The Nuts and Bolts of Neurocritical Care

Acute brain injury is common in the ICU. Many times, it's due to something else going on with the patient—septic encephalopathy, delirium, hypotension, electrolyte imbalance, etc. In these cases, correcting the cause usually improves brain function. Sometimes, the patient is in the ICU because of direct injury to the brain. This can usually be divided into one of two camps—"toxic-metabolic" injury or "structural" injury. Structural brain injury can be from trauma, spontaneous hemorrhage, or vascular occlusion. These terms, of course, are not mutually exclusive—structural brain lesions can be associated with metabolic derangements as well.

Acute brain injury can present with either focal or generalized deficits. It can be subtle (mild confusion, weakness in one extremity) or dramatic (coma, seizures, toxic agitation). Coma, delirium tremens, and status epilepticus could be better described as "acute brain failure" and are true medical emergencies. There are many causes of acute brain injury, and it's beyond the scope of this handout to discuss the diagnosis and treatment of each one. The purpose of this document is to outline the general principles of neurocritical care—in other words, the things you should do to help the patient (or at least not make him worse!).

First Things First

The human brain is dependent on a nearly continuous delivery of oxygen and glucose in order to function normally. There are very few glycogen stores that can be broken down, and brain cells begin to die off after around 4 minutes of anoxia. Therefore, your <u>first</u> priority is to provide **oxygen and substrate** to the brain-injured patient. Substrate refers to glucose (fuel) and thiamine (helps neurons use glucose to maintain normal cellular function). Give 100 mg of thiamine IV or IM and either check the patient's blood sugar or give 50 mL of D50 intravenously. Provide supplemental oxygen by cannula or face mask while you're determining what to do next.

A and B

Intubation should be considered for any patient with significant brain dysfunction. Unlike most MICU patients (who are intubated for hypoxemia or ventilatory failure), stuporous or comatose patients require intubation for airway protection. The usual threshold cited is the Glasgow Coma Score being 8 or less, because most protective airway reflexes are depressed or absent at that level. Other reasons to intubate include inability to handle secretions, hemodynamic instability, rapidly declining level of consciousness (GCS 15, then 13, then 10 over the last 30 minutes—don't wait for it to hit 8), planned surgical intervention, or if the patient is agitated and requires significant sedation for diagnostic testing. Don't forget to immobilize the cervical spine if there is any suspicion of trauma or if the person was "found down." Cervical spine *clearance* is not a priority; cervical spine *protection* is.

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BiPAP has become quite popular in the last few years, and for good reason. It's great for patients with decompensated heart failure, COPD exacerbations, and obstructive sleep apnea. BiPAP is NOT good for brain-injured people, however! It doesn't provide good control over ventilation and does nothing to protect the airway; if the person is obtunded, it increases the risk of aspiration. In order to truly benefit from BiPAP a patient needs to be somewhat awake and cooperative, which usually isn't the case in neurocritical care.

Mechanical Ventilation

Patients who are mechanically ventilated should be treated just like patients without brain injury—avoidance of ventilator-induced lung injury, pneumonia, and mechanical complications are all important to the ultimate outcome. PEEP can be used in patients with brain injury, even those with elevated ICP (despite what the neurosurgeons may tell you). The effect of extremely high PEEP (> 15 cm H_2O) is not known, and the effect of APRV on ICP has not been studied either. One study did show an improvement in PaO_2 and reduction in ICP with high frequency oscillatory ventilation.

While the patient is intubated, the goal should be normal gas exchange. Prophylactic hyperventilation is not helpful, so the $PaCO_2$ should be kept between 35 and 40 mm Hg. If there are clinical signs of impending herniation (dilated pupil, posturing, etc.), then mild hyperventilation ($PaCO_2$ 30-35) may help by inducing slight cerebral vasoconstriction, thereby lowering intracranial pressure. If the intracranial pressure remains elevated despite this and other measures, lower the $PaCO_2$ to the range of 28-32 mm Hg. Hyperventilation below 28 mm Hg doesn't help and can actually hurt the patient by causing excessive cerebral vasoconstriction.

