and Young People

Isotonic crystalloids that contain sodium in the range 131–154 mmol/liter				
Fluid type	**Osmolality (compared with plasma)**	**Tonicity (with reference to cell membrane)**	**Sodium content (mmol/liter)**	**Potassium content (mmol/liter)**
0.9% sodium chloride	Isosmolar	Isotonic	154	0

Hartmann's solution	Isosmolar	Isotonic	131	5
Isotonic crystalloids with glucose that contain sodium in the range 131–154 mmol/liter				
Fluid type	**Osmolality (compared with plasma)**	**Tonicity (with reference to cell membrane)**	**Sodium content (mmol/liter)**	**Potassium content (mmol/liter)**
0.9% sodium chloride with 5% glucose	Hyperosmolar	Isotonic	150	0
Hypotonic fluids				
Fluid type	**Osmolality (compared with plasma)**	**Tonicity (with reference to cell membrane)**	**Sodium content (mmol/liter)**	**Potassium content (mmol/liter)**
0.45% sodium chloride with 5% glucose	Hyperosmolar	Hypotonic	75	0
0.45% sodium chloride with 2.5% glucose	Isosmolar	Hypotonic	75	0
0.45% sodium chloride	Hyperosmolar	Hypotonic	75	0
5% glucose	Isosmolar	Hypotonic	0	0
10% glucose	Hyperosmolar	Hypotonic	0	0

1.1.3 American Academy of Pediatrics Clinical Practice Guideline: Maintenance Intravenous Fluids in Children (2018)

*Please refer to **Section 1.3** of CHI Report.*

There are no new updates. The recommendations of this guideline remain unchanged [4].

1.1.4 American Academy of Family Physicians (AAFP) Diabetic Ketoacidosis: Evaluation and Treatment (2013)

*Please refer to **Section 1.4** of CHI Report.*

There are no new updates. The recommendations of this guideline remain unchanged[5].

1.1.5 Japan Society of Transfusion Medicine and Cell Therapy Evidence-Based Guidelines for the Use of Albumin Products (2017)

*Please refer to **Section 1.5** of CHI Report.*

There are no new updates. The recommendations of this guideline remain unchanged[6].

1.2 New Guidelines

This part includes the added guidelines to the previous CHI Fluids and Volume Expanders report, along with their recommendations.

Table 6. List of Additional Guidelines

Additional Guidelines
Intravenous fluids - The Royal Children's Hospital (RCH) Melbourne (2020)[10]
Surviving Sepsis Campaign by the Society of Critical Care Medicine (2021)[7]
The Saudi Diabetes Clinical Practice Guidelines by the Saudi National Diabetes Center (SDCPG, SNDC, 2021)[8]
The Management of Diabetic Ketoacidosis in Adults by the Joint British Diabetes Societies for inpatient care (2023)[9]

1.2.1 Intravenous fluids - The Royal Children's Hospital (RCH) Melbourne (2020)

Evidence levels and recommendation grades are not outlined[10].

The following recommendations are provided by the Royal Children's Hospital (RCH) Melbourne on the management of IV fluids[10]:

- **Assessment: Red Flags:**
    - Check for abnormal serum sodium levels <135 mmol/L or >145 mmol/L (or significant change of >0.5 mmol/L/hr on a repeat measure)

- Consider increased antidiuretic hormone (ADH) secretion- especially with acute CNS and pulmonary conditions.
- Short gut or other significant gastrointestinal pathology
- Fluid resuscitation >20 mL/kg required.
- Situations where specialized fluid management is required.

- Examination
  - Examine hydration status for signs of dehydration and fluid overload including edema (e.g., periorbital, genital, sacral, peripheral), especially in children already receiving IV fluid treatment.
  - Weigh children on IV fluids at the start of treatment and at least daily.
  - Children with severe dehydration or ongoing losses need to be weighed more often.
- **Management:**
  - Measure serum electrolytes and glucose before starting IV fluid treatment and at least every 24 hours if IV fluids are continued at more than 50% maintenance.
  - For more unwell children and children with large fluid losses or abnormal electrolytes, check the electrolytes and glucose 4-6 hours after starting fluid therapy, and then according to the clinical situation.
  - Repeated weights are the best measure of fluid status.
  - Keep track of fluid balance with repeated weights and documentation of intake/outputs.
- **Treatment:**
  - For shock treatment, give a bolus of 10–20 mL/kg of sodium chloride 0.9% as fast as possible, and reassess for additional IV fluid needs.
  - Alternative resuscitation fluids such as Plasma-Lyte 148, Hartmann's, packed red blood cells, or albumin may sometimes be used on senior advice.
  - For rehydration, calculate the degree of dehydration. For children with mild or moderate dehydration, enteral (oral or NG) rehydration is preferable. IV fluid rehydration may be required for children with severe dehydration or those who cannot tolerate enteral intake. The following figure provides the calculations:

Table 7. Calculations of Fluid Requirements and Fluid Deficit

Calculation of Fluid Requirements
Total fluid requirement = Maintenance + Replacement of deficit + Replacement of ongoing losses
Calculating Fluid Deficit
The most accurate way to calculate a child's fluid deficit is: **Deficit (mL) = [Premorbid weight (kg) minus current weight (kg)] x 1000** If a pre-morbid weight is not available, use: Deficit (mL) = weight (kg) x % dehydration x 10

- Replace deficit over 24–48 hours based on dehydration severity:
    - For children with ≤5% dehydration, replace deficit in the first 24 hours.
    - For children with >5% dehydration, replace deficit more slowly. Replace the 5% deficit in the first 24 hours and the remainder over the following 24 hours.
    - Serial clinical assessment of hydration status must be made at regular intervals for all children with dehydration.
- **Ongoing Fluid Losses:**
    - Replace ongoing losses based on the previous hour or 4-hour period (e.g., replace a 200 mL loss over the previous 4 hours by giving 50 mL/hr for the next 4 hours).
    - Gastrointestinal tract losses are often replaced with sodium chloride 0.9% + potassium chloride 20 mmol/L.
- **Maintenance:**
    - Use the figure below to calculate full maintenance fluid rates, primarily for well children. Adjust fluid rates for all unwell children.

Table 8. Calculations of full maintenance fluid rates. Adapted from the 2020 Royal Children's Hospital Guideline.

