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**Vascular Disease**

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## Commentaries

### Do Quality of Life Measures Measure Anything We Want To Measure?

**For many years I've been sharing a** thought with some of my Parkinson's disease patients who complain about their problems in walking. Advanced Parkinson's disease patients have trouble walking, and I always try to ask about falls, not that I can often do something about it but sometimes I can. Appreciating and sharing the misery is helpful in and of itself, I think, and probably more important is knowing that the problem has been acknowledged and addressed, whether successfully or not.

I have observed that the patients who complained the most were those who had isolated episodes of inability to walk, not the ones who could barely walk all the time. It was the paroxysmal nature of the problem, it seemed to me, rather than the disability itself, that was more trying for the patients. Those who could walk some of the time but not all the time felt like they should be able to walk all the time, whereas those who could barely walk, but were like that all day, learned to bear their disability. The hard thing was to have a disability which fluctuated. Now I can walk, now I can't, and yet the legs are strong! I don't know how much of this is the obvious frustration of living with a variable deficit, and how much was the concern that others wouldn't understand and assume that their was a bit of fakery involved.

I used to share this observation with these patients. I told them that I thought that if they had lost their legs in a car accident they'd have accommodated better to their disability than if the problem came and went, so that sometimes they walked reliably without a cane, while at others they needed a walker or even a wheelchair, when they turned "off" and their PD medications stopped working.

A recent article in *Neurology* (F. de N. Abrantes-Pais et al. *Neurology* 2007;69:261) supports this, albeit I am certainly warping their observations and deductions to fit my own thoughts. These authors had been impressed with their observation that tetraplegics seemed to be more contented with their lives than paraplegics, and that the higher the level of the spinal cord lesion, the better the pa-

tients accommodated to their disability, the greater their optimism and the higher their quality of life. It was a small study involving only 41 subjects, 20 with "high cord," 10 with "low cord" and 11 able-bodied controls. They compared a number of measures of quality of life and optimism, and found that the higher the level of the cord transection, the better and more optimistic the subjects felt. Not only that, but the cord transected patients endorsed a higher quality of life than the able-bodied controls!

This was obviously counterintuitive, so they eliminated any subjects who had also suffered traumatic brain injury, to keep brain changes from confounding the issue. No change. Then they decided to examine the issue of "high cord." In this study, "high cord" was defined as T6 or above. The lowest level in this category had numbness and paralysis from a level between the nipples and the umbilicus down to the toes, and therefore includes paraplegics and tetraplegics. All subjects had complete cord transections, that is, no feeling and no voluntary movement at all below the level of the injury. In the final subgroup analysis they compared only those with cervical injuries above C6, and therefore were tetraplegic (or at least couldn't raise their arms, although they might be able to use their hands). In all subgroup analyses, the higher the level of the injury and therefore the greater the disability, the better the patients felt.

We know that certain brain injuries are self-protecting with regard to insight into the disability. The most classic of the neurological syndromes, due to a right parietal lesion, usually a stroke, the patient suffers left-sided paralysis, can't see to the left and acts as though the left side of the universe doesn't exist, including the left side of their own body. The worse the deficit, the better the patient feels. In dementing syndromes, as patients lose insight into their disabilities they sometimes change from being depressed to being happy, manic even, causing great problems in their care because of their lack of awareness of their limitations. But a spinal cord injury should not cause problems above

the level of the injury, other than an anticipated grief or depressive reaction.

This article was not alluding to inappropriate reactions to injury, but rather the opposite, the lack of what outsiders would consider appropriate resignation and anger.

Then Supreme Court Justice William Douglass suffered a right middle cerebral artery stroke, with left hemiparesis, left hemianesthesia, denial and neglect, like most such patients, he felt great and couldn't get back to the court. "Nothing wrong with me," he said, that is, *nothing wrong that he was aware of*. And the press ate it up. But this is obviously different.

How can we understand this? On the one hand we can cheer. "Isn't it terrific that these guys (these subjects, and most seriously injured Americans are male) are reacting so well?" But it is a bit disturbing, isn't it, that they feel better than able-bodied controls? What's going on?

The authors of the article thought that the greater the amount of spinal cord separated from the brain, the better the patient felt, but couldn't explain why. I can't either. They wondered if it had to do with sympathetic disconnection from the brain. I guess that parasympathetic disconnection would work just as well. My own thought is that there are hormones, peptides, growth factors, unrecognized chemicals, humors, if you will, that are secreted by non-central nervous system tissue controlled, indirectly from the brain via the spinal cord, and when they are disconnected they produce some rose-colored tint to life. It is not likely to produce an evolutionary advantage. Until the last century, anyone with a spinal cord transection died from infections, either in the skin or the bladder, or renal failure. This trick of the body must be unrelated to evolution.

Another question that arises, which the authors failed to ask is: how useful are the measures of quality of life, despite passing every statistical test in the books on validity? Would you ask your neurosurgery friend to transect your spinal cord to trade up to a better score on a quality of life scale?

—JOSEPH H. FRIEDMAN, MD

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# Osler and the Art of Procrastination

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**Hasty, precipitous judgment was once the symbol of flightiness,** pubescent exuberance or intemperate actions. Haste in every business, said Herodotus [c. 485 – 425 BCE], only brings failures. Haste, then, was deplored except in those rare instances of human passion as when the Scriptural Song of Solomon declared: “Make haste, my beloved, and be thou like a roe or to a young hart upon the mountains of spices.”

But somewhere along the line, a lack of haste underwent a tidal transformation and was labeled as procrastination, perhaps at the same time as the invention of such societal contrivances as deadlines, progress reports and production quotas. In a 1749 letter to an acquaintance, Lord Chesterfield [1694 – 1773] wrote the following oft-quoted manifesto: “No idleness, no laziness, no procrastination: never put off till tomorrow what you can do today.” The emerging Industrial Revolution in England had its battle anthem.

Slowly, ever so slowly, reflective judgment, once a hallmark of maturity and Socratic wisdom, was tainted as the outer face of lazy indecision and was further stigmatized as the thief of time. The waking moments of each day were now zealously counted and each minute was to be shielded against wanton wastage. Thomas de Quincey [1785 – 1859] wrote: “If once a man indulges himself in murder, very soon he comes to think little of robbing; and from robbing he comes next to drinking and Sabbath-breaking, and from that to incivility and procrastination.” Admittedly, de Quincey was exhibiting his customary perverse humor and hyperbole, but still he managed to equate procrastination with society’s most egregious crimes.

The word, procrastination, carries the unpleasant aroma of laziness, wasteful dawdling, indolence and dilatory dithering while the world impatiently yearns for forthright, assertive decision-making. Procrastination bespeaks of deliberate misuse of that precious gift called time. And thus, inevitably, procrastination has become the unyielding enemy of human progress. The humble Latin origins of the word, however, tell us that its original meaning and intent was less declaratory: the word was based upon the Latin, *crastinus*, meaning ‘of tomorrow’; and with the prefix, *pro-*, it was meant to yield a word meaning ‘to give unto tomorrow.’ [Procrastination should not be confused with the word, *procrastination* which means a breathless desire to visit a city south of Providence.]

Well, if procrastination is not naked laziness then surely it bespeaks of rank indecision. Indecision is one of those words that can signify something pejorative; or, on the other hand, can be the sign of patient wisdom. Time usually decides whether a person’s stance had been pathologically hesitant, vacillating and irresolute or, on the other hand, appropriately and wisely hesitant until further information had been gathered. The equation between resolution and irresolution is frequently the historic report-card on whether one is a Neville Chamberlain or a Winston Churchill.

And where, in the evolution of the practice of medicine, does decision and indecision play any role? Certainly in the maturation of the profession, from its activity, millennia ago, as

a subset of magic, through its struggle over the centuries to become, ultimately, a helpful calling. There had been nodal points in this plodding evolution when the profession had overreached itself – and thus did more harm than good in exploiting its meager and dubious armamentarium of interventions: blood-letting and agents fostering emesis and purging. After all, if one’s sole tool is a hammer, nails inevitably will look attractive.

The 18<sup>th</sup> Century physician was taught to intervene according to the precepts of Galen, who had lived 17 centuries before. Galenic medicine had supplanted an older paradigm which declared: Observe, use few medicines and encourage Nature in its healing paths.

A Canadian physician, William Osler [1849 – 1919], did much to bring merit and purpose to the act of indecision. Osler’s career in Canada, then the United States and finally as the Regius Professor of Medicine at Oxford University brought him to be the most revered and honored physician in the Western World. Much of his teaching, however, sounded regressive. For example, he deplored the fact that the desire to take medicine was the most outstanding feature that distinguished humans from animals. And since he had little faith in the great majority of medications available at the beginning of the 20<sup>th</sup> Century, he urged that they all be dumped into the Atlantic Ocean, noting in passing that the only harm would be to the fishes.

His advice to younger physicians, beyond his belief in pharmacologic nihilism, was to observe before you intervene. Certainly Osler recognized the existence of surgical emergencies, but the overwhelming causes for humans seeking medical aid, he believed, did not require precipitous action. It was Osler’s practice to stare at the patient at great length while listening carefully to his concerns, complaints and anxieties. It was not out of reticence that Osler was reluctant to employ one drug or another. Rather, he believed that they were essentially worthless if not actually harmful. And so Oslerian medicine was constructed, first, on the art of assertive bedside indecisiveness furthered by the belief that only rational research, not charisma, will eventually yield medications with proven merit. Osler died in 1919. In the three decades following his death, medicine added such proven medicines as insulin, antibiotics such as penicillin, a variety of therapeutic hormones such as ACTH, and a spectrum of objective biochemical and radiological diagnostic procedures to convert a noble profession into a scientific and competent enterprise.

– STANLEY M. ARONSON, MD

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Stanley M. Aronson, MD, has no financial interests to disclose.

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# Vascular Disease: Medical Therapy, Surgery and Interventional Technologies

Kenneth S. Korr, MD

**Thirty years since the advent of balloon coronary angioplasty** have seen dramatic advances in percutaneous interventional technologies, not just in the coronary vasculature, but also in other arterial territories affected by atherosclerosis. Multiple disciplines have developed expertise in the treatment of these disorders including interventional cardiologists, vascular surgeons, interventional radiologists, and vascular medicine specialists. An increased diagnostic awareness of the clinical manifestations of atherosclerotic vascular disease and major advances in the medical management of their common risk factors has had a major affect on the natural history of these disorders. Yet considerable controversy still exists surrounding the exact role and indication for medical vs revascularization therapies and whether percutaneous or surgery revascularization is equivalent or even preferable in any given vascular territory. In this issue of *Medicine & Health/Rhode Island* we attempt to clarify some the controversies surrounding four distinct vascular entities and provide the most current guidelines for the evaluation and management of these patients.

"Current Status of Drug-Eluting Coronary Stents" reviews the risks and benefits of drug eluting vs bare metal stents, and the importance of long-term dual anti-platelet therapy in reducing the incidence of subacute stent thrombosis. "An Update on Carotid Artery Stenosis" focuses on the importance of Duplex carotid ultrasound imaging for the diagnosis and serial follow-up of carotid artery disease, and reviews recent clinical trials comparing medical therapy, carotid endarterectomy and

carotid artery stenting. "Contemporary Management of Peripheral Arterial Disease (PAD)" examines the differential diagnosis of lower extremity discomfort, the importance of the ankle-brachial index as a screening test for PAD and an algorithm of different treatment modalities. "The Clinical and Therapeutic Implications of Renal Artery Stenosis" compares the distinctive clinical presentations of Atherosclerotic Renal Artery Stenosis and Fibromuscular Dysplasia and reviews the roles of medical therapy, and endovascular and surgical revascularization in the management of these patients.