Remember how important oxygen is? In neurocritical care, we try to keep the SpO_2 at least 95% and the PaO_2 at least 90 mm Hg. There's not a whole lot of evidence that defines the "critical threshold" of oxygen tension in the brain, but it makes sense to keep the patient well-oxygenated. Therapeutic hyperoxia (i.e., a $PaO_2 \geq 150$) has some experimental data supporting it, but isn't part of clinical practice yet. Theoretically, hyperoxia could cause cerebral vasoconstriction and might make things worse. One study of patients who were resuscitated from cardiac arrest showed poorer outcomes with a $PaO_2 > 300$.

Extubation in the brain-injured patient usually depends on the patient's mental status and ability to protect his airway. Many of these patients need tracheostomy and if you think this will be necessary, do it sooner rather than later—early tracheostomy is associated with better mobilization and rehabilitation, lower rates of pneumonia, and less time spent receiving positive-pressure ventilation.

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Circulatory Support

Proper blood pressure management is a cornerstone of neurocritical care. The most important concept to remember has nothing to do with bringing the BP down, however—it is to **AVOID HYPOTENSION AT ALL COSTS!!!** Now that I have your attention….

The perfusion pressure of the brain is referred to as the CPP (cerebral perfusion pressure). The CPP is the difference between the mean arterial pressure (MAP) and the intracranial pressure (ICP). Normally, the brain's vascular system is able to regulate itself to maintain a constant delivery of oxygen to tissue—this is called cerebral autoregulation. Cerebral autoregulation works just fine when the CPP is between 50 and 120 mm Hg. When the CPP falls below 50, oxygen delivery becomes "supply-dependent"; that is, the lower the CPP, the lower the oxygen delivered. When the CPP exceeds 120 a situation called "luxury perfusion" occurs, which can lead to cerebral edema. Patients with chronic hypertension may have a rightward shift of this relationship.

When brain tissue is injured, much of the cerebral autoregulation is lost (at least in the injured area). Oxygen delivery becomes supply-dependent over a much wider range of pressure and when the CPP falls below 50 mm Hg, irreversible ischemia can occur. For this reason, and to maintain a margin of safety, we try to keep the CPP between 60 and 90 mm Hg. If an intracranial measuring device is in place, the CPP can be calculated easily (MAP – ICP). If there is no ICP monitor, the MAP should be kept ≥ 80. This is usually accomplished with IV fluids, but vasopressors may be required. Fluids should obviously be given first if the patient is volume-depleted, and the patient should be kept euvolemic at all times (especially important with cerebral salt wasting and diabetes insipidus).

Now, what about hypertension? There's something about an elevated blood pressure that seems to drive doctors and nurses crazy. It probably has a lot to do with all of those "Silent Killer" PSAs that run on TV. So we all know that the blood pressure needs to come down. NOW. A LOT. But should it really come down? If so, how much? And how should this be done?

The most important factor in deciding what to do about hypertension is the patient's clinical condition. The asymptomatic woman who is sitting in your office eating salted potato chips with a BP of 220/105 needs counseling, a prescription, and a stern lecture about her diet. She does not need admission to the ICU, a nitroprusside drip, and an arterial line. The same patient who shows up in the ED a week later with the same blood pressure and a thalamic hemorrhage needs a different approach.

When you're considering how much to lower a patient's blood pressure, it helps to know why the blood pressure needs to be reduced and what the consequences of not controlling the blood pressure are. Here are some guidelines:

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Emergency	**Target BP**	**Why the BP Needs to Come Down**
Subarachnoid Hemorrhage	MAP 70-90 SBP 110-150	Systolic blood pressure spikes above 150 increase the risk of rerupture of the aneurysm, which carries a 75% risk of mortality.
Intracerebral Hemorrhage	MAP 100-120 SBP 140-180	Cerebral perfusion needs to be maintained, but the blood pressure should be lowered rapidly to prevent expansion of the hematoma.
Hypertensive Encephalopathy	Reduction of the MAP by 25% over 1 hour	Rapid lowering of the blood pressure beyond 25% of the initial MAP may cause cerebral ischemia.
Acute Ischemic Stroke	Don't lower the blood pressure unless the SBP exceeds 220 or the DBP exceeds 120, **unless thrombolytics have been given.**	After an ischemic stroke, a "penumbra" of viable, but threatened, brain tissue exists around the infarcted area. This penumbra depends on collateral circulation and adequate perfusion, and dropping the blood pressure can lead to death of this tissue. So, while the temptation to lower the BP is there, RESIST!
Post-Thrombolysis for Stroke	MAP 100-130 SBP 140-180	After tPA, the balance is between adequate perfusion of the penumbra and the risk of hemorrhage with higher blood pressures.

