Congresso Nazionale dei Medici di Bordo della Marina Mercantile

1 Dicembre 2012 Genova

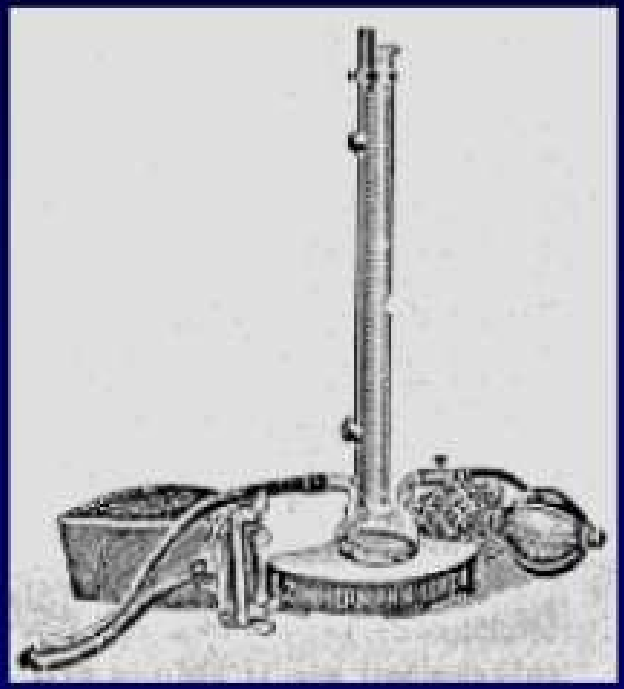
Trattamento della crisi ipertensiva

Carlo Del Prato
Direttore DEA ASL 5

Scipione Riva Rocci.

Un nuovo sfigmomanometro.

Gazzetta Medica di Torino. 1896; 47: 981, 1001



Scelta dell’apparecchio

2 tipi di sfigmomanometri, quello a mercurio e quello aneroide.

- In PS apparecchi elettronici (multiparametrici)
- Gli strumenti a mercurio sono affidabili e hanno bisogno della ricalibrazione periodica come gli strumenti aneroidi.
- Gazzetta ufficiale n.245 del 18 ottobre scorso. Il decreto è entrato in vigore a partire il l **3 aprile 2009:**
- «il mercurio non può più essere commercializzato nei termometri per la misurazione della temperatura corporea e in altre apparecchiature di misura destinate alla vendita al grande pubblico (manometri, barometri, sfigmomanometri, termometri diversi da quelli per la misurazione della temperatura corporea)».

Misurazione della PA

Il paziente deve essere mantenuto a riposo in un ambiente tranquillo.

Questa condotta porta normalmente ad una riduzione di 10-20 mmHg o più della pressione arteriosa.

Più misurazioni, (almeno tre) evidenziano il fenomeno di regressione verso la media

Misurazione pressione arteriosa

- Eseguire almeno due misurazioni intervallate da 1 o 2 minuti e una misurazione aggiuntiva se le prime due sono molto diverse tra loro.
- Usare un bracciale standard (12-13 cm di altezza e 35 cm di lunghezza), ma disporre di bracciali più grandi e più piccoli nel caso rispettivamente di soggetti obesi e magri. Usare bracciali pediatrici nei bambini.
- Posizionare il bracciale a livello del cuore qualunque sia la posizione del paziente.
- Usare le fasi I e V (scomparsa dei toni di Korotkoff) per identificare rispettivamente la pressione sistolica e diastolica.

Procedure per la misurazione della pressione arteriosa

- Misurare la pressione arteriosa in entrambe le braccia in occasione della prima visita per identificare eventuali disparità legate a una vasculopatia periferica. In questa situazione considerare il valore più alto come quello di riferimento nel caso si impieghi la tecnica auscultatoria.

- Misurare la pressione arteriosa dopo 1 e 5 minuti dall'assunzione dell'ortostatismo nei soggetti anziani, nei pazienti diabetici e in altre condizioni in cui può essere frequente o sospettata ipotensione ortostatica.

VARIABILITA' DELLA PRESSIONE ARTERIOSA

A) BIOLOGICA
   1. casuale
   2. sistematica
   - short-term (frequenza cardiaca, respiro, bilancia simpato-vagale)
   - attività fisica e mentale
   - giornaliera (ritmo sonno-veglia)
   - stagionale

B) Legata all'osservatore

C) Legata alla misurazione della pressione

Effetti di alcune attività comuni sulla PA

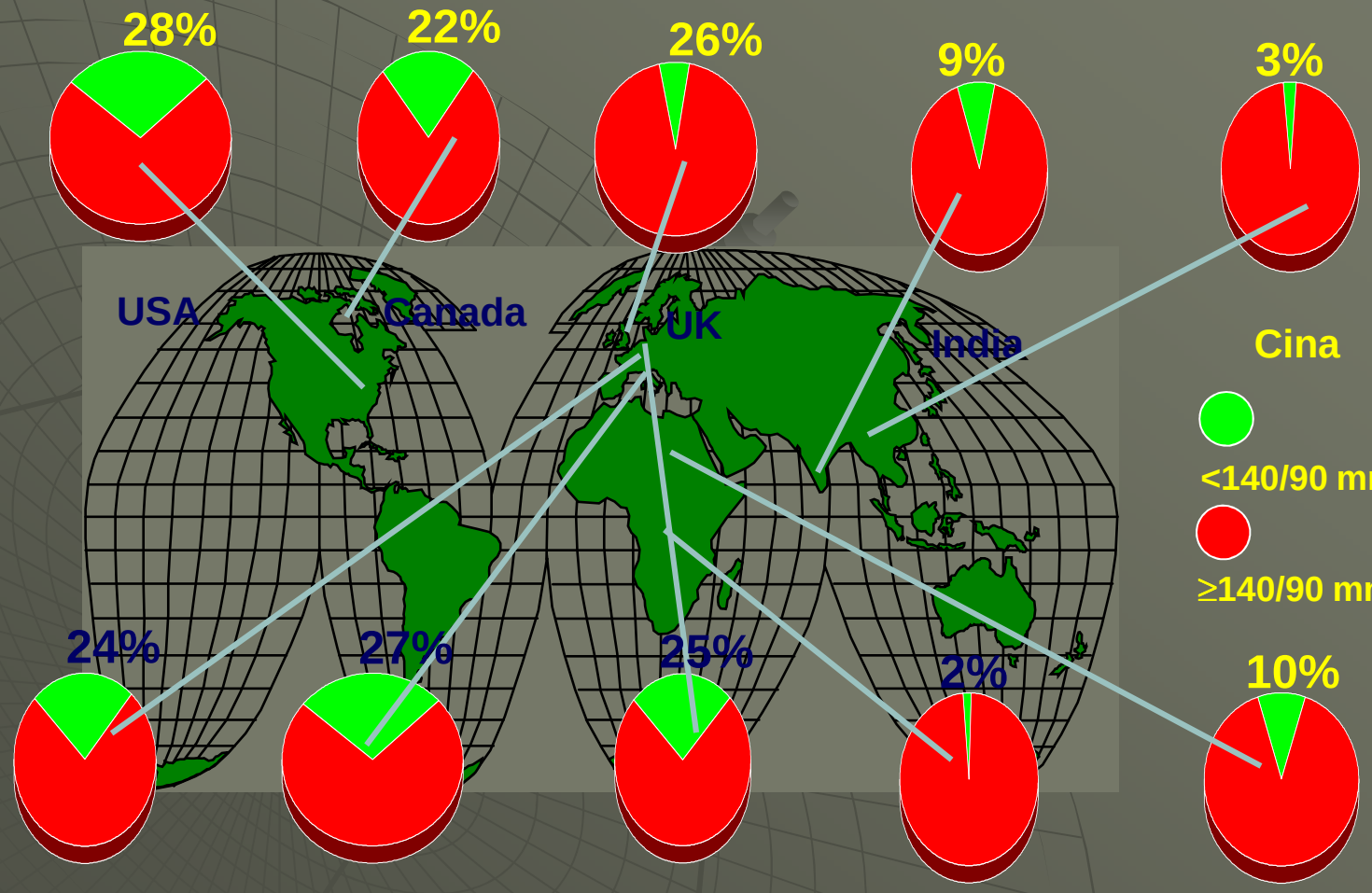
Attività	PA sistolica (*)	PA diastolica (*)
vestirsi	+ 12	+ 10
mangiare	+ 9	+ 10
camminare	+ 12	+ 6
leggere	+ 2	+ 2
vedere la TV	+ 0,3	+ 1
andare a lavorare	+ 16	+ 13
svolgere un lavoro sedentario	+ 6	+ 5
parlare a telefono	+ 10	+ 7
tenere una conferenza	+ 20	+ 15

(*) variazione in mmHg, modificato da BMJ, 2001

Epidemiology

- Sixty million in U.S.
- More than 90% have essential hypertension
- 20% surgical patients
- ¾ of those affected do not have their BP well controlled
- Incidence is higher in African-Americans and the elderly
- 4- 35 % after the surgical procedures