Weight (kg)	Full maintenance mL/day	mL/hour
3-10	100 x weight	4 x weight
10-20	1000 plus 50 x (weight minus 10)	40 plus 2 x (weight minus 10)
20-60	1500 plus 20 x (weight minus 20)	60 plus 1 x (weight minus 20)

> 60	2400 mL/day is the normal maximum amount	100 mL/hour

- This calculation serves to:
  - Determine the per-kilogram volume necessary to sustain hydration in healthy children.
  - Consider insensible losses, which encompass losses through respiration, skin, and stool.
- Account for the excretion of daily excess solutes, such as urea, creatinine, and electrolytes, in a volume of urine with an osmolarity similar to that of plasma.
- Important notes:
  - The maintenance fluid requirement calculation in this table is applicable to all age groups, including young infants. Young infants require a higher volume of enteral milk (150–180 mL/kg/day) to meet their nutritional and growth needs. However, this greater volume should not serve as the basis for prescribing intravenous fluids.
  - When prescribing intravenous fluids for an infant, it should be based on their water requirement, typically 100 mL/kg/day for infants up to 10 kg, with adjustments as clinically indicated (e.g., potentially restricted to 2/3 of the maintenance volume).

Fluid Restriction:

- For most unwell children, it is advisable to utilize 2/3 of the standard maintenance fluid rates, except when they are already dehydrated. Unwell children tend to have increased secretion of antidiuretic hormone (ADH), which means they require less fluid to prevent water overload and hyponatremia.
- Children with the following medical conditions face a heightened risk of excessive ADH secretion and may need further fluid restriction, and it is recommended to consult with a senior medical professional:
  - Acute central nervous system (CNS) conditions such as meningitis, tumors, or head injuries.
  - Pulmonary conditions like pneumonia, bronchiolitis, or cases involving mechanical ventilation.
  - Children in the post-operative phase or those experiencing trauma.

- Hourly fluid rates can be calculated following the table below:
- **Table 9.** Hourly Fluid Rates. Adapted from the 2020 Royal Children's Hospital Guideline.

Weight (kg)	Full maintenance (mL/h) Well child	2/3 maintenance (mL/h) Most unwell children unless dehydrated
5	20	13
10	40	27
15	50	33
20	60	40
25	65	43
30	70	47
35	75	50
40	80	53
45	85	57
50	90	60
55	95	63
≥ 60	100	67

Choice of Fluid

- The preferred choice for intravenous (IV) maintenance fluids is typically sodium chloride 0.9% infused with glucose 5%. However, there are alternative options available for maintenance fluids, including:
    - Plasma-Lyte 148 with glucose 5% (contains 5 mmol/L of potassium) – generally stocked in tertiary pediatric centers and intensive care units.
    - Hartmann's solution with glucose 5%.
- Glucose 5% is suitable for maintenance fluids in children without other glucose sources.
- **High glucose containing fluids**:
    - Glucose 10% (with or without additional sodium chloride) is commonly used in neonates and occasionally in children with metabolic disorders. It's important to follow local injectable guidelines for preparing IV fluids containing glucose 10%.

    - Glucose solutions with concentrations of 15–20% are rarely used, typically in neonates and children with metabolic disorders. These solutions are best administered via central venous access.
    - Solutions containing glucose concentrations exceeding 20% are seldom necessary for children. Their use should be limited to intensive care units and must be discussed with senior medical staff, as inappropriate use can lead to severe adverse events.
- **When it comes to including potassium in maintenance fluids**:
    - This should be considered once baseline electrolytes and renal function have been evaluated.
    - Use pre-prepared fluid bags containing potassium to minimize risks of errors.
    - Avoid adding concentrated solutions (sodium chloride, potassium chloride, or glucose) to fluid bags unless there is a clear clinical need, as this can pose safety risks.
    - The standard concentration for most cases is 20 mmol/L of potassium chloride.
- **Non-standard fluids:**
    - For non-standard fluids, they should only be prescribed with a well-defined clinical indication, in consultation with a senior clinician.
    - Regularly monitor serum sodium and blood glucose levels when using these fluids.
- Hypotonic fluids, which have a sodium concentration lower than that of plasma, are not recommended for routine use in children due to the associated risks of hyponatremia.
    - Avoid administering glucose 4% with sodium chloride 0.18%.
    - Sodium chloride 0.45% solutions are rarely needed and should only be prescribed in consultation with a senior clinician.
- **Consider consultation with local pediatric team:**
    - In cases where there is uncertainty about the choice or volume of fluid to use, electrolyte abnormalities, or when significant comorbidities are present, it is advisable to consult with the local pediatric team.
    - For severe electrolyte or glucose abnormalities and when dealing with shock requiring large IV fluid boluses (≥40 mL/kg), it may be necessary to consider transferring the child to a facility with higher-level care than what the local hospital can provide.

Figure 8 shows an algorithm to approach IV fluid prescription:

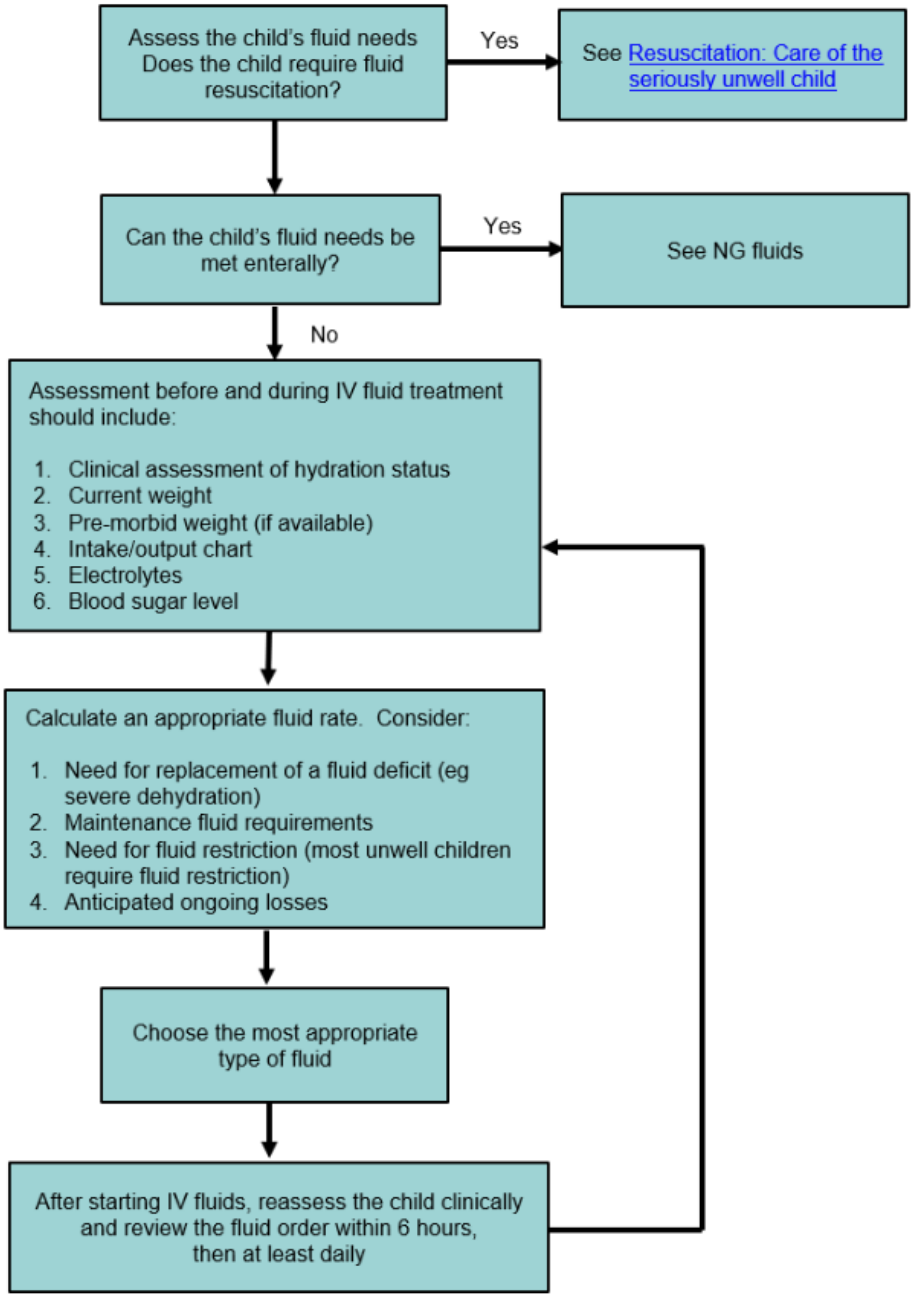

Figure 8. *Approach to IV Fluid Prescription. Retrieved from the 2020 Royal Children's Hospital Guideline.*

- To calculate a child's fluid deficit accurately, you can use the following formula:
    - Fluid Deficit (mL) = [Pre-illness weight (kg) - Current weight (kg)] x 1000
- If you don't have the pre-illness weight, you can use this formula:

- Fluid Deficit (mL) = Weight (kg) x % dehydration x 10

- The total fluid requirement is the sum of maintenance, replacement of deficit, and replacement of ongoing losses.

Table 10. Electrolyte Content of Intravenous Fluids. Retrieved from the 2020 Royal Children's Hospital Guideline.

Fluid	Na mmol/L	Cl mmol/L	K mmol/L	Ca mmol/L	Lactate mmol/L	Mg mmol/L	Acetate mmol/L	Gluconate mmol/L	Glucose %	Osmolality mOsm/L
Normal human plasma	135 - 145	96 - 106	3.5 – 5.0	2.1 – 2.6	0.5 – 1.8	0.7 – 1.2	0		3.5 – 8.0	275 – 295
Sodium chloride 0.9%	154	154	0	0	0	0	0	0	0	308
Sodium chloride 0.9% + glucose 5%	154	154	0	0	0	0	0	0	5	586
Sodium chloride 0.9% + glucose 5% + potassium 20 mmol/L	154	174	20	0	0	0	0	0	5	626
Plasma-Lyte 148 + glucose 5%	140	98	5	0	0	1.5	27	23	5	584
Compound Sodium Lactate (Hartmann's)	130	110	5	2	30	0	0	0	0	274
Sodium chloride 0.45% + glucose 5% *	77	77	0	0	0	0	0	0	5	428
*Note – Fluids with a sodium concentration <125 mmol/L are not recommended for routine use										

1.2.2 Society of Critical Care Medicine Surviving Sepsis Campaign (2021)

Recommendations from the 2021 Surviving Sepsis Campaign (SCC) by the Society of Critical Care Medicine (SCCM) are intended to provide guidance for the clinician caring for adult patients with sepsis or septic shock in the hospital setting[7]. They are an update on the 2016 recommendations previously published.

Evidence levels and grades of recommendations are outlined in the table below:

Table 11. Grading Scheme for Recommendations

Description of implications of strength of recommendation for patients, clinicians, and policymakers.		
	Strong Recommendation	**Weak Recommendation**
For patients	Most individuals would want the recommended course of action. A small proportion would not.	The majority of individuals would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action.	Different choices are likely to be appropriate for different patients and therapy should be tailored to the individual patient's circumstances.
For policy makers	The recommendation can be adapted as policy in most situations, including use as performance indicators	Policymaking will require substantial debates and involvement of many stakeholders.

Main recommendations related to fluid and volume expanders are summarized below:

- For patients experiencing sepsis-induced hypoperfusion or septic shock, consider administering a minimum of 30 mL/kg of IV crystalloid fluid within the initial 3 hours of resuscitation (Weak, low quality of evidence).
- In adults with sepsis or septic shock, prioritize using dynamic measures to guide fluid resuscitation rather than relying solely on physical examination or static parameters (Weak, very low quality of evidence).
- It is recommended to guide the resuscitation process by aiming to reduce serum lactate levels in patients with elevated lactate, rather than disregarding serum lactate in the treatment plan (Weak, low quality of evidence).

- When dealing with adults in septic shock, consider using capillary refill time as an additional method for guiding resuscitation alongside other measures of perfusion (Weak, low quality of evidence).
- In the case of adults with sepsis or septic shock, our recommendation is to use crystalloids as the primary choice for fluid resuscitation (Strong, moderate-quality evidence).
- Adults dealing with sepsis or septic shock may want to consider using balanced crystalloids instead of normal saline for resuscitation, as we suggest (Weak, low quality of evidence).
- In adults with sepsis or septic shock who have received significant quantities of crystalloids, we recommend considering the use of albumin (Weak, moderate-quality evidence).
- The use of starches for resuscitation in adults with sepsis or septic shock is not recommended (Strong, high-quality evidence).
- In the context of sepsis and septic shock in adults, our suggestion is to avoid using gelatin for resuscitation (Weak, moderate-quality evidence).
- When it comes to the choice between restrictive and liberal fluid strategies in the first 24 hours of resuscitation for patients with sepsis and septic shock who still exhibit signs of hypoperfusion and volume depletion after initial resuscitation, there is insufficient evidence to make a clear recommendation (No recommendation).
- Use a restrictive transfusion strategy over a liberal one for adults with sepsis or septic shock (Strong recommendation, moderate quality of evidence).