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So, now that you've decided to lower the blood pressure, what drug do you use? Again, much of this depends on the clinical situation. Here are some drugs that are commonly used in neurocritical care.

Drug	**Dose**	**Mechanism, Pros and Cons**
Nicardipine	5-15 mg/hour infusion	Calcium channel blocker with no suppression of the AV node; acts as a cerebral arterial vasodilator. Very titratable with few side effects, and preferred for most neurocritical care patients.
Labetalol	10-20 mg IV PRN 0.5-2.0 mg/min infusion	Combined alpha and beta receptor blocker; especially useful in hyperadrenergic conditions (cocaine intoxication, thyrotoxicosis). Can cause bradycardia and bronchospasm.
Fenoldopam	0.1-1.6 mcg/kg/min infusion	DA1 receptor agonist; lowers systemic blood pressure while increasing renal blood flow, so it can be useful when there is evidence of acute renal failure. It may increase ICP, so it isn't used too often.
Sodium Nitroprusside	Doesn't matter	Sodium nitroprusside dilates both arterioles and veins, which increases cerebral edema and ICP. It also worsens cerebral autoregulation and has no place in neurocritical care.

Cardiac Concerns

Most of the time, the blood pressure is too high and needs to be lowered. Occasionally, though, patients will be hypotensive. This needs to be treated just as urgently as hypertension, since cerebral perfusion needs to be maintained.

Subarachnoid hemorrhage (and to a lesser extent, intraparenchymal hemorrhage) causes a tremendous surge in catecholamines. This leads to diffuse coronary vasoconstriction and can cause myocardial injury even in patients without coronary artery disease. The classic EKG findings are deep inverted T waves, but ST depression, ST elevation, and conduction delays can all occur. Pathologically, "contraction band necrosis" is what's found, which can

range from complete reversibility to full-thickness infarction. Troponin levels can be elevated, reflecting the degree of myocyte injury.

The principal treatment is supportive. There's no role for heparin since there's no thrombosis of a coronary artery (and heparin would be contraindicated anyway in the setting of SAH). Inotropic support and vasopressor support (if necessary) should be provided to maintain adequate CPP. Dopamine and dobutamine are most commonly used.

Ischemic strokes can occur following myocardial infarction—in this case, anticoagulants are indicated and early revascularization of the coronary (as well as the cerebral) circulation should be considered.

Dysrhythmias of all shapes and speeds can occur with the brain-injured patient (20-40% of ischemic strokes, and nearly 100% of SAH), and should be treated aggressively with the usual drugs. Unstable rhythms should be cardioverted.

Reversal of Anticoagulation

Patients with intracranial bleeding who are coagulopathic require rapid reversal to prevent hematoma expansion.

Coagulopathy	**Reversal Agent**
Warfarin	FFP—15 mL/kg (typically 4-6 units); may repeat until INR is less than 1.5. Prothrombin concentrates are becoming more available and may be used as well. Recombinant Factor VIIa is an option for life-threatening hemorrhage that requires emergency surgery, and the dose is 20-40 mcg/kg IV. Vitamin K 10 mg IV daily for 3 days (delayed action)
Heparin or LMWH	Protamine sulfate 1 mg per 100 units heparin, or per 1 mg enoxaparin (one dose), to a maximum dose of 50 mg IV.
Platelet dysfunction	Platelet transfusion (keep platelet count > 100K); may also use DDAVP 0.3 μg/kg IV (one dose). Conjugated estrogens (0.6 mg/kg) IV daily for 5 days for prolonged platelet dysfunction.
Tissue Plasminogen Activator	10 units cryoprecipitate, followed by FFP and Vitamin K

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Thromboelastography is quick and is a good way to evaluate the adequacy of the coagulation cascade. Transfusing to normalize TEG parameters, rather than coagulation values, is becoming more common.