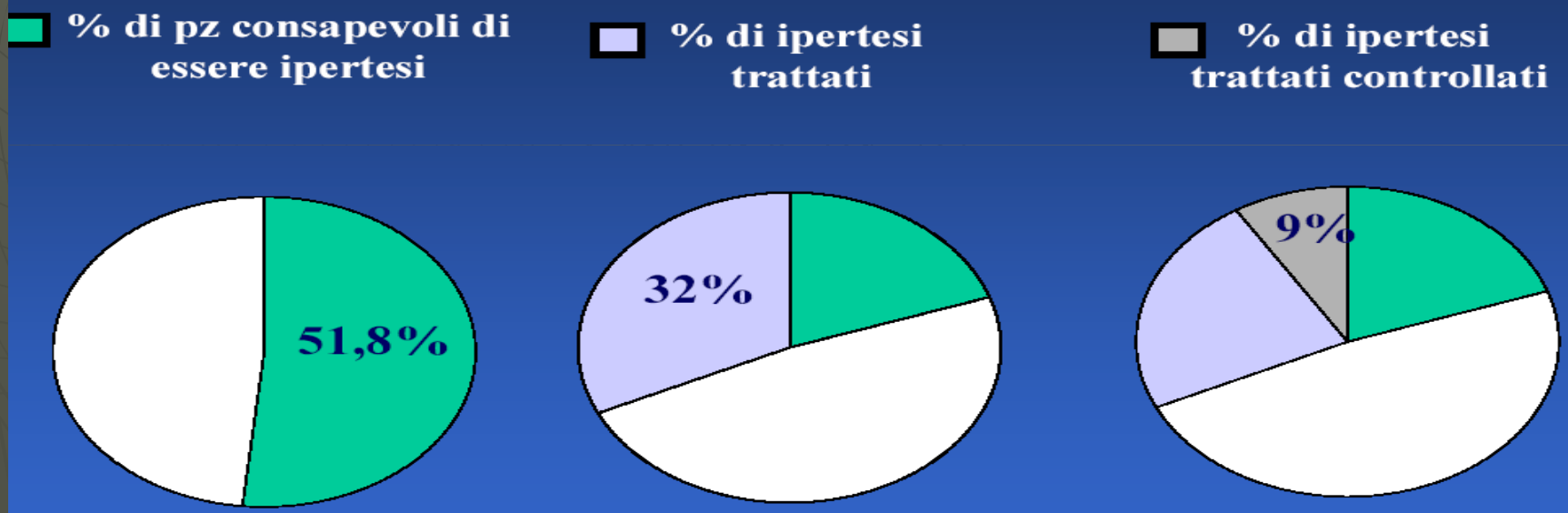
PERCENTUALE DI CONTROLLO DELL'IPERTENSIONE IN DIVERSI PAESI



American Heart Association, 1999

Quanti ipertesi ci sono in Italia e quanti ne stiamo trattando?

Ipertensione in ITALIA: Consapevolezza, Trattamento, Controllo



E in Italia ?

Crisi ipertensive:

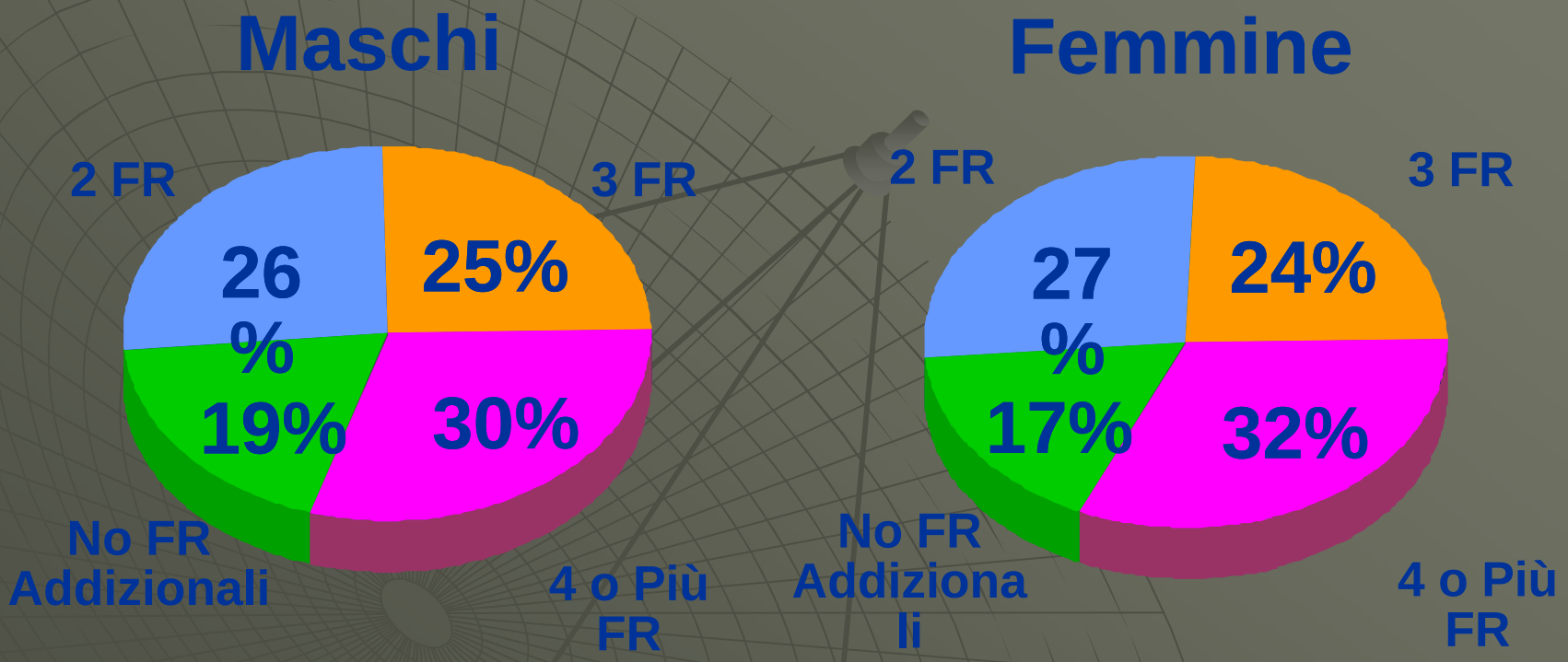
DEA di Torino: il 3% degli accessi era da riferirsi ad una crisi ipertensiva, rappresentando il 27% delle urgenze/emergenze mediche in DEA

- **Dati osservazionali permettono di rilevare una percentuale tra lo 0,3 e lo 0,6% annuo delle presentazioni in Pronto soccorso (linee guida IA Reg. Toscana 2009).**
- **La % nel 2009 ASL 5: 0,61%**

Soltanto un quarto delle crisi ipertensive vanno considerate vere e proprie emergenze mediche.