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# An Update On the Management of Atherosclerotic Carotid Artery Disease

Steven Weinsier, MD, and Immad Sadiq, MD

**Stroke is the third leading cause of death** after heart disease and cancer and is the leading cause of long-term disability.<sup>1</sup> Of the approximately one million new strokes that occur each year, about 20% are due to carotid artery disease, and 5 to 12% of patients with new strokes have carotid vascular disease that would have been amenable to revascularization. The progression of carotid stenosis can be unpredictable; nearly 80% of strokes due to embolization in the carotid distribution may occur without warning.<sup>2</sup> The risk of stroke increases with age, so identifying those patients at risk is increasingly important as our population ages. The benefits of **carotid endarterectomy (CEA)** over medical management in stroke prevention have been clearly established for symptomatic patients with severe stenosis. **Carotid artery stenting (CAS)** is becoming an alternative to CEA in the management of carotid artery stenosis, particularly in higher-risk patients.

## PATIENT EVALUATION

Determining which patients to screen for carotid artery stenosis can be difficult. The evaluation for carotid artery disease begins with a detailed history and physical examination. The symptoms of carotid artery stenosis are typically produced by embolization causing **transient ischemic attacks (TIAs)** or strokes. Common presentations may include monocular blindness with a “shade” coming down over one eye (amaurosis fugax) or hemispheric symptoms like unilateral weakness, sensory loss, speech/language symptoms, or visual field disturbance. Symptoms such as these should trigger a prompt neurologic work-up including a non-invasive imaging study of the carotid arteries to evaluate for carotid artery stenosis.

Patients with asymptomatic carotid stenosis represent 80 to 90% of those undergoing carotid revascularization, so history alone is frequently insufficient in detecting carotid disease.<sup>2</sup> Some believe that auscultation for carotid bruits should be part of the routine physical examination. A bruit can be heard in about 4 to 5% of

patients ages 45 to 80 years old; and although not particularly sensitive or specific for identifying clinically significant stenosis or predicting cerebrovascular events, bruits are usually present if stenosis is greater than 75%.<sup>3</sup> They also correlate with increased cardiovascular events.<sup>4</sup> After detection of a bruit and confirmation of atherosclerotic carotid artery disease by imaging techniques, aggressive cardiovascular risk factor modification should be initiated. The natural history of carotid stenosis is one of gradual progression with the most important risk factors for rapid progression being stenosis greater than 50% and hypertension (systolic blood pressure greater than 160mmHg).<sup>5</sup>

There is no consensus on the routine screening of asymptomatic patients for carotid vascular disease. The only exception are patients with coronary artery disease prior to **coronary artery bypass graft surgery (CABG)**. The stroke risk of patients undergoing CABG is four times higher if there is a prior history of TIA or stroke, four times higher if they have a 50 to 99% carotid artery stenosis, and seven times higher if there is a carotid occlusion.<sup>6</sup> Screening for carotid artery stenosis is suggested in patients for planned CABG who have one of the following risk factors: age greater than 65, left main coronary artery

disease, a history of smoking, a history of a TIA or stroke, or a carotid bruit.<sup>7</sup>

## IMAGING

Of the many imaging modalities available to diagnose carotid artery disease, **carotid duplex ultrasound (CDU)** remains the initial test of choice and is the most common test for evaluating and following patients with carotid artery stenosis. (Table 1). CDU is inexpensive, widely available, reproducible, and highly accurate with excellent correlation to conventional angiography. One meta-analysis found a sensitivity and specificity of 98% and 88% respectively for detecting stenosis greater than 50% and a sensitivity and specificity of 90% and 94% respectively for detecting stenosis greater than 70%.<sup>8</sup> In most patients, ultrasound is able to visualize the carotid artery from the subclavian origin to the retro mandibular entrance into the skull. Although higher resolution imaging modalities are available, ultrasound has the advantage of giving functional data through Doppler flow measurements. The Doppler diagnostic criteria and stenosis measurement rely on peak systolic and end-diastolic velocities in the **internal carotid artery (ICA)** and **common carotid artery (CCA)**, spectral Doppler patterns, and ICA/CCA velocity ratios. B-mode imaging also provides

**Table 1: Indications for Carotid Duplex Ultrasonography**

### Neurologic Symptoms

- Stroke
- Transient ischemic attack (TIA)
- Amaurosis fugax – transient monocular blindness

### Asymptomatic

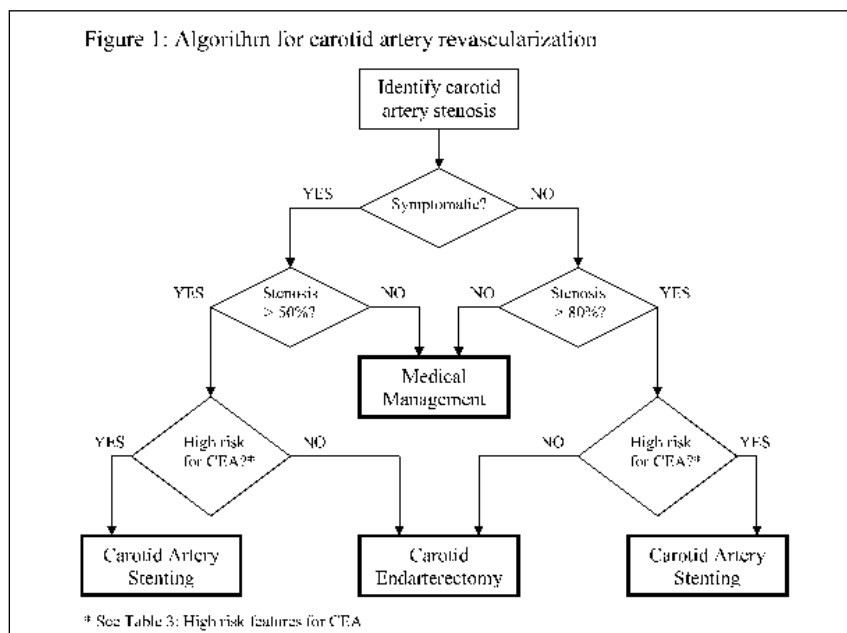
- Carotid bruit
- Pulsatile neck mass
- Patients undergoing CABG with one of the following risk factors
  - Age greater than 65
  - Left main coronary artery disease
  - History of smoking

### Known carotid stenosis based on prior testing

- Moderate carotid stenosis - follow every 6 months for a year and then annually if stable
- Post-CEA check at 1 month, 6 months, 1 year and then annually if stable
- Post-stenting check at 1 month, 6 months, 1 year and then annually if stable



Figure 1: Algorithm for carotid artery revascularization



useful information regarding plaque burden, morphology, ulceration, echolucency, or plaque mobility.

For most patients, CDU is adequate, but other imaging modalities may be helpful when CDU is inconclusive or carotid artery revascularization is considered. **Magnetic resonance angiography (MRA)** images correlate very well with conventional angiograms. The advantages of MRA include plaque characterization and visualization of intrathoracic and intracranial lesions not seen by Doppler. Some limitations of MRA include the inability to assess stented arteries due to artifact, overestimation of stenosis (subtotally occluded vessels may appear totally oc-

cluded), and cost. **Computerized tomographic angiography (CTA)** is better at assessing calcification and less prone than MRA to overestimate the severity of stenosis; however, the radiation exposure and risk of contrast-induced nephropathy is not inconsequential.

The need for revascularization is often assessed on non-invasive imaging studies only, and conventional angiography is reserved for patients undergoing revascularization.

## MEDICAL THERAPY

Most patients with carotid disease die of myocardial infarctions, not strokes, so when carotid artery disease is identified,

cardiovascular risk factor modification should be initiated. This should include medical therapy to limit the progression of atherosclerosis and decrease cardiovascular and cerebrovascular events. Modifiable risk factors (e.g., smoking, hypertension, dyslipidemia, and diabetes) need to be aggressively managed. Elevated blood pressure is linearly related to risk of stroke, and even a small reduction in blood pressure can result in significant risk reduction. Any effective antihypertensive medication will reduce stroke risk, but angiotensin converting enzyme inhibitors and angiotensin receptor blockers may have benefit beyond just their antihypertensive effects.<sup>2</sup> Dyslipidemia should be managed aggressively in patients with carotid vascular disease similarly to patients with coronary artery disease. Statins significantly reduce the risk of stroke in patients with known coronary disease and in patients with prior TIAs and strokes.<sup>9</sup>

All patients with carotid artery disease should be placed on antiplatelet therapy for the prevention of adverse cardiovascular events. Primary prevention trials have shown that aspirin reduces the risk of myocardial infarction in men, but does not significantly reduce the risk of ischemic stroke. One large primary prevention trial in women showed a reduction in the risk of stroke without affecting the risk of myocardial infarction.<sup>10</sup> Large stroke prevention trials support the use of aspirin for secondary prevention in patients with prior TIAs or strokes. In both symptomatic and asymptomatic patients, aspirin is the recom-

Table 2: Medical management and risk factor modification in patients with carotid artery stenosis

Risk Factor	Treatment	Comment
<b>1° prevention of stroke</b>	Aspirin	For primary prevention of stroke and MI
<b>Prior stroke or TIA</b>	Aspirin Extended-release dipyridamole plus aspirin (Aggrenox™) Clopidogrel Other	Found to be superior to aspirin alone in one trial  Similar efficacy to aspirin Aspirin plus clopidogrel, three drug therapy, and warfarin have been used, but are not supported by clinical trial data and may increase risk of bleeding
<b>Hypertension</b>	Goal BP <140/90 mmHg and BP <130/80 in diabetes and chronic kidney disease	Any antihypertensive regimen may be used, but ACE inhibitors and ARBs may have benefits beyond their antihypertensive effects
<b>Smoking</b>	Smoking cessation counseling	
<b>Lipids</b>	Lifestyle and/or medical therapy to reach a goal LDL <100 mg/dl (goal <70 mg/dl if high CAD risk)	Multiple studies have shown that statins reduce risk of stroke in patients with coronary artery disease and elevated total cholesterol or LDL
<b>Diabetes</b>	Goal HbA1c < 7%	



mended initial antiplatelet agent. The addition of dipyridamole to aspirin is not recommended for primary prevention, but dipyridamole should be added when symptoms occur while already on aspirin. One trial showed extended-release dipyridamole plus aspirin (Aggrenox®) to be superior to aspirin alone in preventing the combined outcome of myocardial infarction, stroke, or vascular death in patients with prior neurologic events.<sup>11</sup> Thienopyridines have not been evaluated for primary prevention, but clopidogrel alone is similar to aspirin in secondary prevention. Aspirin plus clopidogrel have no advantage over either drug alone for secondary prevention and in one randomized trial were associated with a significant increase in bleeding risk.

Recurrent events may occur despite adequate anti-platelet therapy. The use of warfarin in such patients is controversial at best. Warfarin is reserved for patients with obvious or suspected thrombus in the carotid arteries with some degree of patency on imaging or in cases of a suspected cardio-embolic or aorto-embolic etiology. Otherwise, it is not indicated for the treatment of carotid artery disease. The mainstay of therapy in patients with symptomatic atherosclerotic carotid artery disease is revascularization.