1.2.3 Saudi National Diabetes Center (SNDC) Saudi Diabetes Clinical Practice Guidelines (SDCPG) (2021)

Evidence levels and grades of recommendations were not outlined. The following recommendations are provided on the **rehydration** in managing DKA by the Saudi National Diabetes Center[8]:

Diabetic ketoacidosis (DKA) for patients older than 14 years old

- Begin with an initial normal saline bolus, followed by a rapid normal saline infusion. Caution should be exercised to avoid overhydration and cerebral edema.
- Be mindful of pseudo hyponatremia due to elevated blood glucose levels and adjust by adding 3 Na+ per 10 glucose over 5.5 mmol/L.

- Initially, use isotonic saline at a rate of 15-20 ml/kg of body weight per hour or 1-1.5 L during the first hour.
- The choice of further fluid replacement depends on the patient's hydration status, serum electrolyte levels, and urinary output.
- Hypernatremic patients may benefit from 0.45% Na Cl at 4-14 ml/kg/hour, while patients with eunatremia or hyponatremia may prefer 0.9% Na Cl at a similar rate.
- The goal is to replace 50% of the estimated water deficit over 12-24 hours. This protocol is not suitable for hemodynamically unstable patients, who should be managed by the ICU team.
- In patients with hypotension, aggressive fluid therapy with isotonic saline should continue until blood pressure stabilizes.

Guidelines for Diagnosis & Management of Diabetic Ketoacidosis (DKA) in Children under 14 years of Age and/or < 50 kg weight

Management in emergency room or urgent care area:

- Fluid replacement as follows: patient could present in shock or only dehydrated but with stable hemodynamics. Fluid management in the first hour is shown in the figure below:

Fluid Management in 1st hour	Dehydrated, not in shock: Estimate the severity of DKA	In clinical shock: (weak peripheral pulses, prolonged capillary refill ≥ 3 seconds, reduced conscious level)
	Mild: venous pH<7.3 or bicarbonate <15mmol/L **Moderate**: pH<7.2 or bicarbonate <10mmol/L **Severe**: pH<7.1 or bicarbonate <5mmol/L	**Shock with hypotension (late sign):** 10 ml/kg 0.9 Saline bolus over 5-10 minutes. Repeat x3 till normal BP (consult expert)
	Start IV 0.9% Saline at: 5 ml/kg/h for mild/moderate DKA 7 ml/kg/h for severe DKA	**Shock, not hypotensive (compensated):** 10 ml/kg 0.9 Saline over 1 hour

***Figure 9**. Fluid Management in the First Hour. Retrieved from SDCPG 2021.*

- Management plan after the 1-2 hours
    - IV maintenance + deficit
        - Maintenance calculation: 100 ml/kg for the first 10 kg+ 50 ml/kg for the next 10kg + 20 ml/kg for the rest BW
        - Deficit calculation: 5% for mild/moderate DKA, 10% for severe DKA

        - Correct slowly over 48 hours:
            - Start 0.9% Saline (with KCl)
            - Potassium: 40 mEq/L KCl (after 1st void & if K level <5.5)
    - The amount of fluid from the insulin bag is to be counted in the overall rehydration fluid (when using a 500 ml bag for mixing). Drop fluid boluses that are > 20 ml/kg from the overall rehydration fluid with no substitution for the ongoing losses. Consider, only, if the fluid balance stays negative (check Q 4 hours). Often call for fluid early (expect 1 hour delay).

Table 12. Conservative total fluid calculation. Adapted from SDCPG 2021.

To minimize calculation burden, errors, and confusion, we recommend the following simplified and slightly more conservative total fluid calculation for the first 28 hours after DKA presentation			
Simplified calculated rate by weight	≤ 15 kg	16-40 kg	> 40 kg
Maintenance + deficit	5 mL/kg/h	4 mL/kg/h	3 mL/kg/h
NB. All fluids given during resuscitation should be documented carefully, particularly in ER			

The following has been associated with a risk of cerebral edema, **DO NOT**:

- Give insulin bolus
- Give IV sodium bicarbonate (except in life-threatening hyperkalemia or life-threating acidosis)
- Give fluid boluses for DKA not in shock
- Give hypotonic fluid (0.45%, 0.22%) for rehydration
- Give more than 10 mL/kg fluid bolus each time if in shock
- Exceed 1.5-2 maintenance/day as a general rule

Table 13. Fluid Adjustments. Adapted from SDCPG 2021.

Adjustment and trouble shooting
When blood glucose (BG) drops to < 14-17 mmol/L (250-300 mg/dL), add dextrose 5% to 0.9% saline
When BG drops to < 8 mmol/L (~ 140-150 mg/dL), add D10% to 0.9% saline

With rapid fall of glucose (> 100 mg/hour), add D10% and can increase to max D12.5% if acidosis is not improving (may decrease insulin to 0.05 u/kg/h or even down to 0.03 /kg/h is acidosis is improving)
Hypoglycemic attack (< 4 mmol), give 2-5 mL/kg D10% bolus, hold insulin for 15-30 min then repeat BG

- When oral fluid is tolerated, the IV fluid should be reduced, and oral fluid intake should be included in total rehydration fluid calculation.
- The following figure shows the recommendations for managing cerebral edema:

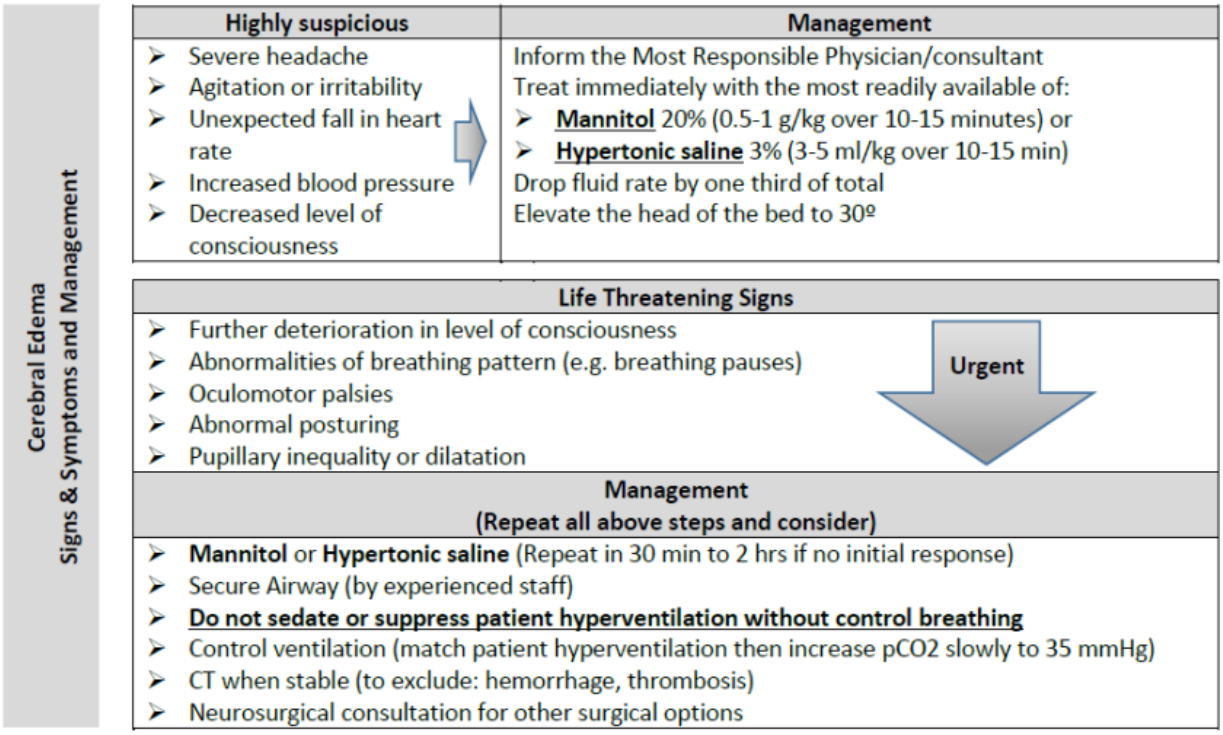

***Figure 10**. Cerebral Edema Management. Retrieved from SDCPG 2021.*

- *Effective Osmolality = 2 Na + Glucose (glucose value in mmol/L)
- **Corrected Na = measured Na + 2 [(plasma glucose-100/100)] mg/dL

1.2.4 The Joint British Diabetes Societies for Inpatient Care: Management of Diabetic Ketoacidosis in Adults (2023)

These guidelines have been developed to advise the treatment and management of diabetic ketoacidosis in adults. The guideline recommendations have been developed and reviewed by a multidisciplinary team led by the Joint British Diabetes Society (JBDS) and including representation from Primary Care Diabetes Society,

Diabetes UK[9]. The main recommendations related to fluid management are detailed below:

- The primary and universally agreed initial treatment for DKA involves administering fluids and subsequently providing insulin. This approach serves several crucial purposes, including restoring circulatory volume, eliminating ketones, and rectifying electrolyte imbalances.
- The typical deficits in fluids and electrolytes for individuals with DKA are outlined below. For instance, a 70 kg adult experiencing DKA may have a deficit of up to 7 liters, which should be replenished with crystalloid solutions. In certain cases, such as individuals with kidney or heart issues, the elderly, and adolescents, adjustments may be necessary in terms of the rate and volume of fluid replacement. The primary objective of the initial few liters of fluid is to address hypotension, restore the intravascular deficit, and counteract the effects of osmotic diuresis while correcting electrolyte disturbances.
- Common Deficits in DKA for Adults
    - Water: 100 ml/kg
    - Sodium: 7-10 mmol/kg
    - Chloride: 3-5 mmol/kg
    - Potassium: 3-5 mmol/kg
    - The specific choice of fluid is discussed in greater detail in the section titled "Controversial Areas."
- Crystalloid rather than colloid solutions are recommended for fluid resuscitation.
- 0.9% sodium chloride solution (‘normal saline’) is the fluid resuscitation of choice.
- Cautious fluid replacement in young adults
- Bicarbonate administration is not recommended routinely.
- In patients with end stage renal failure or on dialysis: When an osmotic diuresis doesn’t develop, it’s possible for dialysis-related hyperglycemia and ketosis to occur without significant dehydration. Due to the elevated serum tonicity, a mixed presentation of both DKA and HHS can also manifest. Furthermore, the volume of fluid circulating in the bloodstream may increase at the expense of the fluid within cells, which resolves as glucose and ketone levels return to normal. Consequently, individuals with end-stage renal failure or those undergoing dialysis may not require fluid replacement. However, for

individuals considered hypovolemic, small amounts of 250 ml (either 0.9% sodium chloride or 10% dextrose) can be administered, alongside frequent clinical assessments.

- DKA Immediate management:
    - First hour:
        - Restoring Circulating Volume
        - Evaluate the degree of dehydration by examining the pulse and blood pressure. As a general guideline, a systolic blood pressure (SBP) of 90 mmHg can be used as an indicator of hydration, but consider factors like age, gender, and concurrent medications.
        - If the SBP upon admission is below 90 mmHg, hypotension is likely due to insufficient circulating volume. However, also consider other potential causes such as heart failure or sepsis.
        - Administer 500 ml of 0.9% sodium chloride solution over 10-15 minutes. If the SBP remains below 90 mmHg, this can be repeated while awaiting input from senior medical staff. Typically, most individuals require a rapid infusion of 500 to 1000 ml in practice.
        - If there is no improvement in clinical condition, reconsider other causes of hypotension and seek an immediate assessment by a senior medical professional. It may be necessary to involve the Intensive Care Unit (ICU) or critical care team.
        - When the SBP is 90 mmHg or higher upon admission, the following table outlines a typical fluid replacement plan for a previously healthy 70 kg adult. Please note that this is a representative guideline, and a slower infusion rate should be considered for young adults (refer to the Controversial Areas section). Mandatory reassessment of cardiovascular status at 12 hours may indicate the need for further fluid.