Keep Cool

There is a growing body of both laboratory and clinical evidence that hyperthermia (core body temperature ≥ 38º C) worsens brain injury. Elevated body temperature increases cerebral metabolic requirements and oxygen consumption and can also increase the production of lactic acid, which can be deleterious. The goal for most neurocritical care patients is **normothermia**, which can be accomplished with cooling blankets, antipyretics, and specialized devices like the Arctic Sun cooling vest. Rarely, pharmacologic adjuncts like bromocriptine and paralytic agents may be necessary.

Two large studies have shown the benefit of therapeutic hypothermia on survivors of cardiac arrest. The patients who improved had a primary cardiac cause of arrest—ventricular tachycardia or ventricular fibrillation. They were cooled to 32-34˚C for 12-24 hours and then rewarmed to normal temperature. Concerns that this merely robs the undertaker to pay the nursing home are not founded—survivors demonstrated a significantly better neurologic recovery.

Therapeutic hypothermia has not been shown to improve outcomes in patients with traumatic brain injury. It's still being studied in ischemic stroke and refractory intracranial hypertension. Right now, it should be considered an experimental "rescue therapy" in those cases.

Sugar

Sugar ain't always sweet. Obviously, hypoglycemia poses the most immediate threat to brain tissue, but hyperglycemia can also be dangerous. Cerebral lactate/pyruvate ratios increase whenever the blood glucose level is above normal, and outcomes following neurosurgery, subarachnoid hemorrhage, and ischemic stroke have been shown to be adversely affected by poor glycemic control, even in non-diabetics. Tight glucose control is essential to good neurocritical care. We aim to keep the blood glucose between 100 and 150 mg/dL, which helps avoid the hypoglycemic episodes that occur with tighter protocols.

Salt

Hyponatremia can exacerbate neurologic deficits by increasing the free water content of brain tissue. Hyponatremia is commonly due to SIADH and is treated with free water restriction and low-dose diuretics. Another less frequent cause is cerebral salt wasting (CSW), which is most often seen after subarachnoid hemorrhage but has also been associated with brain tumors, ICH, and surgery. The major difference between SIADH and CSW is the patient's volume status—cerebral salt wasting causes polyuria and rapidly leads to volume depletion and hypotension. It is essential to check the urine osmolality and

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make sure that the replacement fluid is more tonic than the urine. For example, a patient whose serum sodium is 129 mEq/L and whose urine osmolality is 450 mEq/L will become more hyponatremic if he is given normal saline (osmolality 308 mEq/L). That patient should be rehydrated with 1.8% saline (616 mEq/L) or 3% saline (1026 mEq/L). Fludrocortisone, 0.1 mg PO daily, may also help with salt retention.

Hypernatremia in neurocritical care patients is most often due to central diabetes insipidus, which is the absence of ADH. These patients are also polyuric and can quickly become volume depleted. The first goal of treatment should be to restore the intravascular volume with isotonic fluids (normal saline or lactated Ringer's) and to replace ADH, which can be done with DDAVP. The usual dose is 2-4 mcg IV every 6-8 hours. If the urinary output continues to exceed 400-500 cc/hour, a vasopressin drip may be required—start at 1 unit/hour, and titrate to keep urine output < 200 cc/hour. Free water losses can be replaced with either 0.45% saline or D5W.

Intracranial Hypertension

Monitors

Several types of intracranial pressure monitors are available. A ventriculostomy allows both measurement of ICP and therapeutic drainage, and is therefore the most preferred. Other devices include intraparenchymal fiberoptic monitors and epidural bolts—these measure ICP, but do not allow drainage of CSF. These devices also tend to "drift" and cannot be recalibrated.

Cerebral Perfusion

The cerebral perfusion pressure (CPP) is defined as the difference between the mean arterial pressure (MAP) and the intracranial pressure (ICP). When the CPP falls below 50 mm Hg, autoregulation is lost and brain ischemia occurs. Excessively high CPP (over 110 mg Hg) can also be detrimental. At this pressure the upper autoregulatory threshold is exceeded and cerebral edema can occur. In general, the CPP should be kept between 60 and 90 mm Hg.