## REVASCULARIZATION

After carotid atherosclerotic disease is detected, the goal is to minimize risk of stroke or death. To determine whether revascularization is an option for a patient, the risk of stroke over time should be weighed against the risk of a procedure-related major complication (myocardial infarction, stroke, or death). The major determinants of risk of stroke or death in patients with carotid stenosis are symptom status and degree of stenosis. For less than 50% stenosis, revascularization provides no benefit over medical therapy in either symptomatic or asymptomatic patients. As the degree of stenosis increases, the risk of stroke increases and the benefit of revascularization may outweigh the risk of the procedure. Recent guidelines from American College of Cardiology and the American Heart Association for the prevention of stroke recommend revascularization in symptomatic patients with greater than 50% stenosis if the risk of procedure-related major complication(s) is less than 6%. In asymptomatic patients with greater than 80%

**Table 3: High risk features for CEA**

### Significant comorbidities

- Congestive Heart failure class III-IV
- Left Ventricular Ejection Fraction < 30%
- Unstable angina
- Recent myocardial infarction
- Untreated left main or three-vessel coronary artery disease
- Awaiting heart surgery
- Severe chronic lung disease

### Anatomical risk factors

- Contralateral carotid occlusion
- Previous CEA with recurrent stenosis
- Prior radiation treatment to the neck
- High or low carotid bifurcation
- Tracheostomy

stenosis the threshold of acceptable risk is higher; a peri-operative complication rate of 3% or less is considered appropriate.<sup>12</sup>

**Carotid endarterectomy (CEA)** was first performed in the 1950s. In the late 1980s and 1990s, randomized clinical trials comparing CEA to medical therapy clearly established a role for revascularization in the prevention of strokes in patients with carotid bifurcation stenosis.<sup>2</sup> A pooled analysis looking at stroke or death found significant benefit of CEA compared to aspirin after 5 years of follow up in symptomatic patients with 50-99% carotid stenosis. The relative risk reduction in ipsilateral stroke was 48% ( $p=0.00001$ ) if the stenosis was 70-99% and 28% ( $p=0.002$ ) with a stenosis of 50-69%. No benefit was seen when the stenosis is less than 50%.

In asymptomatic patients, the benefit was limited to men, younger patients, and stenosis greater than 60%.<sup>13</sup> In contemporary practice asymptomatic patients are considered for CEA if the stenosis is greater than or equal to 80%.

Although CEA is very effective, like any other surgery it has limitations. Some patients may not be candidates for this surgery either due to anatomical reasons or other risks specifically related to the surgery. (Table 3). In most of these patients carotid artery stenting may be a feasible alternative. This less invasive approach is performed under local anesthesia.

The recent SAPHIRE trial compared CAS and CEA in patients at high risk for stroke. Symptomatic patients with greater than 50% stenosis or asymptomatic patients with greater than 80% stenosis were included. The 30 day incidence of myocardial infarction, stroke, or death was

4.8% after CAS and 9.8% after CEA,  $p=0.09$ . The primary end point of myocardial infarction, stroke or death between 31 days and 1 year occurred in 12.2% after CAS and 20.1% after CEA,  $p=0.053$  for superiority. In asymptomatic high-risk patients, CAS significantly reduced the incidence the primary end-point. CEA was associated with a higher incidence of cranial nerve palsy and target-lesion revascularization at one year. Death, stroke and target-lesion revascularization were similar between the groups at three years.<sup>17</sup>

## GUIDELINES

The most recent American Heart Association/American Stroke Association (AHA/ASA) guidelines (2006) recommend CEA in symptomatic patients (TIA or stroke within 6 months) with 50 to 99% stenosis if the risk of perioperative morbidity and mortality is less than 6% (class I, Level of Evidence A).<sup>12</sup> In asymptomatic patients, guidelines recommend CEA for 60 to 99% if the risk of perioperative morbidity and mortality is less than 3% although revascularization is typically reserved for patient with greater than 80% stenosis. In addition, the American Academy of Neurology recommends that eligible patients should be between 40 to 75 years old and have a life expectancy of at least five years.<sup>18</sup> The guidelines for CAS are less clear. The AHA/ASA guidelines state that in patients with carotid stenosis greater than 70% in whom stenosis is difficult to access surgically, medical conditions increase the risk of surgery, or other conditions such as radiation to the neck or restenosis after CEA, CAS is not inferior to CEA and may be considered (Class IIB, Level of Evidence B). CAS is also reasonable when performed by



# Contemporary Management of Peripheral Arterial Disease – A Review

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## “Peripheral arterial disease” (PAD)

refers to disease of the aorta and its branches, excluding the coronary and cerebral arteries. This review will focus primarily on the recognition, evaluation and management of atherosclerotic lower extremity arterial disease, an important subset of PAD. In 2005, Hirsch et al published the most recent ACC/AHA guidelines for the management of PAD.<sup>1</sup> This important document should serve as a helpful reference for all clinicians. This review will attempt to highlight the most important recommendations from this document.

## EPIDEMIOLOGY

The prevalence of PAD rises with advancing age, increasing sharply after age 40. In the **National Health and Nutrition Examination Survey (NHANES)**, the prevalence was 0.9% between the ages of 40-49, 2.5% between the ages of 50-59, 4.7% between the ages of 60-69, and 14.5% above 70.<sup>2</sup> Overall prevalence in the study was

4.3% (over 5 million adults in the United States). The prevalence is likely to rise as the proportion of elderly patients in the population increases. Also, in an age and gender-adjusted analysis, patients of non-Hispanic black ethnicity were approximately 3 times more likely to have PAD than their non-Hispanic white counterparts.

## RISK FACTORS

The major risk factors for PAD are: cigarette smoking, diabetes mellitus, hypertension, dyslipidemia, renal insufficiency, family history and hyperhomocysteinemia. Age greater than 70 years, post-menopausal state and non-hispanic black ethnicity are also considered risk factors for PAD, as well as for concomitant coronary artery and cerebrovascular disease. Indeed, these diseases very frequently coexist. Management of all relevant risk factors is a critical component in the optimal care for patients with PAD.

## PRESENTING SIGNS AND SYMPTOMS

The vast majority of PAD is asymptomatic. This disease is frequently overlooked, and often goes undiagnosed. Among patients diagnosed with PAD, 20-50% are asymptomatic at the time of their initial diagnosis. These patients deny ischemic leg symptoms, but often report significant functional impairment. 40-50% of patients with PAD present with atypical leg pain. 10-35% of patients present with typical claudication, which usually reflects the presence of advanced disease. 1-2% of PAD patients present with critical limb ischemia, defined as the presence of ischemic pain at rest, ulceration and/or gangrene. This small subset is at very high risk of morbidity and mortality within the next 6 months. Another common presentation is Leriche's syndrome, related to bilateral occlusive aorto-iliac disease. (Image 1) This syndrome consists of buttock and hip claudication, which may be accompanied by weakness in these muscle groups when walking. In men, this syndrome almost always leads to erectile dysfunction. With sufficient vigilance on the part of health care providers, many PAD patients can be identified before the development of any symptoms. This early recognition will allow many patients to avoid the more severe morbidity associated with advanced PAD.

## DIAGNOSIS

All patients with risk factors for PAD should undergo a thorough vascular assessment. This includes taking a careful history and review of systems, focusing on the presence of intermittent claudication, ischemic rest pain, non-healing wounds and any functional limitations. These components of a thorough review of systems are particularly important in patients greater than 50 years of age with cardiovascular risk factors, and in all individuals 70 years of age or older. The classic description of intermittent claudication is that of reproducible exertional discomfort or weakness in the buttock,



Image 1: Aorto-iliac occlusive disease, in a patient with Leriche's syndrome.

**Table #1: Differential Diagnosis of Lower Extremity Discomfort**

Cause	Description	Effect of Activity	Other Features
<b>Vascular</b>			
Intermittent Claudication (Arterial)	Discomfort or weakness in the buttocks, hip, thigh, calf or foot	Provoked by a predictable amount of exertion, alleviated promptly with rest (usually within 5 minutes)	Symptoms typically occur one segment below the level of stenosis
Venous Claudication	Tightness or squeezing sensation, usually in the calf	Worsens with walking, gradually resolves with rest; relief often accelerated with limb elevation	Signs of DVT and/or chronic venous insufficiency may be present
Lymphedema	Tension, pressure, non-pitting edema within calf, foot and toes	Present at rest and with activity	"Peau d'orange" appearance of thickened skin
<b>Spinal</b>			
Spinal stenosis	Weakness, pain and/or sensory changes	Worse upon standing or walking, may be positional, may be alleviated by sitting, flexion at the waist or squatting	Usually related to arthritis of the spine impinging on the spinal column; may have history of back pain
Radiculopathy	Sharp or burning pain along the posterior or lateral aspect of the leg, often with associated tingling sensation	Worsens with postural changes, cough, sneezing, Valsalva maneuver, not relieved with rest; may be relieved by changes in posture	May be related to degenerative spinal arthritis or herniated nucleus pulposus
<b>Musculoskeletal</b>			
Arthritis	Aching discomfort, often continuous; severity related to intensity of activity	Worse with activity and weight-bearing, often not relieved by rest	Few symptoms in non-weight-bearing activities; symptoms may be sensitive to changes in weather
Chronic Compartment Syndrome	Aching or cramping pain in the area of the affected compartment	Episodic, usually occurring following strenuous activity	Compartment pressure > 20 mmHg confirms Dx; Treatment is surgical
Baker's Cyst	Tenderness and swelling in the popliteal fossa	Worsens with activity, not relieved with rest	Signs of inflammation in the popliteal fossa
<b>Other</b>			
Benign Nocturnal Cramps	Cramping pain, usually in calves, most often at night	Occurs at rest, usually resolves spontaneously	Very common, usually idiopathic; may be related to electrolyte disturbances

A detailed physical examination should also be performed, including a careful evaluation of pulses and an evaluation of the legs and feet. PAD may present with a unilateral cool extremity with significant pallor. Poor wound healing, hair loss, and skin atrophy may occur distal to the point of occlusion. Auscultation of the corresponding arteries should be performed, to identify and localize any bruits.

thigh or calf muscles, which resolves promptly with rest. The amount of exercise which produces symptoms is usually reproducible. Atypical presentations are common, and differentiating claudication from other causes of lower extremity pain can be challenging. (Table #1)

## DIAGNOSTIC TESTING

The ankle-brachial index (ABI) is a simple, easily reproducible and widely available test for the diagnosis of PAD. The ABI is a ratio of the blood pressure measured in the ankle, to the blood pressure measured in the brachial artery. This test is usually accompanied by pulse volume recording (PVR) or by assessing Doppler waveforms at sequential locations along the extremities. (Image #2) These techniques greatly enhance the

diagnostic yield of the ABI study by allowing for the determination of the approximate level of disease. This may help differentiate "inflow" disease, (referring to disease of the aorta or iliac arteries), from disease in more distal arteries. The use of PVR or Doppler techniques may also allow for an estimate of the severity of disease. Finally, PVR may assist with diagnosing PAD in patients with stiff, non-compressible vessels, in whom the ABI may be falsely elevated.

The ABI (with PVR or Doppler) should be performed in all patients with claudication or other symptoms suggesting PAD.