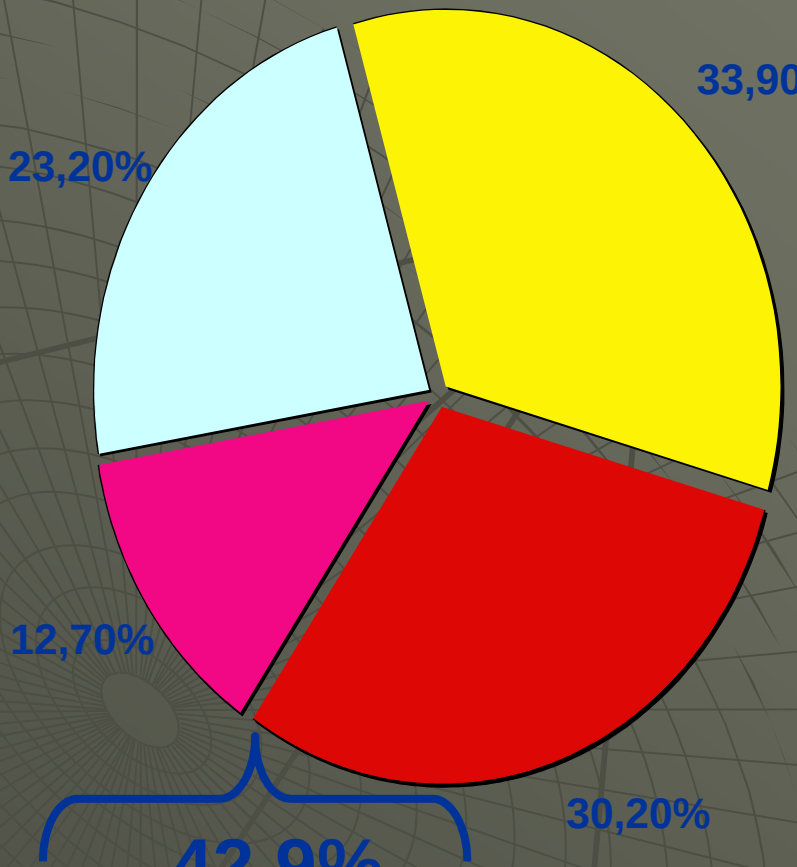
Da: U. Marchisio, P. Riva

La maggioranza degli ipertesi ha fattori di rischio addizionali



Kannel. Am J Hypertens 2000;13:3S-10S

Profilo del rischio CV totale in recenti studi italiani sull'ipertensione



42.9%

5.800.000 ipertesi in Italia a rischio alto o molto alto

Volpe M, et al. J Hypertens 2007; in p

Stratificazione del rischio cardiovascolare

Altri fattori di rischio, danno d'organo o presenza di patologia concomitante	Pressione arteriosa (mmHg)				
	Normale PAS 120-129 o PAD 80-84	Normale alta PAS 130-139 o PAD 85-89	Grado 1 PAS 140-159 o PAD 90-99	Grado 2 PAS 160-179 o PAD 100-109	Grado 3 PAS ≥180 o PAD ≥110
Nessun fattore di rischio aggiunto	Rischio nella media	Rischio nella media	Rischio aggiunto basso	Rischio aggiunto moderato	Rischio aggiunto elevato
1-2 fattori di rischio	Rischio aggiunto basso	Rischio aggiunto basso	Rischio aggiunto moderato	Rischio aggiunto moderato	Rischio aggiunto molto elevato
3 o più fattori di rischio, SM, danno d'organo o diabete	Rischio aggiunto moderato	Rischio aggiunto elevato	Rischio aggiunto elevato	Rischio aggiunto elevato	Rischio aggiunto molto elevato
Malattia cardiovascolare o renale	Rischio aggiunto molto elevato	Rischio aggiunto molto elevato	Rischio aggiunto molto elevato	Rischio aggiunto molto elevato	Rischio aggiunto molto elevato

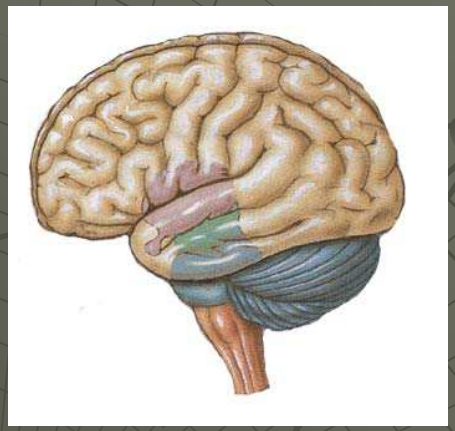
SM: sindrome metabolica; PAS: pressione arteriosa sistolica; PAD: pressione arteriosa diastolica

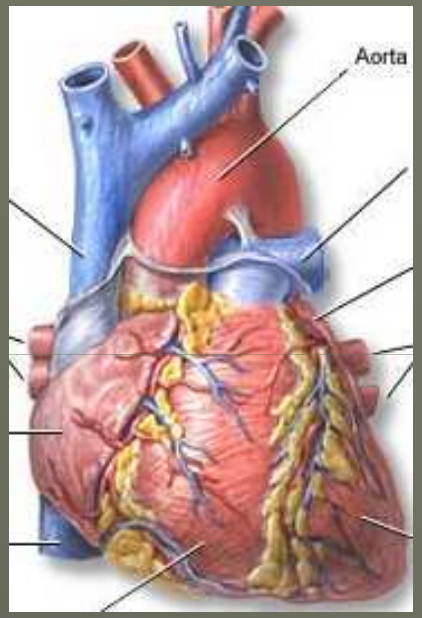
- L’pertensione costituisce una delle cause principali di aterosclerosi
- Colpisce prevalentemente arterie di grande e medio calibro in particolare le coronarie
- Meccanismo d’azione: aumenta la permeabilità vasale alle lipoproteine plasmatiche favorendo la formazione di placche ateromasiche
- Può coinvolgere anche organi singoli:

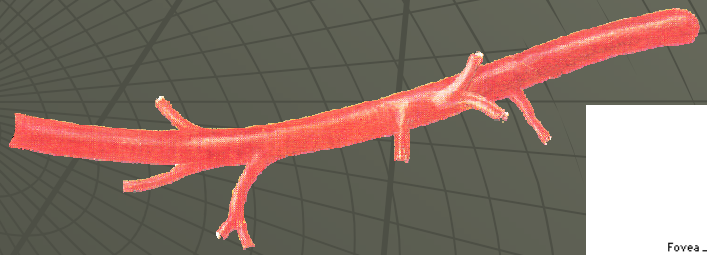
  Cuore
  Encefalo: si creano disturbi vascolari sotto forma di trombosi e di emorragie comunemente definiti “ictus cerebrali”.
  Rene: la sofferenza renale può essere la conseguenza di processi aterosclerotici che determinano una riduzione del flusso ematico renale con danno alla struttura e quindi alla funzionalità renale.
  Occhio: il danno si verifica a livello delle arteriose oculari alcune delle quali può rompersi dando origine a microemorragie; i segni clinici sono dovuti ad una sofferenza retinica che si manifesta inizialmente con visione **offuscata,chiazze scure o scintillanti** all’interno del campo visivo, **mosche volanti**, fino ad arrivare ad una cecità progressiva .

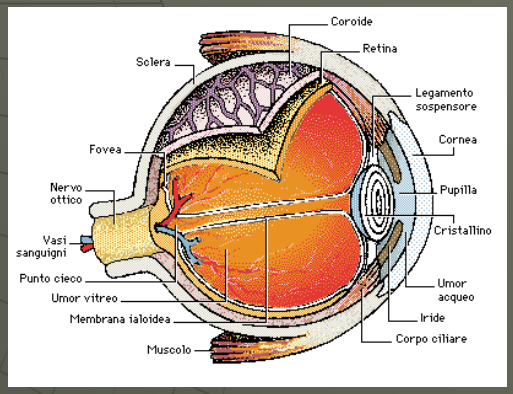
Organi bersaglio dell'ipertensione arteriosa sistemica

- Vasi arteriosi
- Miocardio
- Encefalo
- Reni
- Occhi



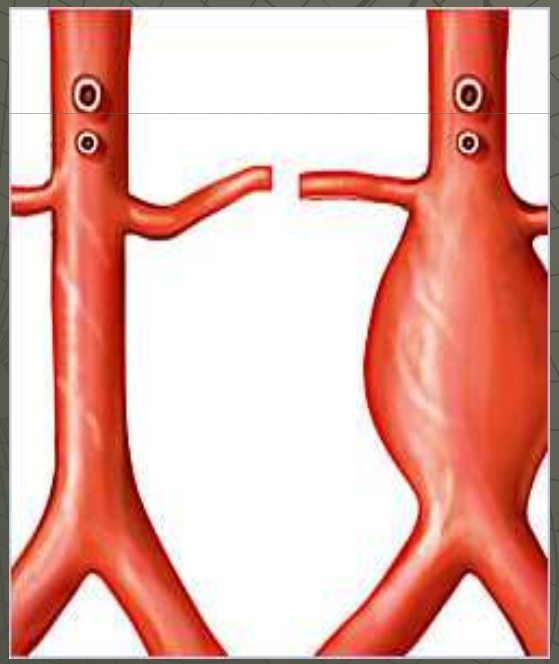


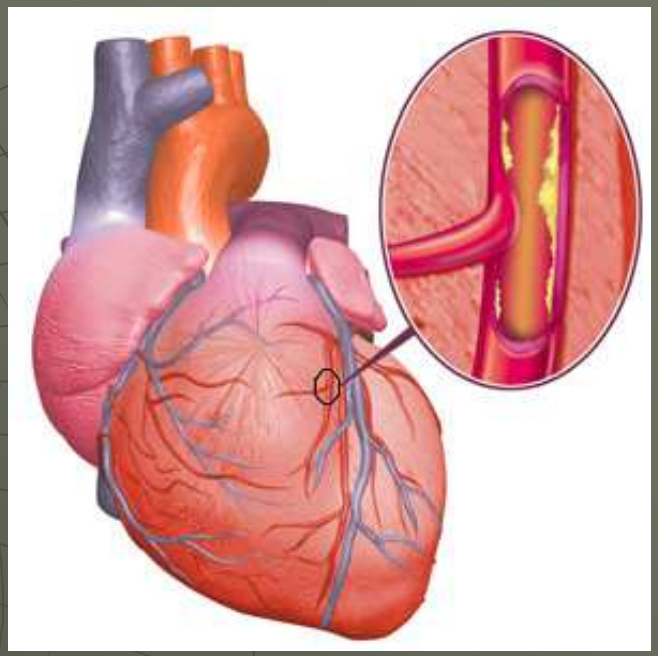




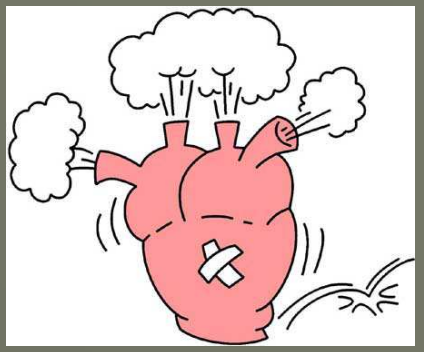
QUADRI CLINICI FINALI:

- **Le arterie maggiormente colpite sono i vasi di grande e medio calibro**
- **Il rimodellamento vasale può evolvere come rimodellamento positivo (stenosi) o negativo (dilatazione/aneurisma)**
- **I quadri clinici di presentazione variano in base al distretto coinvolto e spesso il coinvolgimento è multidistrettuale**





