



The *REDOXS*[®] Study
REducing Deaths due to OXidative Stress

**A randomized trial of glutamine and antioxidant supplementation in
critically ill patients**

Protocol Violations

This study is registered at Clinicaltrials.gov.
Identification number NCT00133978

Definition of Protocol Violation

For the purpose of the REDOX[®] study, a protocol violation or protocol deviation occurs when the volume of study supplements received is actually less than the prescribed volume.

The prescribed volume of enteral study supplement is **480mls/day** (20 ml/hr X 24 hrs) for all patients.

The prescribed volume of parenteral study supplements is **240 mls/day** (10 mL/hr X 24 hrs). In rare cases, if the patient is extremely tall, the prescribed volumes may be higher. Refer to the label on the parenteral bag for the prescribed volume.

The threshold volume for the protocol violation for the enteral study supplements differs from the parenteral study supplement threshold.

For the Enteral Study Supplements

A protocol violation is defined as receiving < 80% of the prescribed volume in one day.

For example, the prescribed volume is 20mls/hr x 24hrs= 480mls per day.
If the volume actually received is < 80% of 480mls or is between 0-383mls per day, this is a protocol violation.

For the Parenteral Study Supplements

A protocol violation is defined as receiving < 90% of the prescribed volume in one day.

For example, the prescribed volume is 10mls/hr x 24hrs= 240 mls per day.
If the volume actually received is < 90% of 240mls or is between 0-215 mls per day, this is a protocol violation.

Refer to Protocol Violation and Deviation Reporting Algorithm on page 8.

Reporting of Protocol Violation

If a protocol violation does occur, a Protocol Violation Form must be completed and faxed to CERU *within 24 hours* of becoming aware of the violation.

Record the following details on the Protocol Violation Form (see next page):

- site name, patient enrollment number, name of study coordinator reporting the violation and site investigator name.
- date and time the protocol violation occurred.
- date and time the protocol violation was discovered.
- type of violation i.e. enteral or parenteral study supplements
- was the site investigator informed and if no, indicate why not.
- reasons for the protocol violation and comments.
- action taken by study coordinator.

Fax the completed form to the Project Leader who will follow up with the Study Coordinator as needed.

The Protocol Violation Form and the Enteral Feeding Protocol may be downloaded from the REDOXS[®] website under the Welcome, Home Page (Site Status Page).

A Protocol Violation Form does **not** need to be completed on the following days:

- day of enrollment
- day of discharge from ICU (unless the patient has received less than 5 days of the supplements)
- day of death.

Monitoring Study Supplement Volumes

The volumes of study supplements actually received must be monitored daily and the use of a daily checklist is highly recommended to identify if a Protocol Violation/deviation has occurred.

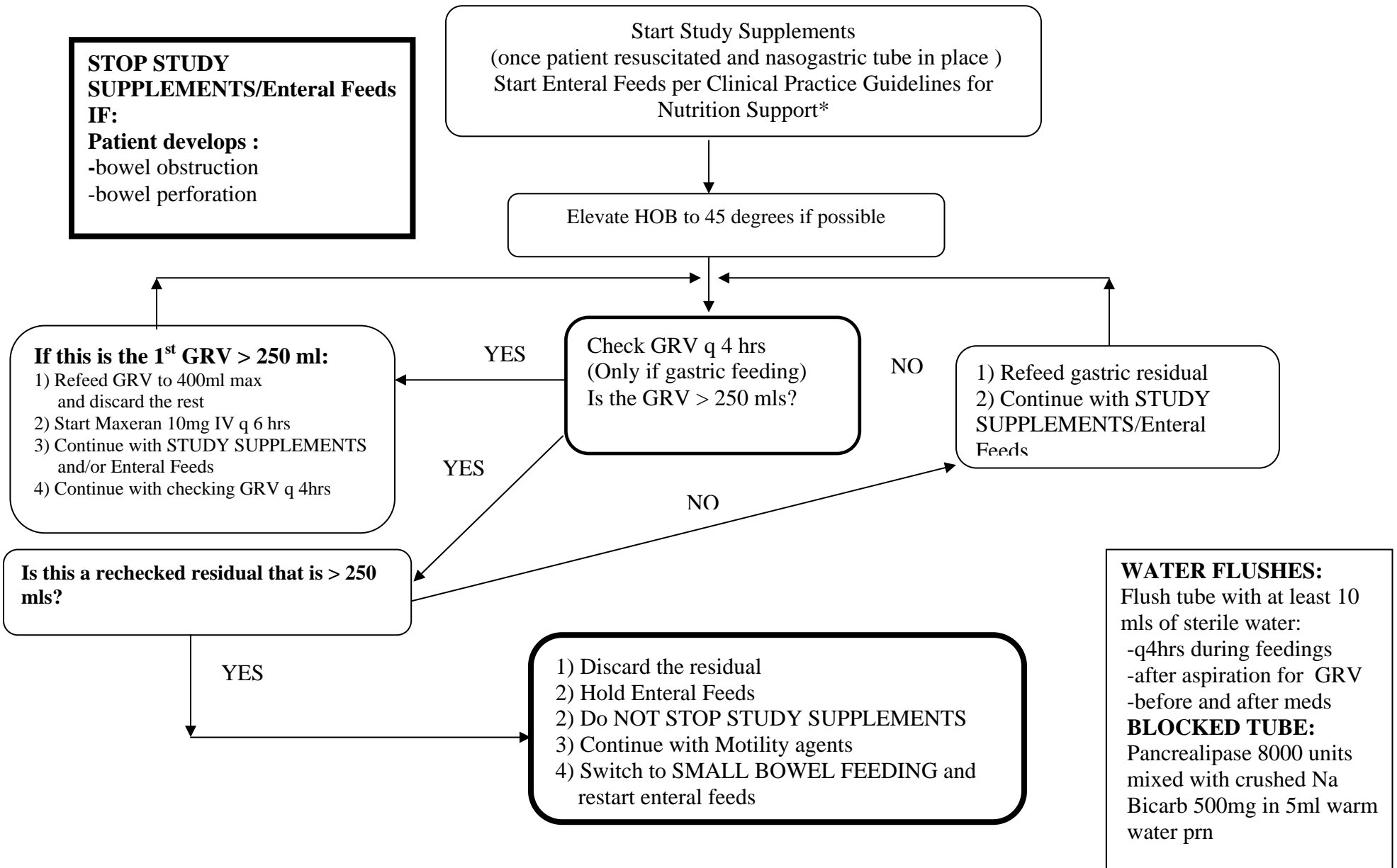
When entering the volumes on the electronic data capture system (Study Supplement Compliance page), you will be reminded to fill out a Protocol Violation Form or provide an explanation.