Table 14. Typical Fluid Replacement Plan for a Previously Healthy 70 kg Adult (Adapted from the JBDS 2023 DKA Guideline)

Fluid	Volume
0.9% sodium chloride 1 L	1000 mL over 1st hour
0.9% sodium chloride 1 L with potassium chloride	1000 mL over next 2 hours
0.9% sodium chloride 1 L with potassium chloride	1000 mL over next 2 hours
0.9% sodium chloride 1 L with potassium chloride	1000 mL over next 4 hours

0.9% sodium chloride 1 L with potassium chloride	1000 mL over next 4 hours
0.9% sodium chloride 1 L with potassium chloride	1000 mL over next 6 hours

        - If more than 1 liter of sodium chloride has been administered to resuscitate hypotensive patients, it may be necessary to provide potassium chloride. Exercise caution in specific groups, including young adults aged 18-25 years, the elderly, pregnant individuals, those with heart or kidney failure, and those with other significant comorbidities. In these cases, consider admission to a Level 2/High Dependency Unit (HDU) facility and replace fluids cautiously.
    - Hours 6-12:
        - Continue IV fluids and assess for treatment complications such as fluid overload or cerebral edema.
    - Hours 12-24
        - Continue IV fluids if the person is not eating or drinking.
        - Re-assess for treatment complications such as fluid overload.

Section 2.0 Drug Therapy in Fluids and Volume Expanders

This section comprises three subsections: the first one contains the newly recommended drugs, the second one covers drug modifications, and the third one outlines the drugs that have been withdrawn from the market.

2.1 Additions

There are no newly SFDA-registered drugs as fluid and volume expanders. Balanced electrolytes were added to the drug summary spreadsheet.

2.2 Modifications

Remove the "Prior Authorization (PA)" as a prescribing edit for Sodium Chloride, Mannitol, Albumin, the combination of Dextrose and Sodium Chloride, and the combination of Dextrose, Calcium Chloride Dihydrate, Magnesium Chloride 6h2o, Sodium Chloride, Potassium Chloride, Disodium Phosphate Dihydrate, Sodium Hydrogen Carbonate

2.3 Delisting

The medications below are no longer SFDA registered[11], therefore, it is advisable to delist the following drugs from CHI formulary. *Please refer to* ***Drug Therapy in Fluids and Volume Expanders- Section 2*** *of CHI* ***Fluids and Volume Expanders*** *original clinical guidance*

- Dextrose 10% w/v in 0.225% w/v Sodium Chloride

Section 3.0 Key Recommendations Synthesis

- **Intravenous fluid therapy in adults in hospital NICE (2017)**[2]
  - Resuscitation: If patients need IV fluid resuscitation, use crystalloids that contain sodium in the range 130–154 mmol/l, with a bolus of 500 ml over less than 15 minutes.
  - Routine maintenance: If patients need IV fluids for routine maintenance alone, restrict the initial prescription to: ·
    - 25–30 ml/kg/day of water and
    - approximately 1 mmol/kg/day of potassium, sodium and chloride and
    - approximately 50–100 g/day of glucose to limit starvation ketosis.
  - Replacement and redistribution: Adjust the IV prescription (add to or subtract from maintenance needs) to account for existing fluid and/or electrolyte deficits or excesses, ongoing losses or abnormal distribution.
- **Intravenous fluid therapy in children and young people in hospital NICE (2020)**[3]
  - Fluid Resuscitation:
    - Use glucose-free crystalloids containing sodium in the range of 131–154 mmol/liter, administering a bolus of 20 ml/kg in less than 10 minutes. Adjust volumes considering pre-existing conditions, such as cardiac or kidney disease.
    - For term neonates requiring IV fluid resuscitation, use glucose-free crystalloids with sodium in the range of 131–154 mmol/liter, administering a bolus of 10–20 ml/kg in less than 10 minutes.
    - Avoid using tetrastarch for fluid resuscitation.
    - Seek expert advice, such as from the pediatric intensive care team, if the initial fluid resuscitation requires 40–60 ml/kg of IV fluid or more.
  - Routine Maintenance:
    - Calculate routine maintenance IV fluid rates for children and young people using the Holliday–Segar formula (100 ml/kg/day for the first 10 kg of weight, 50 ml/kg/day for the next 10 kg and 20 ml/kg/day for the weight over 20 kg). Over a 24-hour period, males generally require up to 2,500 ml, and females up to 2,000 ml of fluids.

- Calculate routine maintenance IV fluid rates for term neonates based on their age:
- From birth to day 1: 50 to 60 ml/kg/day.
- Day 2: 70 to 80 ml/kg/day.
- Day 3: 80 to 100 ml/kg/day.
- Day 4: 100 to 120 ml/kg/day.
- Days 5 to 28: 120 to 150 ml/kg/day.
- When children and young people require IV fluids for routine maintenance, initially use isotonic crystalloids with sodium in the range of 131 to 154 mmol/liter.

- Replacement and Redistribution
  - Adjust the IV fluid prescription to consider existing fluid and electrolyte imbalances, ongoing losses, and abnormal distribution (e.g., tissue edema in sepsis).
  - For redistribution, consider isotonic crystalloids with sodium in the range of 131 to 154 mmol/liter.
  - To replace ongoing losses, use 0.9% sodium chloride containing potassium.
- Managing Hypernatremia that develops during intravenous fluid therapy:
  - Consider switching from isotonic to hypotonic fluids (e.g., 0.45% sodium chloride with glucose) if no dehydration is evident.
  - If dehydration is diagnosed, calculate, and replace the water deficit over 48 hours, starting with 0.9% sodium chloride.
  - If hypernatremia persists or worsens after replacing the deficit, consider shifting to a hypotonic solution (e.g., 0.45% sodium chloride with glucose).
  - When correcting hypernatremia, ensure that the rate of plasma sodium decrease does not exceed 12 mmol/liter within a 24-hour period.
- Managing Hyponatremia that develops during intravenous fluid therapy:
  - Restrict maintenance IV fluids in individuals at risk of hypervolemia by either reducing to 50-80% of routine maintenance or calculating based on insensible losses within the range 300–400 ml/m2 /24 hours plus urinary output.

- Administer a bolus of 2 ml/kg (maximum 100 ml) of 2.7% sodium chloride over 10–15 minutes.
- Consider a further bolus of 2 ml/kg (maximum 100 ml) of 2.7% sodium chloride over the next 10 to 15 minutes if symptoms persist.
- If symptoms are still present after the second bolus, check the plasma sodium level and consider a third bolus of 2 ml/kg (maximum 100 ml) of 2.7% sodium chloride over 10 to 15 minutes.