This test is also helpful in establishing the initial diagnosis of patients with asymptomatic PAD. The American Diabetes Association, in a consensus statement

from 2004<sup>4</sup>, recommends obtaining screening ABI in diabetic patients greater than 50 years of age. If normal, they recommend repeating the test every 5 years. They also recommend obtaining ABI in diabetic patients younger than age 50 who have other PAD risk factors (e.g. smoking, hypertension, hyperlipidemia, or duration of diabetes greater than 10 years)

In patients with high risk features for PAD, but with a normal or near-normal resting ABI (and PVR or Doppler), additional diagnostic yield can be obtained via measurement of ABI following exercise. (Figure #1) Post-exercise ABI may also help differentiate true claudication from pseudoclaudication, and also helps objectively document the magnitude of any functional limitations.

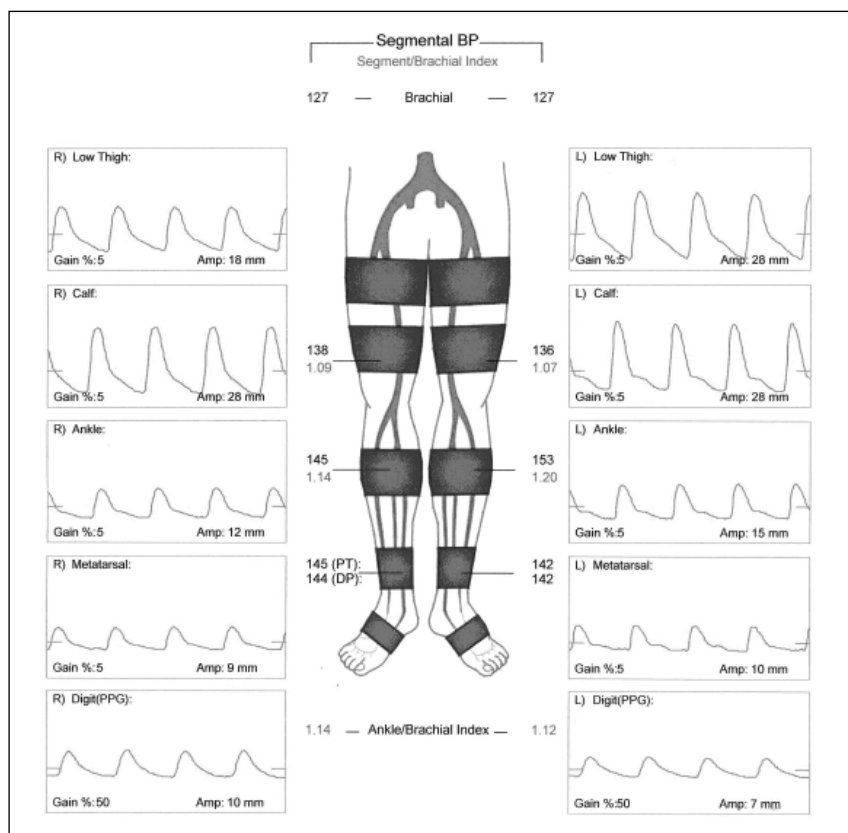


Image #2: Ankle-brachial index (ABI) with pulse volume recording (PVR).

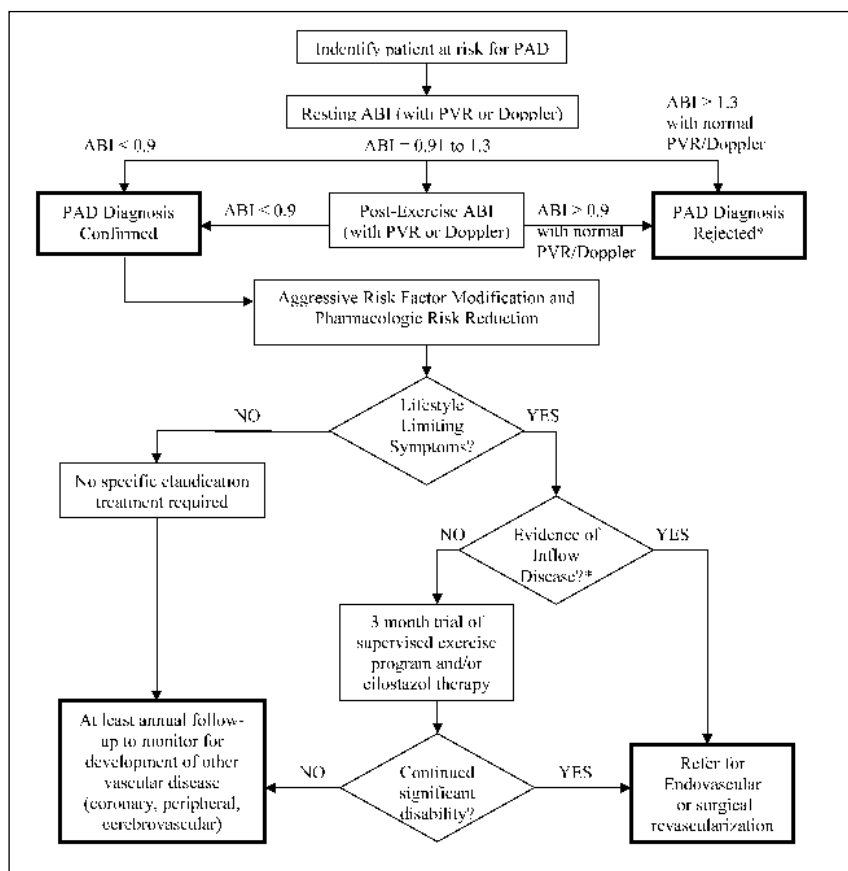


Figure 1: Algorithm for the initial evaluation and management of PAD

For some patients with a high likelihood of PAD, but in whom ABI and post-exercise ABI (with PVR or Doppler) are normal, more advanced imaging techniques may be necessary to allow for a more thorough evaluation for PAD.

Other advanced imaging techniques such as Duplex ultrasonography, **Magnetic resonance angiography (MRA)**, **Computed tomography angiography (CTA)** and contrast angiography can be very useful for a detailed evaluation of PAD patients. Usually such studies would be ordered by a vascular medicine or surgery specialist, after the initial diagnosis has been established by a primary care physician.

Duplex ultrasonography provide a detailed assessment of PAD, including determining the precise location and severity of any PAD. It is helpful in following patients for progression of disease, and may be helpful in assessing patients with stiff, non-compressible vessels. This technique is often useful in providing quantitative data following revascularization procedures. Duplex ultrasonography is limiting in its ability to assess very proximal vessels, and may be limited by dense arterial calcifications.

MRA, using Gadolinium enhancement is very useful in determining the details of peripheral arterial anatomy including the degree and severity of obstruction, and may assist in selecting patients who may benefit from revascularization. CTA may have benefits similar to that of MRA, particularly in patients with contraindications to MRA. Contrast angiography is still considered to gold standard for assessment of PAD, and is typically reserved for patients undergoing revascularization procedures.

## MANAGEMENT

All PAD patients should undergo aggressive risk factor and lifestyle modification, including smoking cessation, an exercise program, as well as careful control of diabetes, hypertension and dyslipidemia.

In the absence of contraindications, all PAD patients (regardless of the presence or absence of symptoms) should receive anti-platelet therapy for primary prevention of adverse cardiovascular events including myocardial infarction (MI), stroke and vascular death. Aspirin

(75 to 325mg daily) is recommended in this setting, and has been shown to reduce adverse cardiovascular events by up to 32% in PAD patients. Clopidogrel (75mg daily) is considered a reasonable alternative therapy in this setting, particularly in patients with symptomatic PAD or who are unable to tolerate aspirin. No supports the use of a combination of aspirin and clopidogrel in this setting. Warfarin therapy is not indicated for the reduction of adverse cardiovascular events in PAD patients.

Cilostazol (100mg twice daily) is an effective agent for improving symptoms and increasing walking distance in patients with PAD and intermittent claudication. Although no trials have found a significant increase in major cardiovascular events with this agent, it is contraindicated in patients with heart failure. Pentoxifylline (400mg three times daily) may be considered as a second-line agent to Cilostazol, but the clinical effectiveness of this agent is not well established.

Exercise rehabilitation has been well documented to reduce symptoms of claudication. Multiple trials have shown that exercise increases maximum walking time and peak oxygen consumption. Some studies have also suggested that exercise rehabilitation improves survival in PAD patients. Stable PAD patients should be referred to an exercise rehabilitation program before being considered for any revascularization procedures.

Revascularization should be reserved for patients with lifestyle-limiting symptoms related to their PAD, a reasonable likelihood of success of the revascularization procedure, and preferably a low risk associated with such a procedure. There are a wide variety of procedures which have been developed to establish revascularization to the lower extremities. In recent years, percutaneous options have begun to supplant many surgical options. However, in some cases, surgical revascularization remains the best options to obtain a satisfactory revascularization.

Critical limb ischemia is a subset of PAD which is characterized by particularly high morbidity and mortality. This is usually defined as the presence of ischemic rest pain, ulceration or gangrene. These patients usually present with resting leg pain which is worse when in a supine position, improving somewhat when the limb is maintained in a dependent position. If left untreated, a large proportion of these patients will require amputation within 6 months. If the clinical course of these patients suggests rapid progression, an expedited evaluation and prompt revascularization should be considered.

Acute limb ischemia represents another subset of PAD with high morbidity and mortality. This occurs when a sudden decrease in limb perfusion threatens limb viability. Patients who present with evidence of acute limb ischemia who are determined to have a salvageable limb should undergo an emergent evaluation to determine the anatomic level of obstruction, and should undergo a prompt revascularization procedure.

## OUTCOMES

PAD is a cause of significant morbidity and mortality. The PAD leads directly to major functional impairments and decreased quality of life. The diffuse atherosclerotic disease that accompanies PAD also leads to significant morbidity and mortality from myocardial infarction and stroke.

## CONCLUSIONS

PAD illness places a large financial burden on the healthcare system, and will increase in prevalence with the aging population in the United States. The prompt recognition, diagnosis and management of PAD should improve the quality of life of patients with PAD and reduced the overall morbidity and mortality of this serious entity.

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# Status of Drug-Eluting Coronary Stents

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## EVOLUTION OF PERCUTANEOUS CORONARY INTERVENTIONAL TECHNOLOGIES

The introduction of **percutaneous transluminal coronary angioplasty (PTCA)** in the late 1970s provided a new, non-surgical approach to the treatment of selected patients with symptomatic coronary artery disease. Throughout the next decade, adjunctive technologies, including rotational and directional atherectomy, expanded the range of coronary lesions which could be approached percutaneously. PTCA continued to be limited, however, by the problems of abrupt vessel closure and late restenosis.