Intracranial Hypertension

Intracranial hypertension is defined as an ICP exceeding 20 mm Hg. Clinical manifestations of intracranial hypertension include mental status changes, worsening peripheral deficits, vomiting, and autonomic changes. Unilateral pupillary dilatation may signal impending uncal herniation. Cushing's Triad may be present in cases of severely increased intracranial pressure. The components of the triad are:

- Bradycardia
- Respiratory Irregularity
- Systolic Hypertension

Airway protection is essential. Measures should be taken to rapidly lower the ICP. If untreated, herniation may occur.

Measures to Lower the ICP

When confronted with a sustained increase in ICP, a few basic steps will usually suffice. First, ensure adequate arterial pressure—fluids or vasopressors should be used. If the patient has a ventriculostomy, CSF can be drained in 3-5 cc increments until adequate CPP is restored. Alternatively, the ventriculostomy can be left open to drain, set at a desired height (usually 20 mm Hg). Repeat CT scanning should be performed to see if there is anything that can be corrected surgically.

If this does not work, or the patient does not have a ventriculostomy, mild hyperventilation can be initiated, but it's really just something that can buy some time (until the mannitol gets infused, or the ventriculostomy gets placed). Hypocapnia causes cerebral vasoconstriction and reduces intracranial blood flow. The goal $PaCO_2$ is 28-32—lower than this can impair oxygen delivery. Sustained hyperventilation becomes ineffective after 6-12 hours, and there is no role for prophylactic hyperventilation. The patient's head should be kept at 30 degrees elevation and the head should be in a neutral position so venous blood flow is not obstructed.

If the ICP is still elevated, osmotherapy can be used. Mannitol (0.25-1.0 g/kg IV) can be used as an osmotic diuretic to lower the ICP. Mannitol should not be used if the patient does not have adequate intravascular volume, however, as this can cause dangerous hypotension. An alternative, which does not deplete the intravascular volume, is hypertonic saline (7.5%, given in 2 cc/kg boluses). Volume overload and pulmonary edema are possible side effects of hypertonic saline. The serum sodium can be raised to 150-155 mEq/L without adverse effects. Serum osmolarity should be followed when using either of these agents, and should generally not exceed 320 mEq/L.

If the ICP is still elevated despite hyperventilation, CSF drainage, and osmotherapy, consider reducing cerebral metabolic oxygen consumption with a drug-induced coma. Propofol is the drug of choice for this—it reduces cerebral oxygen consumption and intracranial pressure and it's easy to titrate. Dosages of up to 150-200 mcg/kg/min may be necessary, so there is the risk of propofol infusion syndrome. Pentobarbital is another, older therapy—a 10 mg/kg bolus is followed by a 1-5 mg/hr infusion. Continuous EEG monitoring should be used in these cases.

Induced hypothermia is currently being studied for this purpose, and decompressive bifrontal craniectomy may also be of benefit. This should be considered for patients on an individual basis.

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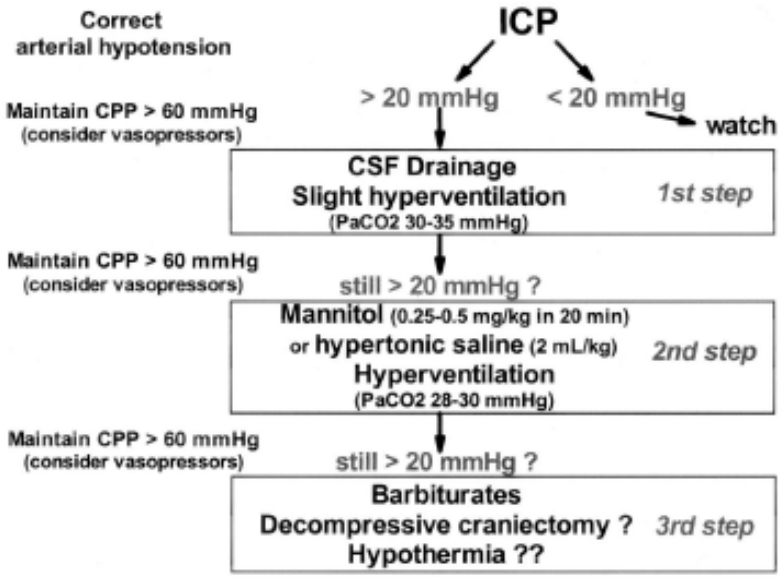