Miocardio



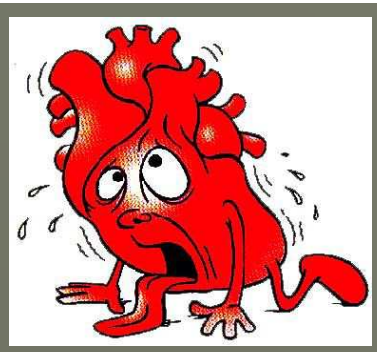
FISIOPATOLOGIA:

- **Aumentato carico di lavoro** → **IPERTROFIA COMPENSATORIA** → **DILATAZIONE VENTRICOLARE**
  → **ISCHEMIA**
- **Aumentato volume** → **DILATAZIONE VENTRICOLARE**

QUADRI CLINICI FINALI:

- **Scompenso cardiaco (cardiopatia ipertensiva)**
- **Cardiopatia ischemica**

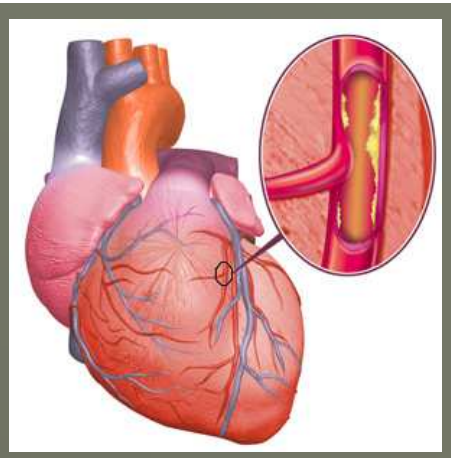
SCOMPENSO CARDIACO



- **Lo sviluppo di ipertrofia ventricolare sinistra, dovuto all'aumentato post-carico, INIZIALMENTE COMPENSATORIA, nel tempo si traduce in una riduzione della frazione di eiezione**

- **La gittata cardiaca viene mantenuta a spese della tachicardia e di un incremento del volume telediastolico, con conseguente aumento della tensione di parete e del consumo miocardico di O_2**

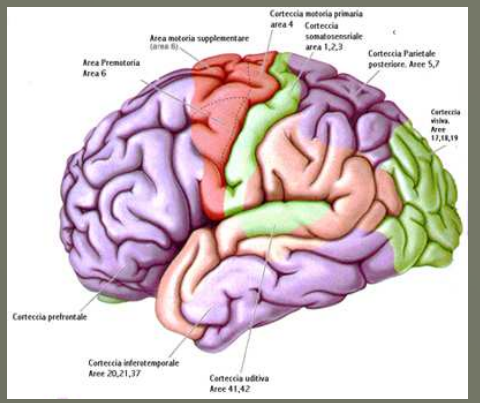
CORONAROPATIA



Aspetti caratteristici rispetto a pazienti non ipertesi:

- ***Elevata percentuale di pazienti con angina tipica e coronarie normali***
- ***Alterazione della vasomotricità coronarica, dovuta a fattori sia locali (disfunzione endoteliale) sia sistemici (iperattività del sistema nervoso simpatico)***
- ***Alta prevalenza di ischemia silente***
- ***Frequente riscontro di microangiopatia***

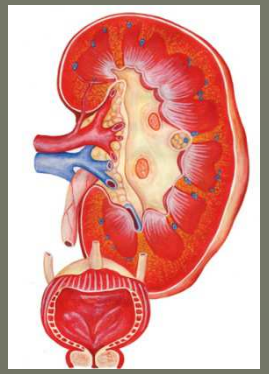
Encefalo



L’ipertensione è la causa più frequente degli eventi cerebrali acuti.

- **Ischemia**
- **Emorragia**

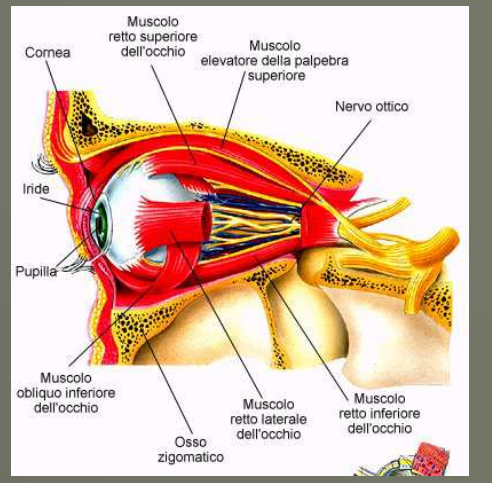
Rene



- Il danno renale si instaura progressivamente e in modo silente nel corso degli anni, manifestandosi esclusivamente con alterazioni di alcuni parametri di laboratorio

- Occasionalmente: insufficienza renale talmente avanzata da rendere necessario un trattamento sostitutivo (Dialisi o Trapianto renale)

Occhio

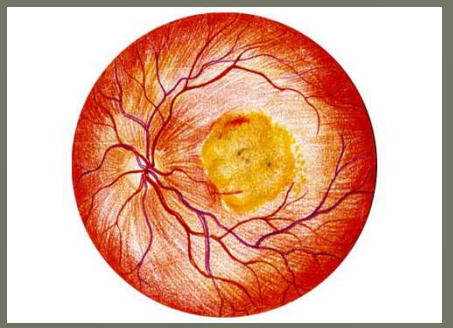


Disturbi visivi si manifestano per compressione, occlusione o rottura o comparsa di essudati dei piccoli vasi della retina

Fattori che influenzano l'entità del danno

- **durata dello stato ipertensivo**
- **livelli dell'aumento pressorio**
- **preesistente stato dei vasi retinici**

Le alterazioni retiniche



- Le alterazioni retiniche, secondarie all'ipertensione arteriosa, costituiscono spesso il primo segno della malattia ipertensiva

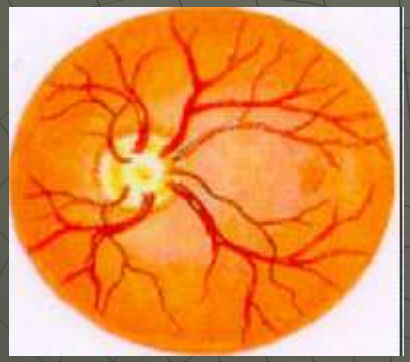
- Il riscontro di tali alterazioni è talvolta occasionale durante una visita oculistica di routine

- Il reperto di alterazioni retiniche a carico del microcircolo può contribuire alla diagnosi precoce di uno stato ipertensivo latente e consentire un trattamento farmacologico adeguato e tempestivo

- Controlli nel tempo del fondo oculare concorrono nel formulare un giudizio sull'efficacia della terapia antipertensiva in atto

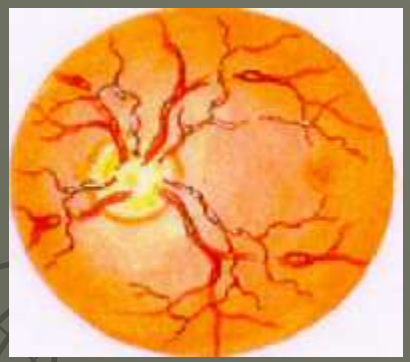
Classificazione del fondo oculare nella retinopatia ipertensiva
Keith, Wagener e Barker,1939

GRADO 1



Simile al quadro del paziente anziano: alterazioni minime, con restringimento del calibro vascolare, aumento del riflesso di parete arteriolare e lieve tortuosità vascolare

GRADO 2



vena si dispone perpendicolarmente rispetto all'arteria (segno di Salus); incroci arterovenosi patologici (segno di Gunn):vena interrotta dall'arteria, e i segmenti interrotti si dilatano; restringimento "segmentario"dell'arteria; aumento riflesso di parete arteriolare

GRADO 3

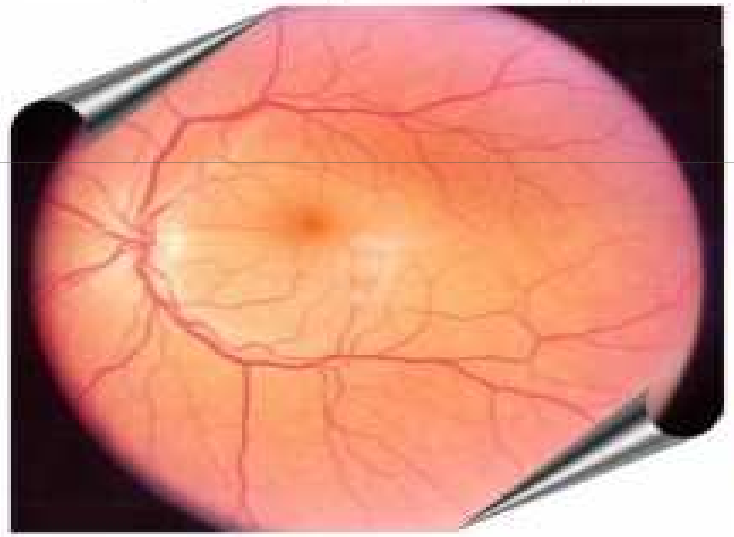
arterie appaiono biancastre e filiformi; compaiono essudati molli (detti anche a fiocco di cotone, espressione di danno ischemico) ed emorragie a fiamma, soprattutto in corrispondenza degli incroci arterovenosi

GRADO 4

coinvolgimento della regione maculare e un edema della papilla ottica. Il grado 3 e 4 possono avere compromissione del visus.