Abrupt vessel closure occurred as a consequence of large intimal dissections, vasospasm and thrombus formation and usually happened during or immediately after the procedure. As a consequence, surgical backup was required for all PTCA procedures and the incidence of emergency CABG, acute myocardial infarction and death was about 1.0%.<sup>1</sup>

Late restenosis tended to occur about 3-6 months after the procedure and was usually heralded by the recurrence of anginal symptoms. Restenosis was a significant problem with 40% of patients demonstrating angiographic re-narrowing (of  $\geq 50\%$  of the vessel diameter), and 20 to 30% of patients requiring repeat revascularization within the year. Intravascular ultrasound studies demonstrated a dual mechanism for restenosis, including components of elastic recoil of the vessel wall and intimal hyperplasia of the underlying smooth muscle cells of the medial layer.<sup>1</sup>

## CORONARY STENTING

Coronary stents were developed in the late 1980s to improve the results of PTCA and better manage the problems of abrupt vessel closure and restenosis. Stents produced better immediate in-lab results with less residual stenosis, and more importantly the ability to stabilize dissection flaps, resulting in significantly lower rates of emergency CABG, periprocedural MI and death (0.1%). In

addition, stents virtually eliminated the elastic recoil component of restenosis, allowing for a greater acute luminal gain and reducing the overall incidence of restenosis. Following **Food and Drug Administration (FDA)** approval of **bare metal stents (BMS)** in 1994, there was a significant reduction in the rate of angiographic restenosis (20-30%) and in the frequency of target lesion revascularization (10-15%).<sup>1</sup>

The improved and very predictable clinical and angiographic success of BMS expanded the scope of **percutaneous coronary interventions (PCI)** to multiple lesions, more complex coronary anatomy and to patients with acute myocardial infarction. Clinical restenosis after bare-metal stenting continued to occur within the first 12 months and was related predominantly to intimal hyperplasia. Increased risk factors for restenosis included longer lesion segments ( $>20\text{mm}$ ) and smaller vessel diameters ( $<2.5\text{mm}$ ) frequently found in women and diabetics. Recurrent ischemia more than a year after stenting was much more likely to be due to new or progressive disease at another site rather than to restenosis.<sup>2</sup>

The significant advantages of stenting, however, were associated with a new and previously unrecognized clinical event, "sub-acute" vessel closure, related to thrombus formation at the stent site, and occurring several days to weeks after the procedure. The initial incidence of "sub-acute thrombosis" was not insignificant—ranging from 0.5 – 2%.

Pioneering work from Antonio Colombo and others demonstrated that the risk of sub-acute stent thrombosis could be minimized by optimal stent deployment with high pressure balloon inflations. In addition, large multi-center trials (STARS) of different post-stent anticoagulation regimens demonstrated that aspirin plus a thienopyridine—"dual anti-platelet therapy" (DAT)—substantially reduced the risk of sub-acute thrombosis to ~ 0.5%.

Continued improvements in stent design, allowing for greater flexibility and improved access to more distal stenotic

lesions, combined with the efficacy of DAT, propelled bare metal stents into the forefront of percutaneous coronary intervention. By 2001, almost two million coronary interventions were performed worldwide, with an estimated annual increase of 8%.

## DRUG-ELUTING STENTS

Restenosis rates, however, remained in the 10 – 15% range, and in-stent restenosis was particularly difficult to treat. Initial forays with brachytherapy (localized radiation therapy) for in-stent restenosis demonstrated some clinical benefit compared to PTCA alone but the technique was clinically cumbersome, requiring the collaboration of interventionalists, radiation oncologists and radiation physicists, and necessitating life-long DAT due to the risk of sub-acute stent thrombosis at the irradiated site.

Ongoing research to reduce the incidence of in-stent restenosis ultimately led to the development of "drug-eluting" stents (DES). DES consist of a standard stainless steel stent backbone, a polymer coating, and an anti-inflammatory drug affixed to the polymer and gradually released or "eluted" into the surrounding tissues over a period of several weeks to modify the local healing response.

Clinical trials of **sirolimus-eluting stents (SES)** and **paclitaxel-eluting stents (PES)** demonstrated a marked reduction in the incidence of restenosis and target lesion revascularization compared to bare metal stents. The benefit of drug-eluting stents compared to BMS resulted from the inhibition of neointimal hyperplasia, leading to a lesser degree of late in-stent lumen loss at six to twelve months. In fact, long-term follow up studies with intra-vascular ultrasound have shown that the neointimal suppression following DES placement may be present as long as two years following stent deployment.<sup>3,4</sup>

Based on the significant reduction in restenosis rates with DES, in 2003 and 2004 the FDA approved two drug-eluting stents for routine clinical use in selected patients.



## CLINICAL TRIALS OF DES

A 2006 meta-analysis of 19 clinical trials with 7060 patients (the three largest trials were SIRIUS, TAXUS IV, and TAXUS V) concluded that, compared to BMS, DES conferred a significant reduction in both angiographic restenosis as well as in target vessel revascularization. In particular, target lesion revascularization was reduced from 16.6 % (BMS) to 6.2% (DES). Despite the reduction in restenosis, however, there was no significant difference in either one-year mortality or myocardial infarction, consistent with previous findings that the majority of restenosis patients present with recurrent symptoms of angina, as opposed to acute myocardial infarction or sudden cardiac death.<sup>5</sup>

As a result of the marked reduction in restenosis and target vessel revascularization, DES usage, particularly in the United States, grew exponentially from 2004 through 2006, accounting for almost 90% of all stent implantations.

In the fall of 2006 the long-term safety of DES came into question with reports in the European literature of an increased incidence of “late” stent thrombosis.

## TIMING OF STENT THROMBOSIS

Stent thrombosis can occur “acutely” (within 24 hours), “sub-acutely” (between one and 30 days), “late” (from 30 days to one year), or “very late” (more than one year) after stent placement. Stent thrombosis within the first year following implantation appears to occur with equal frequency in patients with BMS or DES, as long as patients with DES are treated with the recommended duration of dual anti-platelet therapy.

Two studies published in 2006—one a small randomized trial of BMS versus DES, and the other a meta-analysis of previously published DES trials—raised concerns of an increased incidence of “very late” stent thrombosis in DES patients, which caused an uproar in the lay press. [In both studies, the protocols called for discontinuation of the thienopyridine after six months of DAT therapy.] These concerns led to intense scrutiny and retrospective examination of the use of drug-eluting stents. Risk factors predisposing to a higher rate of DES thrombosis were more frequently related to off-label usage,

including longer stented segments, complex bifurcation lesions, and smaller vessel diameters. Technical and clinical factors were also identified and included suboptimal stent expansion and inadequate stent strut apposition, diabetes mellitus, chronic renal insufficiency, and resistance to anti-platelet agents. Perhaps most importantly, premature discontinuation of dual anti-platelet therapy was identified as one of the major risk factors for late stent thrombosis.<sup>5,6</sup>

In 2007, several larger studies re-examined the risk of late thrombosis in DES-treated patients. In one study, angiographically proven stent thrombosis occurred in 152 of 8146 patients (1.9%) who received DES for both on and off-label indications during up to three years (mean 1.73 years) of follow up. “Sub-acute” stent thrombosis was seen in 91 patients (1.1 %), with a median timing of four days. This figure alone was higher than the historically reported rate of 0.5 – 1.0% seen in BMS patients who were treated with DAT therapy. In addition, both “late” and “very late” thrombosis were seen in an additional 61 patients (0.75%), and events continued at a steady rate of 0.6% per year during the first three years. The estimated cumulative incidence of stent thrombosis was 2.9% at three years.<sup>4</sup>

In a series of 38 cases of stent thrombosis occurring after DES implantation in 2974 consecutive patients, stent thrombosis was significantly more common following premature discontinuation of clopidogrel (37% of patients with stent thrombosis versus 11% in those without stent thrombosis). The mean duration between cessation of clopidogrel and stent thrombosis was nine days in patients with sub-acute stent thrombosis and 153 days in those with late stent thrombosis. A similar analysis from Rotterdam described a cohort of 2,006 patients who received DES, and in whom 8 cases of late stent thrombosis occurred (0.4%). All 8 patients developed late stent thrombosis following discontinuation of clopidogrel (5 continued on aspirin monotherapy).<sup>7,8</sup>

## “OFF-LABEL” USAGE OF STENTS

The FDA approved DES for “stable patients, without serious co-morbidities, who have newly diagnosed lesions, less than 28 to 30 mm in length, greater than

2.5 mm in vessel diameter, and not involving a major vessel bifurcation”. Less is known about the risk for patients in whom stents are placed for off-label indications, which may account for as many as 50-60% of all stent procedures in this country. Off-label indications include patients with complex anatomy (vessels with high risk features including multiple lesions, small vessel diameter, long lesion segments, ostial and bifurcation lesions, restenotic lesions and saphenous vein graft lesions) and patients with acute MI. Preliminary data from the DEScover and EVENT registries suggested worse cardiovascular outcomes in this setting. However, a retrospective analysis in the *New England Journal of Medicine* evaluated adverse events in 6551 patients enrolled in the NHLBI Dynamic Registry. This study concluded that the use of drug-eluting stents was not associated with an increased risk of death or myocardial infarction in patients with off-label indications but was associated with a lower rate of repeat revascularization at 1 year, as compared with bare-metal stents. These findings support the use of drug-eluting stents for off-label indications, based on a one-year duration of follow-up.<sup>9,10,11</sup>

## PATHOGENESIS OF DES THROMBOSIS

An important explanation for the increased risk of thrombosis in DES compared to BMS patients is delayed endothelial healing, particularly incomplete neointimal coverage of the stent struts. (Figure 1) Delayed neointimal coverage was confirmed in a long-term study of 17 DES and 11 BMS patients in whom angiography was performed at 4, 10, and 21 months. Neointimal coverage was complete in all but one of the BMS patients at 3.6 months while the majority of DES patients still had incomplete neointimal coverage at 21 months. Similarly, an autopsy series comparing 23 DES with 25 BMS patients with evidence of late stent thrombosis (>30days) demonstrated inadequate or absent endothelialization of the stent struts in 14 of the 23 DES patients but in none of the BMS patients. In addition, some DES patients demonstrated areas of local inflammation suggesting the possibility of an additional hypersensitivity reaction.<sup>12,13</sup>

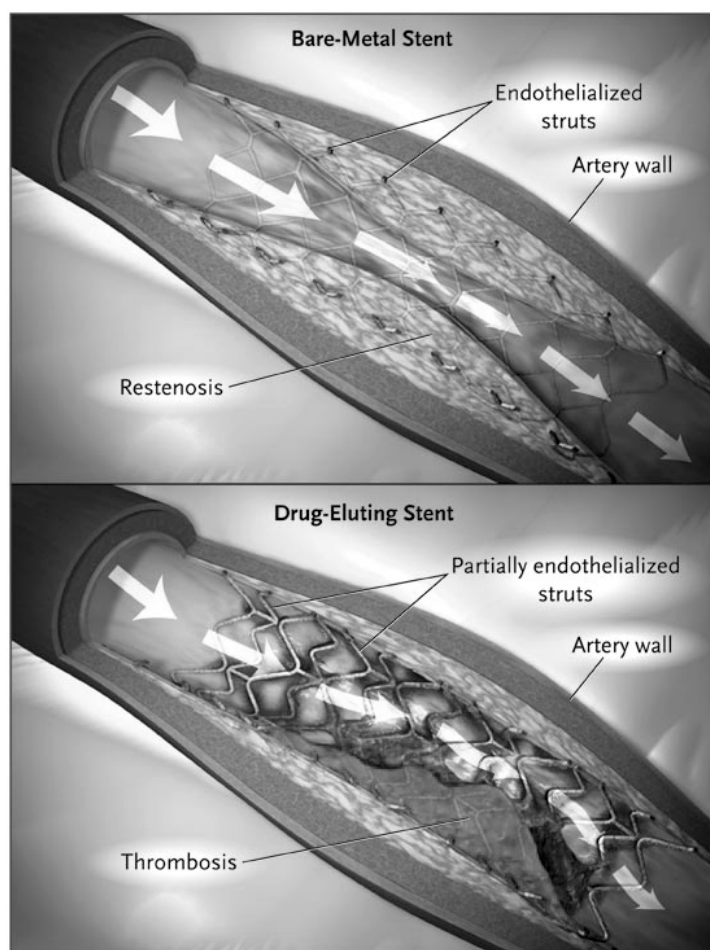


Figure 1. Pathophysiology of restenosis and stent thrombosis (with permission from the NEJM). This figure illustrates the potential complications of coronary stenting: restenosis in a bare-metal stent and late thrombosis in a drug-eluting stent.