Every attempt should be made to ensure that the administration of study supplements is not interrupted and that protocol violations are minimized. Refer to **Enteral Feeding Protocol** to optimize the delivery of the study supplements (and enteral nutrition).

The study supplements are *nutrients*, they are easily absorbed and it is safe to deliver these small amounts regardless of whether enteral feeds are tolerated or not. In the event of enteral feed intolerance, the use of motility agents and small bowel feeding tubes is strongly encouraged.

Deficits in the received volumes can be made up by doubling the infusion rate of the study supplements for up to a maximum of 12 hours. Refer to the **Administration of Study Supplements** (Interruption of Study Supplements) for more details on this.

Enteral Feeding Protocol



Definition of Protocol Deviation

The threshold volume for the protocol deviation for the enteral study supplements differs from the parenteral study supplement threshold.

For the Enteral Study Supplements

A protocol deviation is defined as receiving $\geq 80\%$ but $<100\%$ of the prescribed volume in one day.

For example, the prescribed volume is 20mls/hr x 24hrs= 480mls per day.
If the volume actually received is $\geq 80\%$ of 480mls or between 384mls-479 mls per day, this is a protocol deviation.

Parenteral Study Supplements

A protocol deviation is defined as receiving $\geq 90\%$ but $<100\%$ of the prescribed volume in one day.

For example, the prescribed volume is 10mls/hr x 24hrs= 240mls per day.
If the volume actually received is $\geq 90\%$ of 240mls or between 216-239 mls, this is a protocol deviation.

If a protocol deviation does occur, the Study Coordinator must provide an explanation in as to why the patient did not received the prescribed volume of the study supplements. When entering the volumes on the electronic data capture system (Study Supplement Compliance page), you will be reminded to add an explanation in the comments box.

A Protocol Violation Form is NOT to be filled out if protocol deviation occurs.

Refer to Protocol Violation and Deviation Reporting Algorithm on page 8.

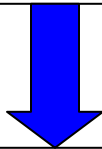
If the patient receives more than the prescribed volumes, you must record the reason for this. When entering this volume on the web based data capture system, you will be prompted to enter a comment explaining why this happened.

Protocol Violation/Deviation Reporting Algorithm

Protocol Violation

Volume of study supplement **actually received** is less than the prescribed volume in 24hrs

Enteral < 80% prescribed
Parenteral < 90% prescribed

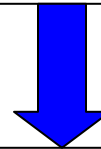


Complete Violation Form
within 24 hours of
discovery
&
Fax to CERU
Attention: Project Leader
(613) 548-2428

Protocol Deviation

Volume of study supplement **actually received** is less than the prescribed volume in 24hrs

Enteral \geq 80% < 100% prescribed
Parenteral \geq 90% < 100%
prescribed



Provide explanation on the
worksheet/web based data
entry (Study Supplement
Compliance)