Esame e foto del fondo oculare

(Keith Wagener Barker)



1° Stadio	"Silver Wiring" Aumentata tortuosità Aumentata la reflettività
2° Stadio	"AV nipping" Compressione delle vene agli incroci artero-venosi
3° Stadio	"Cotton wool" Piccole emorragie a fiamma Essudati a fiocco di cotone
4° Stadio	Edema della papilla Compromissione della macula

Enzo Boncompagni, M.D.

Definitions

- **Hypertensive crisis: SBP > 180 mmHg**
  DBP > 120 mmHg

  Hypertensive emergency: hypertensive crisis with acute end-organ damage.

  BP must to be lowered immediately, although not to "normal levels".

  Hypertensive urgency: hypertensive crisis without acute end-organ damage.

  BP has to be reduced within 24 to 48 hours.

Causes

- Sudden withdrawal of anti-hypertensives
- Increased salt intake
- Abnormal renal function
- Increase in sympathetic tone
  - Stress
  - Drugs
- Drug interactions
- Toxemia of pregnancy

Symptoms/Signs

- Restlessness, confusion
- Vision disturbances
- Severe headache
- Nausea, vomiting
- Seizures
- Focal neurologic deficits
- Chest pain
- Dyspnea
- Pulmonary edema

Symptoms/Signs

Blood Pressure (mm Hg)	Funduscopic Findings	Neurologic Status	Cardiac Findings	Renal Symptoms	Gastrointestinal Symptoms
Usually >220/140	Hemorrhages, exudates, papilledema	Headache, confusion, somnolence, stupor, visual loss, seizures, focal neurologic deficits, coma	Prominent apical pulsation, cardiac enlargement, congestive heart failure	Azotemia, proteinuria, oliguria	Nausea, vomiting

Evaluation Components

- **Medical history**
- **Physical examination**
- **Routine laboratory tests**

Medical hystory

- Use of any prescribed medications
- If patient is known to have hypertension
  - hypertensive story
  - previous control
  - current medications with dosing
  - adherence with regimen
  - time from the last dose
- Use of amphetamines, cocaine
- Use of MAO
- Comorbidities and prior CV or renal disease

Physical examination

- **Confirmation of high BP in *both arms* with an *appropriate-size* BP cuff**

- **Signs of end-organ damage**
  - **Pulses in all extremities**
  - **Lung auscultation**
  - **Heart auscultation**
  - **Neurologic examination**
  - **Fundoscopic examination**

Diagnostic exams to exclude end-organ damage

- Lab analysis
  - Urinalysis with microscopic examination of the urinary sediment *(proteinuria, red blood cells, cellular casts)*
  - Chemistry panel *(renal and/or hepatic dysfunction)*
  - Electrolyte abnormalities *(hypokaliemia, hypomagnesemia)*
- Electrocardiogram *(coronary ischemia, left Ventricular hypertrophy)*
- Chest radiography *(pulmonary edema)*
- CT *(cerebrovascular hemorrhage or ischemia, aortic dissection)*
- Echocardiography

Clinical manifestations of Hypertensive Emergencies

- **Hypertensive encephalopathy**
- **Acute aortic dissection**
- **Acute myocardial infarction**
- **Acute coronary syndrome**
- **Pulmonary edema**
- **Severe pre-eclampsia, eclampsia**
- **Acute renal failure**
- **Microangiopathic hemolytic anemia**

Initial management

Hypertensive urgencies

- **"No acute end-organ damage"**
- **Oral medications to lower the BP gradually over 24 to 48 hours**
- **Rapid reduction in BP below the cerebral, renal, and/or coronary autoregulatory range results in marked reduction in organ blood flow, possibly leading to ischemia and infarction.**

Oral Agents for the Treatment of Hypertensive Agencies

Agent	Dosage	Onset/Duration of Action (after discontinuation)	Precautions
Captopril	25 mg PO; repeat as needed; SL, 25 mg	15-30 min/6-8 hr SL 10-20 min/2-6 hr	Hypotension, renal failure, bilateral renal artery stenosis
Clonidine	0.1-0.2 mg PO, repeat hourly as required to total dosage of 0.6 mg	30-60 min/8-16 hr	Hypotension, drowsiness, dry mouth
Labetalol	200-400 mg PO; repeat every 2-3 hr	1-2 hr/2-12 hr	Bronchoconstriction, heart block, orthostatic hypotension
Amlodipine	2.5-5 mg	1-2 hr/12-18 hr	Tachycardia, hypotension

SL, sublingual.

Cleveland Clinic guidelines

Initial management

Hypertensive emergencies

- **Slow correction of BP to avoid further organ damage**
- **Best management with a continuous infusion of short-acting anti-hypertensive agents**
- **Due to impredictable pharmacodynamics, the sublingual or im route should be avoid**
- **Patients should be managed in ICU with close monitoring**
- **Intra-arterial BP monitoring may be prudent in patients with most severe clinical manifestations**
- **Assess the patient's volume status before**

Initial management

Hypertensive emergencies

- ***Immediate goal*: to reduce diastolic BP by 10 to 15% or to approximately 110 mmHg over a period of 30 to 60 minutes**
- **The anti-hypertensive agent of choice depends on which manifestation of end-organ damage is present and the available monitoring setting**

Sodium Nitroprusside

Potent arterial and venous vasodilator

Dosing in adult:

- 0.3-0.5 μg/kg/min IV initial continuous infusion (50 mg in 250 cc D5W), titrate to effect
  - increase in increments of 0.5 μg/kg/min
  - Average dose: 1-6 mcg/kg/min IV
  - Rates >10 mcg/kg/min may lead to cyanide toxicity
  - Continuous hemodynamic monitoring required
  - Cover IV bag/tubing to avoid exposure to light

Onset/Duration of action: Vasodilation begins in 1 to 2 minutes and effects easily reversible by stopping drip

Interactions: none reported

Contraindications: documented hypersensitivity to nitroprusside or any component of formulation; treatment of compensatory hypertension (aortic coarctation, arteriovenous shunting); high output failure; congenital optic atrophy or tobacco amblyopia.

Precautions

Except when used briefly or at low (<2 mcg/kg/min) infusion rates, nitroprusside gives rise to large cyanide quantities; do not use maximum dose for >10 min; use extreme caution in patients with elevated intracranial pressure and in patients with hepatic or renal dysfunction (watch for cyanide toxicity in patients with impaired hepatic function); use lowest end of dosage range with renal impairment; thiocyanate toxicity occurs in patients with renal impairment or on prolonged infusions (continuous BP monitoring needed).

Nitroglycerin

Vasodilator

Dosing in adult:

NTG continuous IV infusion: Start 5 mcg/min, increase by 5 mcg/min q3-5min to 20 mcg/min; if no response at 20 mcg/min increase by 10 mcg/min q3-5min, up to 200 mcg/min

Onset/Duration of action: 2-3 min/5-10 min

Interactions: Reduces effect of alteplase (tissue plasminogen activator) when used with IV nitroglycerin (avoid concurrent use); ethanol can cause hypotension when nitrates taken 1 h or more after ethanol ingestion; heparin's effect may be reduced by IV nitroglycerin (may affect only a minority of patients); sildenafil, tadalafil, and vardenafil cause significant reduction of systolic and diastolic BP with concurrent use (contraindicated; do not administer sildenafil, tadalafil, or vardenafil within 24 h of a nitrate preparation).

Contraindications: Documented hypersensitivity to organic nitrates, isosorbide, nitroglycerin, or any component of formulation; concurrent use with phosphodiesterase-5 (PDE-5) inhibitors (sildenafil, tadalafil, or vardenafil); angle-closure glaucoma (intraocular pressure may be increased); head trauma or cerebral hemorrhage (increase intracranial pressure); severe anemia additional contraindications for IV product include hypotension, uncorrected hypovolemia, inadequate cerebral circulation, constrictive pericarditis, pericardial tamponade.

Precautions: Severe hypotension can occur; caution in volume depletion, hypotension, and right ventricular infarctions; paradoxical bradycardia and increased angina pectoris can accompany hypotension (orthostatic hypotension can also occur and ethanol can accentuate this); tolerance develops to nitrates and appropriate dosing is needed to minimize this (drug-free interval).

Labetalol (TRANDATE)

Alpha-, beta1-, and beta2-blocker, especially useful with aortic dissection. It lowers BP, reduces incidence of myocardial infarctions and death.

Dosing in adult:

Bolus - 20 mg (0.25 mg/kg for an 80-kg patient) IVP over 2 min; may administer 40-80 mg at 10-min intervals, up to 300 mg total dose.

IV infusion - Initially, 1-2 mg/min; titrate to response up to 300 mg total dose, if needed.