Thus, long-term follow-up of DES patients indicates a short term advantage compared to BMS due to a significant reduction in one year re-stenosis events, but an ongoing, low-level risk of late stent thrombosis which may be reduced by optimal patient selection (Table 1) and a longer duration of dual-anti-platelet therapy.

### CURRENT RECOMMENDATIONS FOR DURATION OF DAT

The initial FDA and manufacturer's recommendations for the prevention of stent thrombosis after coronary stent implantation required dual anti-platelet therapy with 325mg of ASA and 75mg of clopidogrel for 1 month after BMS implantation, 3 months after sirolimus DES implantation and 6 months after paclitaxel DES implantation. These recommendations were based on the anti-

platelet regimens used in the initial pre-market trials that led to FDA approval for DES (i.e. low-risk patients with low-risk lesions).<sup>14</sup>

The current clinical practice has been to continue DAT for a longer period for DES patients, especially for procedures performed for off-label indications, including higher-risk lesions, higher risk patients and multiple vessels

in a single patient. An updated FDA statement on duration of DAT after DES noted that while the "optimal duration of antiplatelet therapy ...is unknown", DAT therapy "should be extended to 12 months in patients at a low risk of bleeding". In our clinical practice we have opted to extend the duration of DAT therapy in DES patients to a minimum of one to two years in all patients, and to continue DAT indefinitely in patients at higher risk of developing late thrombosis (e.g. diabetics and patients with complex lesions or multiple stents), unless bleeding arises.

Long-term therapy with DAT is not without risk. Clearly either aspirin or clopidogrel therapy alone increases the risk of bleeding compared with placebo. And when clopidogrel is combined with aspirin and administered for prolonged duration (up to 28 months), randomized trials have demonstrated a small increase in major bleeding (ranging from 0.4% to 1.0%), compared with aspirin alone.<sup>15</sup>

### CONSEQUENCES OF STENT THROMBOSIS

Sub-acute stent thrombosis carries a high risk of significant morbidity and mortality. In some series mortality rates have been as high as 45%; hence, compliance with the recommended post-stent anti-platelet regimen is crucial.

Premature cessation of thienopyridine drugs may occur for several reasons. The cost of clopidogrel (approximately \$4 per day) has been cited as one reason patients discontinue (or fail to renew) their therapy. In an analysis from the PREMIER registry, factors associated with premature discontinuation of thienopyridine therapy included: older age, not having completed a high school education, not being married, not receiving discharge instructions for medi-

Table 1. Predictors of Drug-Eluting Stent Thrombosis (adapted from Grines, CL et al: *Circulation* 2007; 115: 813-8)

#### CLINICAL

Advanced age  
Acute coronary syndrome  
Diabetes mellitus  
Low ejection fraction  
Prior restenosis or brachytherapy  
Renal failure

#### ANGIOGRAPHIC

Long stented segment  
Multiple lesions  
Overlapping stents  
Ostial or bifurcation lesions  
Small vessel diameter  
Suboptimal stent results

cation use, not being referred for cardiac rehabilitation, greater likelihood of having preexistent cardiovascular disease or anemia, and history of avoiding health care because of cost. The authors concluded that “additional patient education about the rationale for and importance of continuing thienopyridine treatment may be needed—particularly for patients with less formal education.”<sup>16</sup>

Concerned about excessive bleeding, physicians, dentists and other healthcare providers who are planning an invasive or surgical procedure often stop anti-platelet therapy. Unfortunately, many patients are instructed to stop “blood thinners” without distinction be-

tween warfarin and anti-platelet agents and without consideration of the rationale for their use. Many procedures (e.g., minor surgery, dental cleaning, and dental extraction) can usually be performed at no or only minor risk of bleeding with patients on anti-platelet therapy, or could be delayed until the prescribed anti-platelet regimen has been completed.

### DENTAL PROCEDURES IN PATIENTS WHO HAVE RECEIVED DES

Although dental practitioners have long been concerned about the possibility of prolonged bleeding during and after invasive dental procedures on patients receiving anti-platelet drugs, a recent

prospective study of single tooth extractions on patients randomized to aspirin versus a placebo failed to show a statistically significant difference in postoperative bleeding. Although there are no prospective studies of invasive dental procedures on patients taking a thienopyridine alone or in combination with aspirin, there are also no well-documented cases of clinically significant bleeding after dental procedures, including multiple dental extractions. Given the relative ease with which the incidence and severity of oral bleeding can be reduced with local measures during surgery (e.g. absorbable gelatin sponge and sutures) and the unlikely occurrence of bleeding once an initial clot has formed, there is little or no indication to interrupt anti-platelet therapy for dental procedures.

### CONSENSUS STATEMENT FROM THE AHA/ACC/SCAI/ACS AND ADA

In February 2007, a science advisory and consensus statement was published in *Circulation* aimed at prevention of thrombotic events in patients who had received coronary stents. A summary of their recommendations follows:<sup>17</sup>

- 1) Discuss the requirement for anti-platelet drugs with patients prior to stenting and assess their risk for premature discontinuation of DAT.
- 2) Avoid the use of DES, and consider bare-metal stents in:
  - a. Potentially non-compliant patients
  - b. Patients who may discontinue drugs for economic reasons
  - c. Patients likely to require invasive or surgical procedures within the ensuing 12 months
- 3) Increase efforts to educate patients
  - a. Regarding the reasons for prescribing DAT and the risks associated with premature discontinuation
  - b. Not to discontinue any anti-platelet therapy unless specifically cleared to do so by their cardiologist
- 4) Educate healthcare providers who perform invasive or surgical procedures
  - a. Regarding the potentially life-

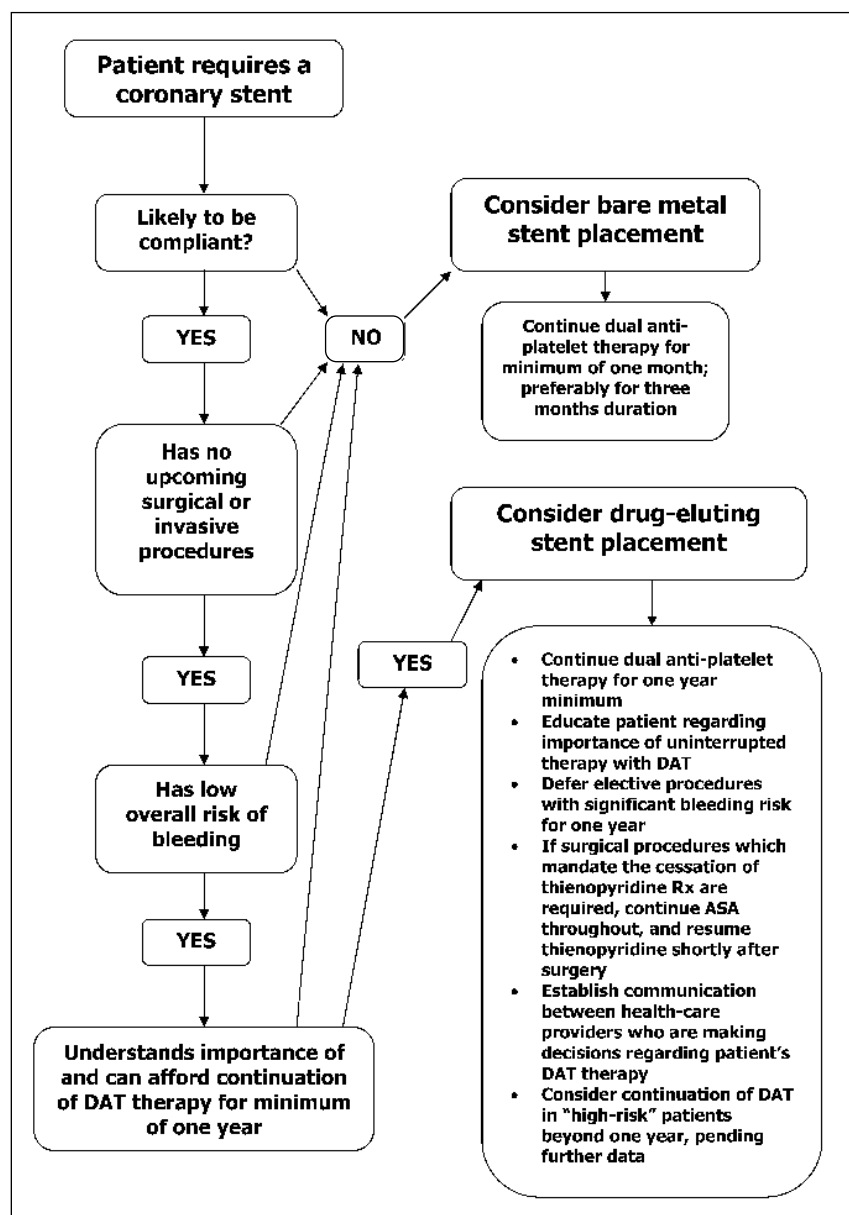
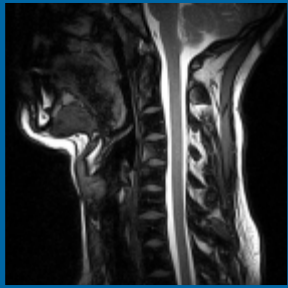


Figure 2. Stent decision-making algorithm

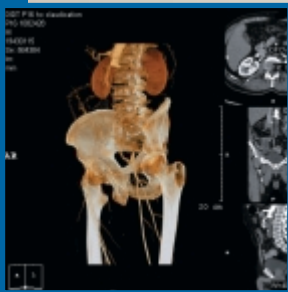


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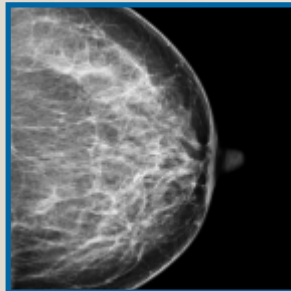
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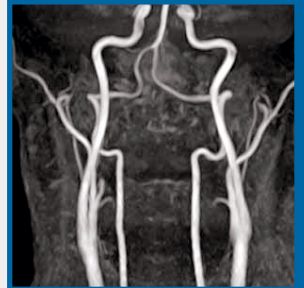
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threatening risk of premature discontinuation of DAT in stented patients  
b. To contact the patient's cardiologist to discuss optimal patient management strategy prior to surgery

- 5) Elective procedures with significant risk of peri- and post-operative bleeding should be deferred for:
  - a. 12 months after DES
  - b. 1 month after bare-metal stenting
- 6) For patients who have received DES within the past year and who must undergo procedures that mandate discontinuation of thienopyridine therapy, aspirin should be continued if at all possible and the thienopyridine restarted as soon as possible after the procedure to reduce the risk of "late" stent thrombosis

Based on these recommendations, we constructed an algorithm regarding the decision making prior to placing a coronary stent, and the recommendations following stent placement. ( Figure 2)

Perhaps the most important guideline to follow in treating patients who have received DES is to ensure adequate communication between the patient, the cardiologist, and other health-care providers who are adjusting the patient's anti-platelet regimen.