- **Clinical Practice Guideline: Maintenance Intravenous Fluids in Children by American Academy of Pediatric 2018**[4]
  - Patients 28 days to 18 years of age requiring maintenance IVFs should receive isotonic solutions with appropriate potassium chloride (KCl) and dextrose because they significantly decrease the risk of developing hyponatremia (evidence quality: A; recommendation strength: strong)
- **Diabetic Ketoacidosis: Evaluation and Treatment at journal of American family physician 2013**[5]
  - In most persons, saline 0.9% is started at 15 to 20 mL per kg per hour, or 1 L per hour initially.
  - As the patient stabilizes, fluids can be lowered to 4 to 14 mL per kg per hour, or 250 to 500 mL per hour. Once the corrected sodium concentration is normal or high (greater than 135 mEq per L [135 mmol per L]), the solution can be changed to saline 0.45%. Dextrose is added when the glucose level decreases to 200 mg per dL (11.10 mmol per L).
- **Evidence-based Guidelines for the Use of Albumin Products; Japan Society of Transfusion Medicine and Cell Therapy (2017)**[6]
  - Spontaneous bacterial peritonitis with renal impairment benefits from the treatment with a hypertonic albumin solution at a 1.5 g/kg body weight within 6 hours after diagnosis, following by 1 g/kg body weight on day3 of illness(1A)
  - Treatment with a hypertonic albumin solution and a vasoconstrictor is effective in improving type-1 hepatorenal syndrome. Albumin should be administered at a dose of 1g/kg body weight on day1 and 20 to 40g/body weight on subsequent days, in combination with terlipressin and other drugs (1A)
  - In burns, Albumin products are indicated in burns involving ≥ 50% of the total body surface area. (2C) [8, p 651]. No paper provides evidence of the efficacy of albumin in severe burns and its benefits to length of stay and mortality (strong recommendation against use,1B). The use of isotonic

albumin should be limited to cases of a serum albumin level of <2g/dl after 18 hours of injury (2B).

- Pulmonary edema: In patients with treatment-resistant pulmonary edema or marked edema, the use of a hypertonic albumin product is considered only in the case of marked hypoalbuminemia (2B).
- The use of isotonic albumin should be considered to maintain circulating blood volume in cases of vasospasm after subarachnoid hemorrhages that do not respond to crystalloids (2C)
- Plasmapheresis: using an isotonic or diluted hypertonic albumin solution as a replacement fluid (1-to1.5-fold plasma volume/ session) is recommended for the treatment of neurological disorders, such as CIDP and GBS (1A).

- **Surviving Sepsis Campaign (2021)**
  - For patients experiencing sepsis-induced hypoperfusion or septic shock, consider administering a minimum of 30 mL/kg of IV crystalloid fluid within the initial 3 hours of resuscitation (Weak, low quality of evidence).
  - In the case of adults with sepsis or septic shock, our recommendation is to use crystalloids as the primary choice for fluid resuscitation (Strong, moderate-quality evidence).
  - Adults dealing with sepsis or septic shock may want to consider using balanced crystalloids instead of normal saline for resuscitation, as we suggest (Weak, low quality of evidence).
  - In adults with sepsis or septic shock who have received significant quantities of crystalloids, we recommend considering the use of albumin (Weak, moderate-quality evidence).
  - The use of starches for resuscitation in adults with sepsis or septic shock is not recommended (Strong, high-quality evidence).
  - In the context of sepsis and septic shock in adults, our suggestion is to avoid using gelatin for resuscitation (Weak, moderate-quality evidence).
  - Use a restrictive transfusion strategy over a liberal one for adults with sepsis or septic shock (Strong recommendation, moderate quality of evidence).

- **The Saudi Diabetes Clinical Practice Guidelines by the Saudi National Diabetes Center (SDCPG, SNDC, 2021)**
- Diabetic ketoacidosis (DKA) for patients older than 14 years old
    - Begin with an initial normal saline bolus, followed by a rapid normal saline infusion. Caution should be exercised to avoid overhydration and cerebral edema.
    - Initially, use isotonic saline at a rate of 15-20 ml/kg of body weight per hour or 1-1.5 L during the first hour.
    - The choice of further fluid replacement depends on the patient's hydration status, serum electrolyte levels, and urinary output.
    - Hypernatremic patients may benefit from 0.45% Na Cl at 4-14 ml/kg/hour, while patients with eunatremia or hyponatremia may prefer 0.9% Na Cl at a similar rate.
    - The goal is to replace 50% of the estimated water deficit over 12-24 hours. This protocol is not suitable for hemodynamically unstable patients, who should be managed by the ICU team.
    - In patients with hypotension, aggressive fluid therapy with isotonic saline should continue until blood pressure stabilizes.
- Guidelines for Diagnosis & Management of Diabetic Ketoacidosis (DKA) in Children under 14 years of Age and/or < 50kg weight
    - Management in Emergency room or urgent care area:
        - Patient could present in shock or only dehydrated but with stable hemodynamics. Fluid management in the first hour:
            - Start IV 0.9% Saline at: 5 ml/kg/h for mild/moderate DKA 7 ml/kg/h for severe DKA
- Management plan after the 1-2 hours
    - IV maintenance + deficit
        - Maintenance calculation: 100 ml/kg for the first 10 kg+ 50 ml/kg for the next 10kg + 20 ml/kg for the rest BW
        - Deficit calculation: 5% for mild/moderate DKA, 10% for severe DKA
        - Correct slowly over 48 hours:
            - Start 0.9% Saline (with KCl)
            - Potassium: 40 mEq/L KCl (after 1st void & if K level <5.5)

The Management of Diabetic Ketoacidosis in Adults by the Joint British Diabetes Societies for Inpatient Care (2023)[9]

- Common Deficits in DKA for Adults
    - Water: 100 ml/kg
    - Sodium: 7-10 mmol/kg
    - Chloride: 3-5 mmol/kg
    - Potassium: 3-5 mmol/kg
- Crystalloid rather than colloid solutions are recommended for fluid resuscitation.
- 0.9% sodium chloride solution ('normal saline') is the fluid resuscitation of choice.
- Cautious fluid replacement in young adults
- Bicarbonate administration is not recommended routinely.
- DKA Immediate management:
    - First hour: Restoring Circulating Volume
        - Administer 500 ml of 0.9% sodium chloride solution over 10-15 minutes. If the SBP remains below 90 mmHg, this can be repeated while awaiting input from senior medical staff. Typically, most individuals require a rapid infusion of 500 to 1000 ml in practice.
        - If there is no improvement in clinical condition, reconsider other causes of hypotension and seek an immediate assessment by a senior medical professional. It may be necessary to involve the Intensive Care Unit (ITU) or critical care team.
        - When the SBP is 90 mmHg or higher upon admission, the following table outlines a typical fluid replacement plan for a previously healthy 70 kg adult.