Onset/Duration of action: *5-10* min/ 1-8 min

Interactions: Concurrent use with alpha-blockers (prazosin, terazosin) may increase risk of orthostasis; decreases effects of sulfonylureas; may have synergistic effects when administered concurrently with verapamil or diltiazem (avoid concurrent IV use); cimetidine increases bioavailability of labetalol; CYP2D6 inhibitors (eg, fluoxetine, miconazole, paroxetine, pergolide, quinidine, quinine) may increase levels/effects of labetalol; NSAIDs may reduce antihypertensive efficacy of labetalol; salicylates may reduce antihypertensive effects of beta-blockers

Contraindications: Documented hypersensitivity to labetalol or any component of formulation; sinus bradycardia; heart block; cardiogenic shock; bronchial asthma; uncompensated cardiac failure; pregnancy (second and third trimesters).

Precautions: Caution in impaired hepatic function; discontinue therapy if signs of liver dysfunction are present; in elderly patients, a lower response rate and higher incidence of toxicity may be observed; avoid concurrent IV use with diltiazem or verapamil; caution in compensated heart failure and monitor for worsening of condition; not for administration to patients with bronchospastic disease; may mask prominent hypoglycemic symptoms and signs of thyrotoxicosis; may cause fetal harm when administered in pregnancy

Esmolol (Brevibloc)

Ideal for use in patients at risk for complications from beta-blockers, especially patients with mild to moderately severe LV dysfunction or peripheral vascular disease.

Dosing in adult:

Loading dose: 250-500 mcg/kg IV infused over 1-3 mim;
Maintenance infusion: 50 mcg/kg/min IV over 4 min;
if adequate effect not observed within 5 min, repeat loading dose and follow with maintenance infusion using increments of 50 mcg/kg/min IV (for 4 min); this regimen may be repeated up to 4 times if necessary. As desired BP approached, skip loading infusion and reduce dose increments in maintenance infusion from 50 mcg/kg/min IV to 25 mcg/kg/min; if necessary, may increase interval between titration steps from 5-10 min

Contraindications: Documented hypersensitivity to esmolol or any component of formulation; sinus bradycardia; heart block; cardiogenic shock; bronchial asthma (relative); uncompensated cardiac failure; hypotension; pregnancy (second and third trimesters).

Onset/Duration of action: 1-5 min/15-30 min

Precautions: Hypotension is common; administer cautiously in compensated heart failure and monitor for a worsening of the condition; use caution in patients with PVD (can aggravate arterial insufficiency); use caution with concurrent use of beta-blockers and either verapamil or diltiazem;use beta-blockers cautiously in patients with bronchospastic disease. Beta-blockers can mask prominent hypoglycemic symptoms and mask signs of thyrotoxicosis; can cause fetal bradycardia when administered in third trimester of pregnancy or at delivery; use caution in patients with renal dysfunction (active metabolite retained); concentrations >10 mg/mL or infusion into small veins or through a butterfly catheter should be avoided (can cause thrombophlebitis); extravasation can lead to skin necrosis and sloughing.

Hydralazine

Principal indication is treatment of eclampsia. Decreases systemic resistance through direct vasodilation of arterioles.

Dosing in adult:

Initial: 10-20 mg/dose IV q30 min as needed, may increase to 40 mg/dose; change to oral therapy as soon as possible

***Onset/Duration of action*:** 10-20 min/3-8 h

Interactions. Beta-blockers (metoprolol, propranolol) serum concentrations and pharmacologic effects may be increased (monitor cardiovascular status); propranolol increases hydralazine's serum concentrations; NSAIDs may decrease hemodynamic effects of hydralazine (avoid use if possible or closely monitor cardiovascular status)

Contraindications. Documented hypersensitivity to hydralazine or any component of formulation; mitral valve rheumatic heart disease

Precautions. May cause a drug-induced lupuslike syndrome; adjust dose in severe renal dysfunction; use with caution in CAD and pulmonary HTN; monitor BP closely following IV administration; response may be delayed and unpredictable in some patients; titrate cautiously to response; hydralazine-induced fluid and sodium retention may require addition or increased dosage of diuretics

Fenoldopam

Short-acting dopamine agonist (DA1) recently approved for management of severe HTN. Increases renal blood flow and sodium excretion. It is x10 more potent than dopamine as renal vasodilator.

Dosing in Adult:

Initial: 0.1-0.3 mcg/kg/min IV (lower initial doses may be associated with less reflex tachycardia); may be increased in increments of 0.05-0.1 mcg/kg/min IV q15 min until target blood pressure reached; maximal infusion rate reported in clinical studies was 1.6 mcg/kg/min

***Onset/Duration of action*:** <5 min/30 min

Interactions. Acetaminophen may increase levels (30-70%) when administered concurrently; beta-blockers increase risk of hypotension, avoid concurrent use (if must use concurrently, close monitoring recommended)

Contraindications. Documented hypersensitivity to fenoldopam or any component of formulation

Precautions. Use caution in patients with glaucoma or intraocular hypertension; dose-related tachycardia can occur, especially at infusion rates >0.1 mcg/kg/min; caution in patients with angina; close monitoring of BP necessary (hypotension can occur); monitor for hypokalemia at 6-h intervals during infusion; continuous infusion only (not for bolus doses); effects of hemodialysis on pharmacokinetics of fenoldopam not evaluated; caution with increased intracranial pressure; contains sulfites (may cause allergic reaction in susceptible individuals)

Phentolamine

Alpha1- and alpha2-adrenergic blocking agent, effective for pheochromocytoma and hypercatecholaminergic-induced hypertension.

Dosing in Adult:

Bolus 5-20 mg IV q5min; Infusion 0.2-0.5 mg/min

Onset/Duration of action**:** 1-2 min/3-10 min

Interactions. Concurrent administration of epinephrine or ephedrine may decrease phentolamine effects; ethanol increases phentolamine toxicity; concurrent administration with sildenafil, tadalafil, or vardenafil cause additive blood pressure-lowering effects

Contraindications. Documented hypersensitivity to phentolamine or any component of the formulation; renal impairment; coronary or cerebral arteriosclerosis; concurrent use with phosphodiesterase-5 (PDE-5) inhibitors including sildenafil (>25 mg), tadalafil, or vardenafil

Precautions. Myocardial infarction, cerebrovascular spasm, and cerebrovascular occlusion have occurred following administration; caution in patients with gastritis or peptic ulcer, tachycardia, or history of cardiac arrhythmias; may use sildenafil with extreme caution

Treatment of Hypertensive Emergencies

Agent	Dosage	Onset/Duration of Action (after discontinuation)	Precautions
Parenteral Vasodilators			
Sodium nitroprusside	0.25-10 µg/kg/min as IV infusion	Immediate/2-3 min after infusion	Nausea, vomiting; prolonged use may cause thiocyanate intoxication, methemoglobinemia, acidosis, cyanide poisoning; bags, bottles, delivery sets must be light resistant
Nitroglycerin	5-100 µg as IV infusion -	2-5 min/5-10 min	Headache, tachycardia, vomiting, flushing, methemoglobinemia; requires special delivery system because of drug binding to PVC tubing
Nicardipine	5-15 mg/hr as IV infusion	1-5 min/15-30 min, but may exceed 12 hr after prolonged infusion	Tachycardia, nausea, vomiting, headache, increased intracranial pressure; hypotension may be protracted after prolonged infusions
Fenoldopam mesylate	0.1-0.3 µg/kg/min as IV infusion	<5 min/30 min	Headache, tachycardia, flushing, local phlebitis, dizziness
Hydralazine	5-20 mg as IV bolus or 10-40 mg IM; repeat every 4-6 hr	10 min IV/>1 hr (IV); 20-30 min IM/4-6 hr (IM)	Tachycardia, headache, vomiting, aggravation of angina pectoris, sodium and water retention, increased intracranial pressure
Enalaprilat	0.625-1.25 mg every 6 hr as IV injection	Within 30 min/12-24 hr	Renal failure in patients with bilateral renal artery stenosis, hypotension

Agent	Dosage	Onset/Duration of Action (after discontinuation)	Precautions
Parenteral Adrenergic Inhibitors			
Labetalol	20-40 mg as IV bolus every 10 min; up to 2 mg/min as IV infusion	5-10 min/2-6 hr	Bronchoconstriction, heart block, orthostatic hypotension, bradycardia
Esmolol	500-µg/kg bolus injection IV or 50-100 µg/kg/min by infusion; may repeat bolus after 5 min or increase infusion rate to 300 µg/kg/min	1-5 min/15-30 min	First-degree heart block, congestive heart failure, asthma
Phentolamine	5-10 mg as IV bolus	1-2 min/10-30 min	Tachycardia, orthostatic hypotension

* Requires special delivery system.
PVC, polyvinyl chloride.

Parental medications according to clinical presentation

Hypertensive encephalopathy	nitroprusside, nicarpidine, labetalol
Malignant hypertension	labetalol, nicarpidine, nitroprusside, enalaprilat
Ischemic stroke/intracerebral bleeding	nicarpidine, labetalol, nitroprusside (controversial)
Acute myocardial infarction/unstable angina	labetalol, esmolol, nitroglycerin, nicardipine
Pulmonary edema	nitroglycerin, nitroprusside, enalaprilat, loop diuretics
Aortic dissection	labetalol, esmolol, nitroprusside
Preeclampsia, eclampsia	labetalol, idralazine, nicardipine
Catecholamine excess	phentolamine, labetalol
Renal emergencies	fenoldopam, nicardipine, labetalol

DECRETI, DELIBERE E ORDINANZE MINISTERIALI

MINISTERO DELL'ECONOMIA E DELLE FINANZE

DECRETO 10 luglio 2012.