## SUMMARY

Significant advances in interventional cardiology have occurred over the past 30 years, leading to substantial increases in the number and anatomic complexity of treated patients, the long-term success of these procedures, and a reduction in the need for coronary bypass surgery. While the risk of restenosis has been dramatically reduced by drug-eluting stents, delayed neo-intimal healing has led to a small, but significant occurrence of "late" stent thrombosis. This thrombotic risk is substantially reduced by continuation of dual-anti-platelet therapy for one or more years following DES placement.

Current guidelines for patient selection for DES, for duration of DAT following DES, and for facing surgical and invasive procedures after DES were discussed, and the avoidance of early discontinuation of anti-platelet therapy following DES was emphasized.

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The authors have no financial interests to disclose.

## Discussion of off-label usage of a product: drug eluting stents

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# Renal Artery Stenosis: Clinical and Therapeutic Implications

Richard A. Regnante, MD, John W. Obell, MD, and Paul Gordon, MD

**Renal artery stenosis is a common cause** of secondary hypertension with a rising incidence due to systemic atherosclerosis in an aging population. Patients with renovascular disease complicated by refractory hypertension, acute pulmonary edema, or progressive renal dysfunction benefit from aggressive medical therapy and may be considered for renal revascularization. **Atherosclerotic renal artery stenosis (ARAS)** accounts for the majority of patients with **renal artery stenosis (RAS)**; however, the subset of patients with **fibromuscular dysplasia (FMD)** and hypertension represents a unique group that benefits from renal artery revascularization.

## CLINICAL FEATURES OF RENAL ARTERY STENOSIS

Renovascular disease can result from a number of pathophysiologic and anatomic abnormalities. Rarely, renal artery congenital malformations, renal artery vasculitides, renal artery aneurysms, embolic phenomena, arteriovenous malformations or fistulas, extrinsic compression of the renal arteries, prior abdominal radiation therapy, neurofibromatosis, William's syn-

drome, spontaneous dissections and traumatic injury to the renal arteries, can result in renal artery pathology.<sup>1-11</sup> Atherosclerotic renal artery disease and renal artery fibromuscular dysplasia are by far the most common causes of RAS, with atherosclerotic disease accounting for 80-90% of RAS.<sup>12,13</sup> ARAS usually occurs in the setting of systemic atherosclerotic cardiovascular disease. It is common to identify coronary, carotid, aortic and peripheral arterial disease in patients with ARAS.

Atherosclerotic disease of the renal artery usually involves the proximal 2 cm of the renal artery, and aorto-ostial segment disease typically represents a continuum of aortic disease extending into the main renal artery branch. (Figure 1)<sup>13</sup> Atherosclerotic disease typically progresses, with 36-71% of lesions progressing to significant stenosis and 16% progressing to total occlusion after 12-60 months of follow-up.<sup>14-18</sup>

The prevalence of ARAS in the general population is difficult to quantify and varies depending on age and other vascular comorbidities. One population-based study that randomly screened elderly patients in the population found a prevalence of 6.8%.<sup>19</sup> Typically patients with ARAS tend to be older, with traditional risk factors for cardiovascular disease and associated comorbidities such as coronary artery disease or cerebral vascular disease. In one study, 30% of patients undergoing cardiac catheterization were incidentally found to have RAS.<sup>20</sup> Significant RAS can be found in up to 70% of patients with evidence of atherosclerosis in other vascular beds.<sup>21</sup>

Hypertension, the most common clinical

manifestation of RAS, is present in nearly a third of patients with malignant or uncontrolled hypertension despite multi-drug therapy. However, half of the patients with significant RAS do not have hypertension, or their blood pressure is well controlled on minimal therapy. Progressive RAS can lead to the development of progressive renal failure, clinically significant renal atrophy, and decreased life expectancy.<sup>22-24</sup>

The impact of RAS on the time to development of renal replacement therapy has not been well established due to multiple confounding factors. However, the life expectancy of a patient on hemodialysis with renovascular disease is much shorter than that of a patient on hemodialysis due to polycystic kidney disease or uncontrolled hypertension without RAS.<sup>25</sup> This is likely due to the association of comorbid atherosclerotic cardiovascular and cerebrovascular disease. In fact, the presence of ARAS, even if not hemodynamically significant, is associated with premature cardiovascular events (myocardial infarction, stroke, and death), and the presence of ARAS in patients with coronary artery disease independently doubles a patient's risk of death, even if coronary revascularization is performed.<sup>26</sup>

## FIBROMUSCULAR DYSPLASIA

FMD usually occurs in younger patients, mainly women age 15-50 years, without systemic vascular disease or cardiovascular risk factors. FMD accounts for 10-20% of adult cases of RAS.<sup>13</sup> Patients with FMD usually present with refractory hypertension and rarely have renal dysfunction.<sup>27</sup> The suspicion for FMD should be raised in a younger woman with severe or newly diagnosed hypertension.

FMD is sub-classified into three categories based on the layer of arterial wall affected, intimal, medial and adventitial. Medial FMD is the most common of the three sub-groups by far in the adult population.<sup>13</sup> While ARAS typically involves the ostial and proximal segments



Figure 1. Non-selective distal abdominal aortic angiography showing bilateral aorto-ostial atherosclerotic renal artery stenoses (single right renal artery and 2 left renal arteries). Note the luminal irregularities in the infrarenal abdominal aorta and proximal portions of the iliac arteries secondary to atherosclerotic plaque.



Figure 2. Selective right renal angiography in a patient with fibromuscular dysplasia extending from the distal third of the main renal artery into the branch vessels. Note the "beaded" appearance of the artery.

of the renal artery, FMD involves the mid to distal segment of the main renal artery and may extend into branches, with a characteristic "beaded" angiographic appearance.<sup>13</sup> (Figure 2)

FMD can affect the carotid, vertebral, iliac and mesenteric arteries, and there is an association with cerebral artery aneurysms.<sup>28</sup> The diagnostic evaluation of patients with suspected RAS from FMD is similar to patients with ARAS.

### Clinical Evaluation and Diagnosis

The clinical evaluation of patients with suspected RAS should begin with the history, physical examination and basic laboratory testing. Patients with hypertension, renal dysfunction or recurrent unexplained flash pulmonary edema should raise suspicion for the diagnosis of RAS, particularly in a patient with known cardiovascular disease or with multiple cardiovascular risk factors.

### HYPERTENSIVE PATIENT

RAS is the most common cause of secondary hypertension. RAS causes or exacerbates hypertension via endocrinologic activation of the renin-angiotensin-aldosterone axis. In patients with unilateral RAS, elevated blood pressure is predominantly secondary to activation of angiotensin II, which is a potent vasoconstrictor, but volume expansion as a result of excess aldosterone secretion is limited

by natriuresis of the contralateral normally functioning kidney.<sup>29,30</sup> In patients with bilateral RAS or with only one functioning kidney, the natriuretic effect of the contralateral kidney is lost and the elevated blood pressure is maintained by volume expansion rather than chronically elevated renin levels.<sup>29,30</sup> In the hypertensive patient, there are several clues that suggest the diagnosis of a secondary cause of hypertension such as RAS.<sup>31</sup> (Table 1) Other causes of secondary hypertension include pheochromocytoma, Cushing's syn-

drome, Conn's syndrome, obstructive sleep apnea, coarctation of the aorta, hypothyroidism, hyperparathyroidism and medications such as oral contraceptives, non-steroidal anti-inflammatory agents, steroids, immunosuppressants, erythropoietin derivatives, and some antidepressants.<sup>32</sup>

### RENAL DYSFUNCTION

RAS should be considered in the patient with renal insufficiency without hematuria or significant proteinuria and bland urinary sediment. Specific patterns of renal dysfunction exist that suggest RAS as the etiology of the renal dysfunction.<sup>31</sup> (Table 2)

### CONGESTIVE HEART FAILURE

Certain patients with congestive heart failure should raise the suspicion of RAS.<sup>31</sup> (Table 3)

### DIAGNOSTIC IMAGING

After a thorough history and physical examination, multiple diagnostic imaging modalities exist to identify RAS. **Magnetic resonance angiography (MRA)**, **computed tomographic angiography (CTA)**, **duplex ultrasound (U/S)** and conventional angiography are the main imaging tests for the evaluation of RAS. All of the non-invasive tests have similar sensitivity and specificity compared to conventional angiography.<sup>31</sup> Captopril renal scintigraphy, selective renal vein renin measurement and plasma renin measurement with or without captopril administration are no longer recommended as initial diagnostic tests for RAS due to their lack of sensitivity and specificity, although they may still be helpful in isolated circumstances.<sup>31</sup> Test availability and patient factors are the main determinants of the test to be used for diagnosis of RAS.

### MAGNETIC RESONANCE ANGIOGRAPHY

MRA is an accurate, comprehensive way to evaluate for RAS, and is now the test of choice to diagnose RAS.<sup>31</sup> The benefits include its lack of ionizing radiation, ability to visualize both main and accessory renal arteries, the renal parenchyma, and the aorta and adjacent mesenteric and iliac arterial branches. MRA requires the infusion of gadolinium as a contrast agent, so caution should be used in patients with renal insufficiency given the recently described potentially fatal nephrogenic systemic fibrosis secondary to gadolinium tissue deposition in patients with renal insufficiency.<sup>33</sup> Other limitations include lack of widespread availability, long acquisition and exam time resulting in claustrophobia in some patients, and limitations of metallic artifact that preclude its use as an imaging tool to follow patients with prior renal stenting.<sup>31</sup>

**Table 1. Clinical Scenarios suggesting renal artery stenosis**

- New onset hypertension at age less than 30 or greater than 55
- Severe, malignant hypertension (refractory to 3 or more medications, including a diuretic)
- Uncontrolled hypertension that was previously well controlled medically
- Hypertension in an individual without a family history of essential hypertension
- Severe hypertension causing refractory angina or congestive heart failure
- Presence of an abdominal bruit on physical examination in a patient with hypertension



**Table 2. Patterns of renal dysfunction that suggest renal artery stenosis**

- Development of worsening renal function after initiation of an ACE-I or ARB (greater than 25% increase in creatinine)
- Unexplained atrophy of kidneys (less than 8cm) or size discrepancy of greater than 1.5cm between each kidney
- Unexplained renal dysfunction, including those patients starting hemodialysis
- Presence of an abdominal bruit on physical examination in a patient with renal insufficiency

**Table 3. Subsets of patients with congestive heart failure that suggest renal artery stenosis**

- Recurrent pulmonary edema without significant coronary artery disease, valvular disease or left ventricular dysfunction
- Severe hypertension and otherwise unexplained congestive heart failure

### COMPUTED TOMOGRAPHIC ANGIOGRAPHY

CTA is a fast, effective, comprehensive way to evaluate for RAS.<sup>31</sup> The advantages include its widespread availability, short exam time, the ability to visualize the main and accessory renal arteries, the renal parenchyma and the abdominal aorta and adjacent mesenteric and iliac arterial branches. However, its use requires the infusion of 100-150ml of iodinated contrast, which may limit its use in patients with renal insufficiency. The exposure to radiation may limit its use in younger patients or in patients who require serial evaluations of a stent after a revascularization procedure. In addition, the metallic artifact of stents may make it difficult to evaluate the severity of in-stent stenoses.