Various and Sundry Items

People with acute brain injury are not that much different from other ICU patients and have the same vulnerabilities to infections, DVT, gastric bleeding, ventilator-induced lung injury, and drug toxicities. Some of the things that have been shown to help all ICU patients are listed here.

- Lung-protective ventilation, with tidal volumes of 6-8 mL/kg (4-6 mL/kg for ARDS)—of course, control of the $PaCO_2$ is more important with acute brain injuries
- Daily sedative interruptions, titration of sedatives to a recognized scale (we use the Richmond Agitation-Sedation Score—a score of -1 is sedated but arousable), and avoidance of unnecessary neuromuscular blockade
- Head-of-bed elevation to 30-45º (helps with the ICP, too)
- Appropriate DVT prophylaxis
- Appropriate stress ulcer prophylaxis
- Subglottic suctioning of endotracheal tubes
- Sterile placement of central venous and arterial lines
- Good oral hygiene

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- Daily review of the medication list
- Early mobility
- Early enteral nutrition

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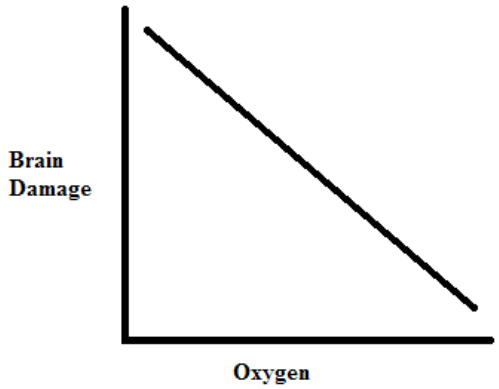
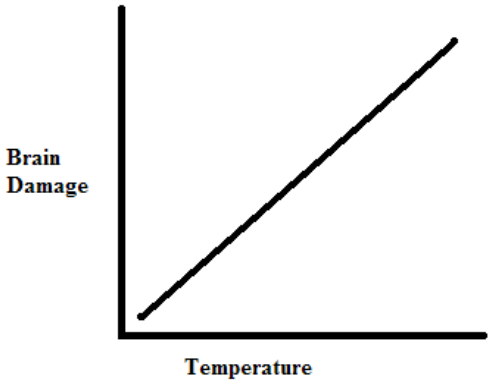
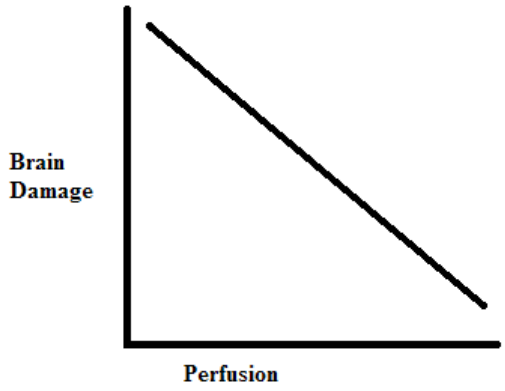
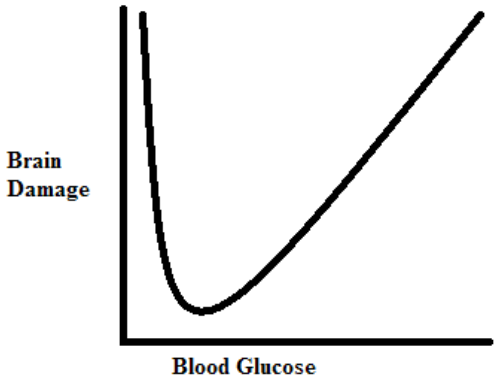
Neurocritical Care—now, in GRAPH FORM!









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