Modifica al decreto 1° dicembre 2011, relativo alle misure del diritto speciale sulla benzina, petrolio, gasolio ed altri generi, istituito nel territorio extradoganale di Livigno, ai sensi della legge 1° novembre 1973, n. 762.

IL MINISTRO DELL'ECONOMIA E DELLE FINANZE

Decreta:

Art. 1.

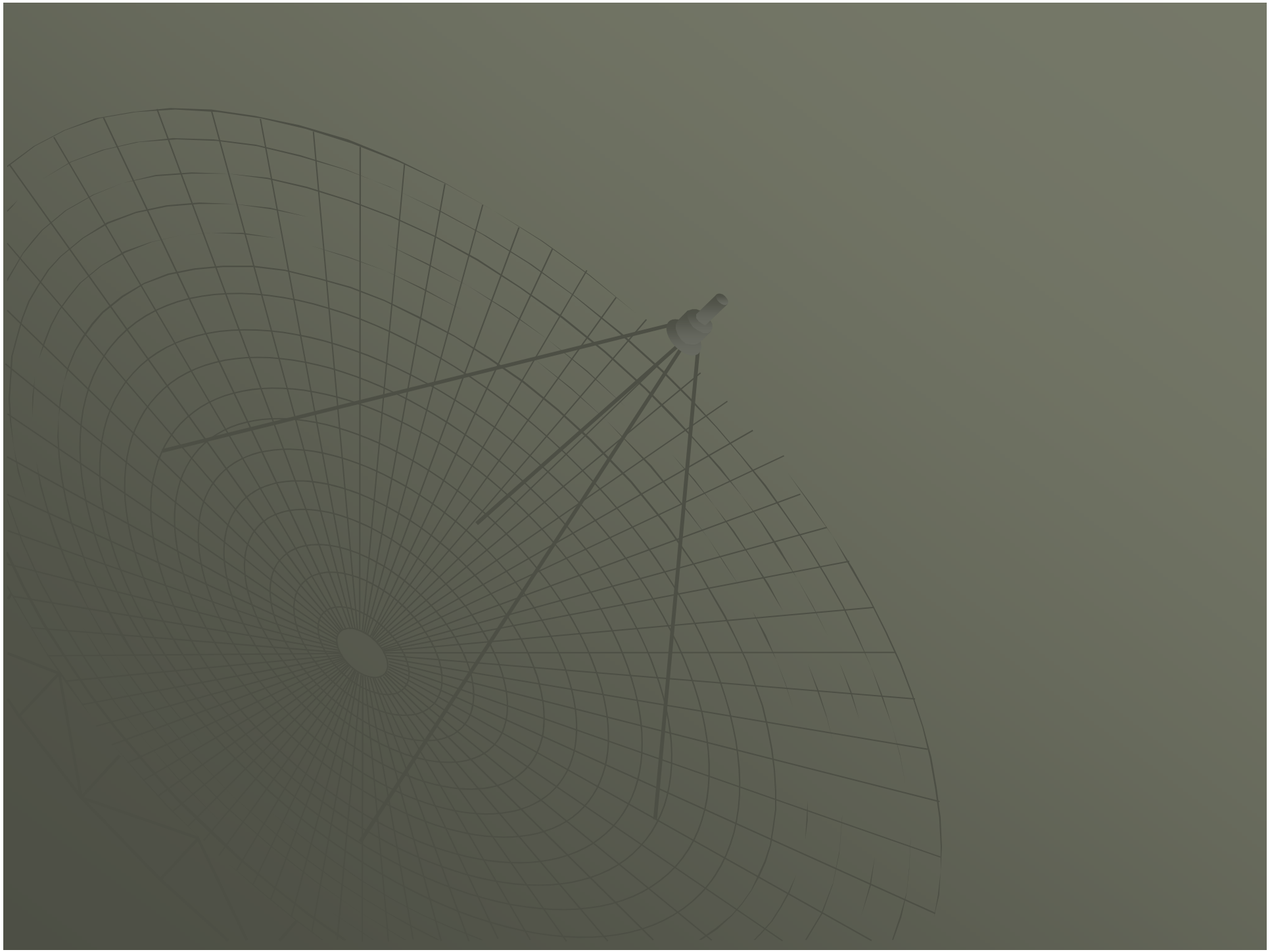
1. La misura del diritto speciale previsto dall'art. 2 della legge 1° novembre 1973, n. 762, con le modifiche successive, viene stabilita in euro 0,155/lit. per il gasolio uso autotrazione.

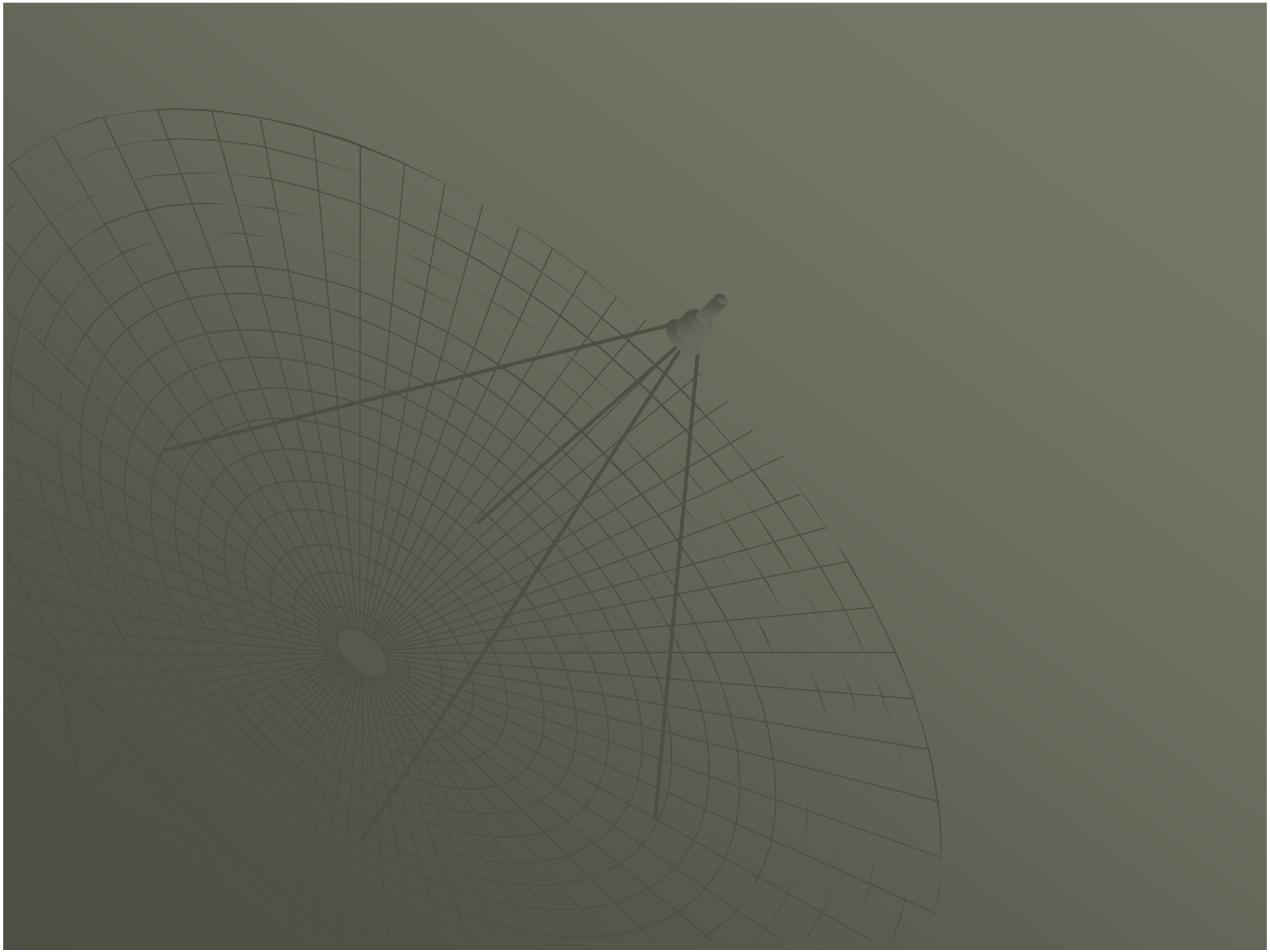
2. La disposizione dell'articolo precedente ha effetto a decorrere dal quindicesimo giorno successivo alla pubblicazione del presente decreto e fino al 31 dicembre 2012.