If more than 1 liter of sodium chloride has been administered to resuscitate hypotensive patients, it may be necessary to provide potassium chloride. Exercise caution in specific groups, including young adults aged 18-25 years, the elderly, pregnant individuals, those with heart or kidney failure, and those with other significant comorbidities. In these cases, consider admission to a Level 2/High Dependency Unit (HDU) facility and replace fluids cautiously.

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Fluids and Volume Expanders report** and aims to provide recommendations to aid in the management of **Fluids and Volume Expanders**. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with **Fluids and Volume Expanders**. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

Section 5.0 References

1. Fluid Resuscitation. Published online 2023. Accessed October 25, 2023. https://www.ncbi.nlm.nih.gov/books/NBK534791/
2. *Intravenous Fluid Therapy in Adults in Hospital*.; 2013. www.nice.org.uk/guidance/cg174
3. *Intravenous Fluid Therapy in Children and Young People in Hospital NICE Guideline*.; 2015. www.nice.org.uk/guidance/ng29
4. Feld LG, Neuspiel DR, Foster BA, et al. *Clinical Practice Guideline: Maintenance Intravenous Fluids in Children*. Vol 142.; 2018. http://publications.aap.org/pediatrics/article-pdf/142/6/e20183083/1076087/peds_20183083.pdf
5. Family A, Westerberg DP. *Diabetic Ketoacidosis: Evaluation and Treatment*. Vol 87.; 2013. www.aafp.org/afp
6. Yasumura S, Makino S, Matsumoto M, et al. Evidence-based Guidelines for the Use of Albumin Products Japan Society of Transfusion Medicine and Cell Therapy. *Japanese Journal of Transfusion and Cell Therapy*. 2017;63(5):641-663.
7. Doi K, Estenssoro E, Ferrer R, et al. *Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2021*. Vol 49.; 2021. www.ccmjournal.org
8. *Saudi Diabetes Clinical Practice Guidelines (SDCPG) Saudi National Diabetes Center (SNDC)*.; 2021.
9. Joint British Diabetes Societies for Inpatient Care (JBDS-IC). The Management of Diabetic Ketoacidosis in Adults. Published online March 2023. Accessed November 12, 2023. https://abcd.care/joint-british-diabetes-societies-jbds-inpatient-care-group
10. The Royal Children's Hospital (RCH) Melbourne. Intravenous fluids . Accessed October 25, 2023. https://www.rch.org.au/clinicalguide/guideline_index/intravenous_fluids/
11. SFDA Drug List J. SFDA Drug List . Published 2023. Accessed June 20, 2023. https://www.sfda.gov.sa/en/drugs-list

Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

II. Adult and Pediatric Quantity Limit?

This is either the adult or pediatric maximum amount of a drug that can be administered per day based on a maximum daily dose. If there is no clinical evidence supporting the quantity limit for that relevant indication, this column will be left as Blank.

III. What information is available in the notes?

"Notes" section provides details of the prescribing edits, extra important drug information and special warning and precautions.

IV. Drug interactions

- A: No known interaction
- B: No action needed
- C: Monitor therapy

- D: Consider therapy modification
- X: Avoid combination

V. Defined Daily Dose

The Defined Daily Dose (DDD) is to be set based on the WHO recommendations https://www.whocc.no/ddd/definition_and_general_considera/

VI. REMS

A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.

Appendix B. Fluids and Volume Expanders Scope

Comparison of the 2020 and the 2023 Report

2020	Changes Performed	2023	Rationale
Section 1.0 Fluids and Volume Expanders Clinical Guidelines			
Intravenous fluid therapy in adults in hospital | Guidance | NICE. (2013, December 10 last update May 2017)[2]	**N/A**	**N/A**	
Intravenous fluid therapy in children and young people in hospital | Guidance | NICE. (2015, December 9)	**Updated**	**Intravenous fluid therapy in children and young people in hospital | Guidance | NICE (2020)**[3]	No new medications.
Clinical Practice Guideline: Maintenance Intravenous Fluids in Children by American Academy of Pediatric 2018[4]	**N/A**	**N/A**	
Diabetic Ketoacidosis: Evaluation and Treatment at journal of American family physician 2013[5]	**N/A**	**N/A**	
Evidence-based Guidelines for the Use of Albumin Products; Japan Society of Transfusion Medicine and Cell Therapy (2017)[6]	**N/A**	**N/A**	
	Missing	**Intravenous fluids - The Royal Children's Hospital (RCH) Melbourne**[10]	Non-SFDA • Plasma-Lyte 148 with glucose 5% (contains 5 mmol/L of

			potassium)

Appendix C. MeSH Terms PubMed

The following is the result of the PubMed search conducted for guideline search:

Query	Filters	Search Details	Results
((((((Plasma Substitutes[MeSH Terms]) OR (Substitutes, Plasma[Title/Abstract])) OR (Blood Expanders[Title/Abstract])) OR (Expanders, Blood[Title/Abstract])) OR (Plasma Volume Expanders[Title/Abstract])) OR (Expanders, Plasma Volume[Title/Abstract])) OR (Volume Expanders, Plasma[Title/Abstract])	Guideline, in the last 5 years	("plasma substitutes"[MeSH Terms] OR "substitutes plasma"[Title/Abstract] OR (("Blood"[MeSH Subheading] OR "Blood"[All Fields] OR "Blood"[MeSH Terms] OR "bloods"[All Fields] OR "haematology"[All Fields] OR "hematology"[MeSH Terms] OR "hematology"[All Fields] OR "haematoma"[All Fields] OR "hematoma"[MeSH Terms] OR "hematoma"[All Fields] OR "haemorrhage"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "haemorrhages"[All Fields] OR "hemorrhages"[All Fields] OR "haemorrhagic"[All Fields] OR "haemorrhaging"[All Fields] OR "hematologies"[All Fields] OR "haematomas"[All Fields] OR "hematomas"[All Fields] OR "hematoma s"[All Fields] OR "hematomae"[All Fields] OR "hemorrhaged"[All Fields] OR "hemorrhagic"[All Fields] OR "hemorrhagical"[All Fields] OR "hemorrhaging"[All Fields]) AND "Expanders"[Title/Abstract]) OR "expanders blood"[Title/Abstract] OR "plasma volume expanders"[Title/Abstract] OR (("expander"[All Fields] OR "Expanders"[All Fields]) AND "plasma	0

		volume"[Title/Abstract]) OR "volume expanders plasma"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	

Appendix D. Treatment Algorithm