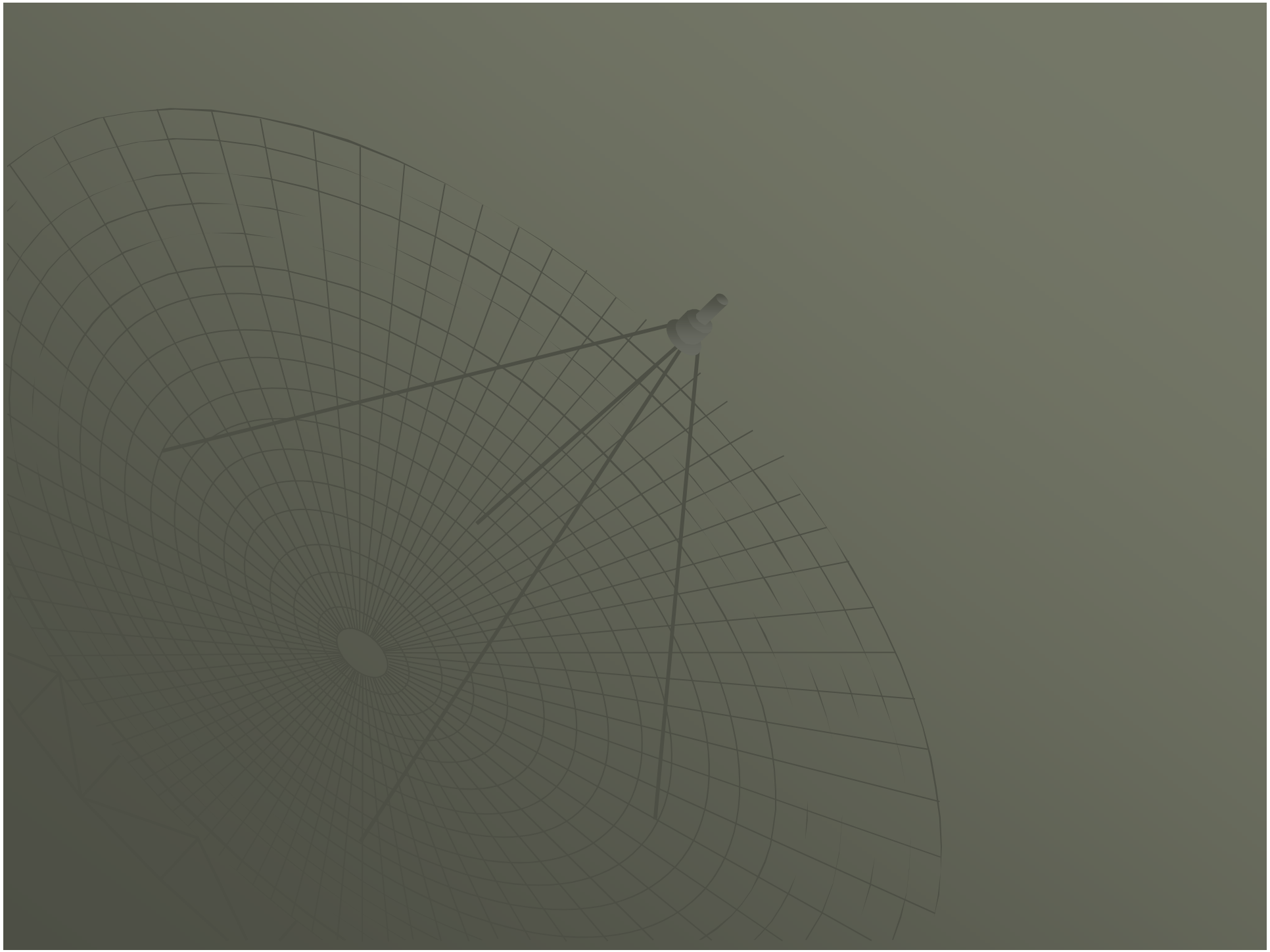
3. L'Ufficio delle Entrate di Tirano è incaricato dell'esecuzione del presente decreto.

ANTIPERTENSIVI E CORONARODILATATORI	41	A BASE DI CLONIDINA CLORIDRATO	fl 150 ug		0	5	10	0		
	42	A BASE DI CLONIDINA CLORIDRATO	cpr 300 ug		0	30	30	0		
	43	NITROGLICERINA	cerotti transdermici		0	5	15	0		
	44	ISOSORBIDE DINITRATO	cpr 10 mg		0	50	50	0		
	45	ISOSORBIDE DINITRATO	cpr sub linguali 5 mg		10	50	100	0		


GRAZIE !!







Cardiovascular emergencies

Aortic dissection

Preferred medications: **Labetalol, nicardipine, nitroprusside (with beta-blocker), esmolol, morphine sulfate.**
Medications to avoid: **Avoid beta-blockers if there is aortic valvular regurgitation or suspected cardiac tamponade.**
Treatment guidelines: **Maintain SBP <110 mm Hg, unless signs of end-organ hypoperfusion are present. Preferred treatment includes a combination of narcotic analgesics (morphine sulfate), beta-blockers (labetalol, esmolol), and vasodilators (nicardipine, nitroprusside). Calcium channel blockers (verapamil, diltiazem) are an alternative to beta-blockers.**

Acute coronary syndrome

Preferred medications: **Beta-blockers, nitroglycerin**
Treatment guidelines: **Treat if SBP >160 mm Hg and/or DBP >100 mm Hg. Reduce BP by 20-30% of baseline. Thrombolytics are contraindicated if BP is >185/100 mm Hg.**

Acute heart failure

Preferred medications: **Nitroglycerin, enalaprilat**
Treatment guidelines: **Treatment with vasodilators (in addition to diuretics) for SBP ≥140 mm Hg. IV or sublingual nitroglycerin is the preferred agent.**

Neurological emergencies

Hypertensive encephalopathy

Preferred medications: **Labetalol, nicardipine, esmolol**
Medications to avoid: **Nitroprusside, hydralazine**
Treatment guidelines: **Reduce mean arterial pressure (MAP) 25% over 8 hours.**

Acute ischemic stroke

Preferred medications: **Labetalol, nicardipine**
Treatment guidelines: **Withhold antihypertensive medications unless the systolic blood pressure (SBP) is >220 mm Hg or the diastolic blood pressure (DBP) is >120 mm Hg UNLESS patient is receiving IV or IA fibrinolysis, then goal BP: SBP <185 mm Hg and DBP <110 mm Hg. After treatment with fibrinolysis, the SBP should be maintained <180 mm Hg and DBP <105 mm Hg for 24 hours.**

Acute intracerebral hemorrhage

Preferred medications: **Labetalol, nicardipine, esmolol**
Medications to avoid: **Nitroprusside, hydralazine**
Treatment guidelines: **Treatment based on clinical/radiographic evidence of increased intracranial pressure (ICP). If signs of increased ICP, maintain MAP just below 130 mm Hg (or SBP <180 mm Hg) for first 24 hours after onset. Patients without increased ICP, maintain MAP <110 mm Hg (or SBP <160 mmHg) for first 24 hours after symptom onset. Recent evidence shows that early intensive BP control is well tolerated and can reduce hematoma growth in patients treated within 6 hours after the onset of an ICH. The target systolic BP for these studies was 140 mm Hg and utilized routine intravenous medications. The target SBP was maintained over 7 days.**

Subarachnoid hemorrhage

Preferred medications: **Nicardipine, labetalol, esmolol**
Medications to avoid: **Nitroprusside, hydralazine**
Treatment guidelines: **Maintain SBP <160 mm Hg until the aneurysm is treated or cerebral vasospasm occurs. Oral nimodipine is used to prevent delayed ischemic neurological deficits, but it is NOT indicated for treating acute hypertension.**

Other disorders

Cocaine toxicity/pheochromocytoma

Preferred medications: **Diazepam, phentolamine, nitroglycerin/nitroprusside**
Medications to avoid: **Beta-adrenergic antagonists prior to phentolamine administration**
Treatment guidelines: **Hypertension and tachycardia from cocaine toxicity rarely require specific treatment. Alpha-adrenergic antagonists (phentolamine) are the preferred agents for cocaine-associated acute coronary syndromes. Pheochromocytoma treatment guidelines are similar to that of cocaine toxicity. Beta-blockers can be added for BP control only after alpha-blockade.**

Preeclampsia/eclampsia

Preferred medications: **Hydralazine, labetalol, nifedipine**
Medications to avoid: **Nitroprusside, angiotensin-converting enzyme inhibitors, esmolol**
Treatment guidelines: **In women with eclampsia or preeclampsia, SBP should be <160 mmHg and DBP <110 mmHg in the prepartum and intrapartum periods. If the platelet count is <100,000 cells mm^3 BP should be maintained below 150/100 mm Hg. Patients with eclampsia or preeclampsia should also be treated with IV magnesium sulfate to avoid seizures.**

Perioperative hypertension

Preferred medications: **Nitroprusside, nitroglycerin, esmolol**
Treatment guidelines: **Target perioperative BP to within 20% of the patient's baseline BP, except if there is the potential for life-threatening arterial bleeding. Perioperative beta-blockers are first choice in patients undergoing vascular procedures or in patients with an intermediate or high risk of cardiac complications.**

Acutely lowering of BP in the ED for clinical situations other than those listed here is controversial and generally should be avoided.