### DUPLEX ULTRASOUND

Duplex ultrasound is a safe, effective and inexpensive way to evaluate for RAS. Ultrasound is portable and there is no radiation or use of potential nephrotoxic contrast agents. Anatomic and functional information can be obtained about the main renal arteries, renal size and appearance. The diagnosis of renal artery stenosis is both based on anatomic appearance and on doppler flow. The *renal resistive index* is calculated based on doppler findings. An abnormal renal resistive index may identify patients with significant renal parenchymal disease who may not benefit from renal revascularization.<sup>31</sup> Unfortunately, ultrasound is highly operator and patient dependent, with limited images in

obese patients or patients with significant bowel gas. There is limited ability to evaluate for accessory renal arteries. Ultrasound is thus limited as an initial diagnostic test for renal artery stenosis. However, ultrasound is an excellent test for serial evaluations of stent patency after percutaneous revascularization since there is no radiation or contrast risk and images are not limited by metallic stent artifact.

### CONVENTIONAL ANGIOGRAPHY

Catheter-based angiography, long considered the “gold standard” for the evaluation of RAS, has largely been replaced by the non-invasive tests, but is still very valuable in patients with equivocal findings on non-invasive tests. Conventional angiography may be especially helpful in patients with suspected FMD, as the sensitivity of non-invasive testing is much lower in patients with FMD.<sup>31</sup> In patients without renal failure, the rate of serious adverse outcomes with non-selective renal angiography, such as contrast-induced nephropathy, bleeding or atheroemboli, is low.<sup>34</sup> American Heart Association guidelines support the use of non-selective renal angiography in patients undergoing diagnostic cardiac catheterization or peripheral angiography in whom there is a high suspicion of RAS, especially if they are candidates for renal revascularization.<sup>34</sup> Conventional angiography is performed in all patients considered for percutaneous renal revascularization.

## CLINICAL MANAGEMENT AND MEDICAL THERAPY

Patients with known renovascular disease should be managed aggressively. The goals of therapy should be normalization of blood pressure, preservation of renal function and prevention of cardiovascular events.<sup>31</sup> The use of multiple medications to control blood pressure is often warranted in patients with RAS. However, lowering the blood pressure too much in patients with RAS may hinder renal perfusion. Most nephrologists will aim for a blood pressure of 140/90 mmHg although data on specific BP targets in this population are lacking. An ideal regimen includes an **angiotensin converting enzyme inhibitor (ACE-I)** or **angiotensin receptor blocker (ARB)**, which directly counter the activation of the renin-angiotensin system. These agents should be used with caution in patients with significant bilateral renal artery disease or with a solitary kidney as they can decrease renal perfusion.<sup>32</sup> A diuretic is frequently employed in this setting to counter intravascular volume overload. Monitoring of electrolytes and creatinine is essential. In patients with concomitant renal dysfunction, nephrotoxic agents and nephrotoxic medications should be avoided. Medical therapy should also include aggressive management of atherosclerotic disease and cardiovascular risk factors. In patients with ARAS, therapy should include aggressive lipid management, aspirin or anti-platelet agents, antihypertensive therapy, aggressive blood sugar control in diabetics, and smoking cessation. A comprehensive history should be obtained in patients with RAS to evaluate for coronary artery disease, cerebrovascular disease and peripheral arterial disease. Patients should be monitored closely for progression of RAS or failure of medical therapy.

Patients with hypertension and FMD can initially be managed medically, but the clinician should have a low threshold for referral for angiography and angioplasty since the success rate of revascularization and improvement in blood pressure control in this patient subset is very high.<sup>27</sup>

### REVASCULARIZATION

Patients with clinically significant RAS due to FMD are almost always referred for revascularization procedures; however, significant controversy exists about the role of revascularization in pa-

tients with ARAS.<sup>35,36</sup> Revascularization can be achieved surgically or endovascularly with **percutaneous transluminal renal angioplasty (PTRA)** and possible stenting.

## SURGERY

Due to the advent of PTRA and the excellent results with stenting, the use of surgical revascularization is now limited to those individuals who have failed PTRA, who have complex anatomy not amenable to PTRA, or have concomitant abdominal aortic disease that warrants surgical repair (such as a abdominal aortic aneurysm).

## ENDOVASCULAR

The use of PTRA has largely replaced surgical techniques due to their less invasive nature with faster recovery times and decreased morbidity. The addition of stenting to PTRA has significantly improved procedural success rates and provided improved long term outcomes with less need for repeat revascularization.<sup>37</sup> Endovascular techniques continue to improve. The use of filter guide wires can limit embolization of atheroma into the distal renal arterioles. Stenting is used mainly for ARAS at the ostium or proximal third of the main renal or accessory renal arteries, whereas balloon angioplasty alone has excellent success and a sustained benefit for FMD.<sup>27</sup>

Significant controversy exists about the role of revascularization in patients with ARAS. Several studies have evaluated medical therapy versus surgery or PTRA.<sup>38</sup> Most do not include the use of modern aggressive medical therapy nor do they represent modern endovascular therapy techniques with the use of stenting and distal protection devices. PTRA alone without stenting is limited by high restenosis rates, and randomized trials have suffered from small sample size and high crossover rates from medical therapy to PTRA. Randomized trials with PTRA and stenting have shown improved blood pressure control.<sup>38</sup> The 2005 ACC/AHA guidelines on the management of peripheral arterial disease address the current expert opinion from multiple professional societies on the role of renal revascularization.<sup>31</sup> (Figure 3) The anatomy of the lesion and the clinical status of the patient must be considered.

Anatomically, lesions are considered significant if they are greater than 70% stenotic or if they are 50-70% stenotic with a pressure gradient greater than 20mmHg measured across them at the time of angiography. Lesions with doppler velocities greater than 300cm/second by U/S are considered hemodynamically significant as well. Clinically symptomatic patients with unilateral or bilateral disease may be considered for revascularization. It is less clear if asymptomatic patients with significant unilateral disease and two functioning kidneys will benefit from revascularization. PTRA is usually performed in patients with FMD even if the lesions appear less than 70% stenotic as the true anatomic caliber of the vessel is often underestimated and clinical improvement can occur in patients with lesions that appear mildly obstructive.

Factors predicting a poor outcome from PTRA with or without stenting include patients with known progressive intrinsic renal disease, known diabetic nephropathy with significant proteinuria,

atrophic kidney (<7 cm), elevated renal resistive index (>80), and advanced renal failure (Cr > 3.5) since the likelihood of renal recovery is low.<sup>31</sup>

Due to the ongoing controversy about the role of renal revascularization in ARAS, ongoing randomized, controlled trials including the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions), STAR (Stenting in Renal Dysfunction Caused by Atherosclerotic Renal Artery Stenosis) and ASTRAL (Angioplasty and Stent for Renal Artery Lesions) trials will help to further define which patients are best treated with aggressive medical therapy versus medical therapy combined with modern day endovascular techniques.

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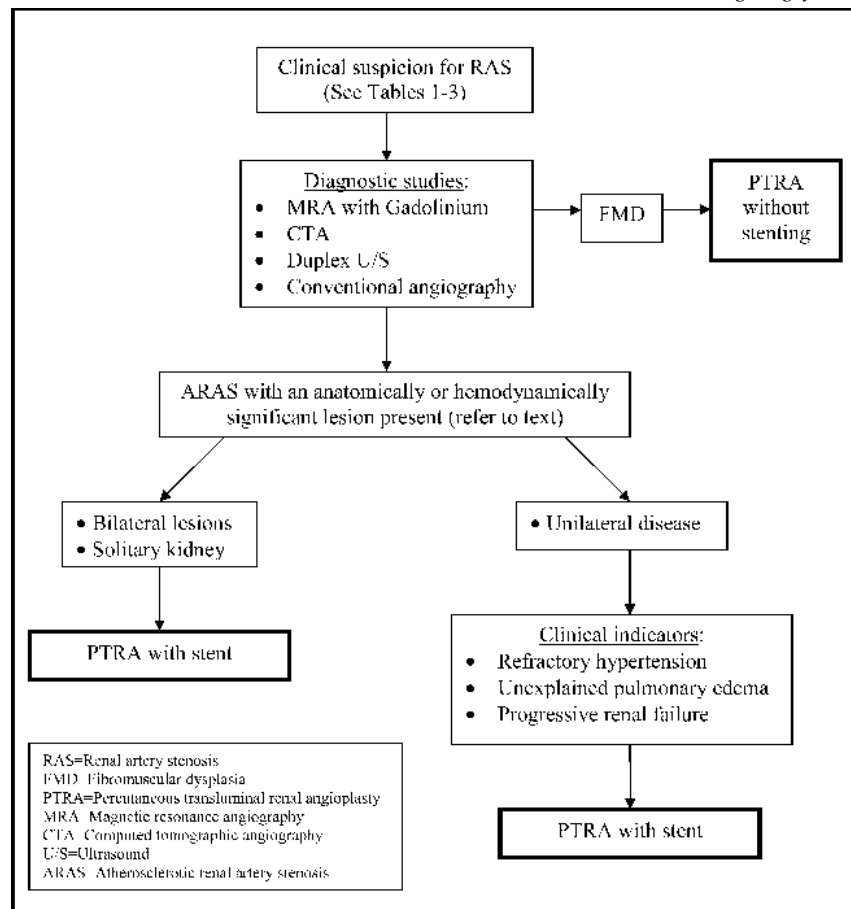


Figure 3. Algorithm for renal revascularization.

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# Images In Medicine

## Chest Pain as the Presenting Features of High Output Heart Disease Due to Congenital Arteriovenous Malformation

Anil T. Taner, Michael K. Atalay, MD, PhD, and Ned H. Gutman, MD

**A 19 year old woman with a right lower extremity arteriovenous malformation (AVM)** status post multiple embolizations presented to the emergency department with chest pain and shortness of breath. An EKG showed sinus tachycardia and left atrial enlargement. Cardiac enzymes were normal but D-dimer was elevated. CT-Angiography showed no pulmonary embolism. The patient was monitored overnight and discharged with a presumed diagnosis of pericarditis. An echo ordered six months later for palpitations showed bi-ventricular dilation and an **atrial septal defect (ASD)** with left to right shunting. Subsequent cardiac MRI confirmed an 8mm ASD with minimal shunting. Cardiac MRI also showed severe 4-chamber enlargement, normal bi-ventricular function, and a cardiac output of 10.8 l/min (Image (a), LA: left atrium; transaxial view. LV/RV: left/right ventricle; sp: spine). The patient was referred to a vascular clinic for surgical evaluation. Images (b)-(d) are from the most recent embolization (2005). Image (b) provides anatomic reference (knee: dashed arrow). Images (c) and (d) are subtraction images showing arterial and venous opacification, respectively, during catheter-based contrast injection. The superficial femoral artery (arrowhead), arteriovenous malformation (\*), and massive draining veins (solid arrows) are readily evident.

### DISCUSSION

Chest pain and shortness of breath in a young person is often attributed to anxiety, musculoskeletal causes, drug use or pulmonary embolism. In the case presented here, it is likely that the symptoms developed secondary to worsening high cardiac output state. The increase in cardiac output from an AVM can

cause both subendocardial perfusion defects as well as structural heart deformities. Treatment of AVMs may restore normal cardiac output and eliminate heart failure symptoms. Given the potential consequences of untreated high-output cardiac failure, it is important for physicians to recognize the condition early in the course and refer the patient for definitive treatment.

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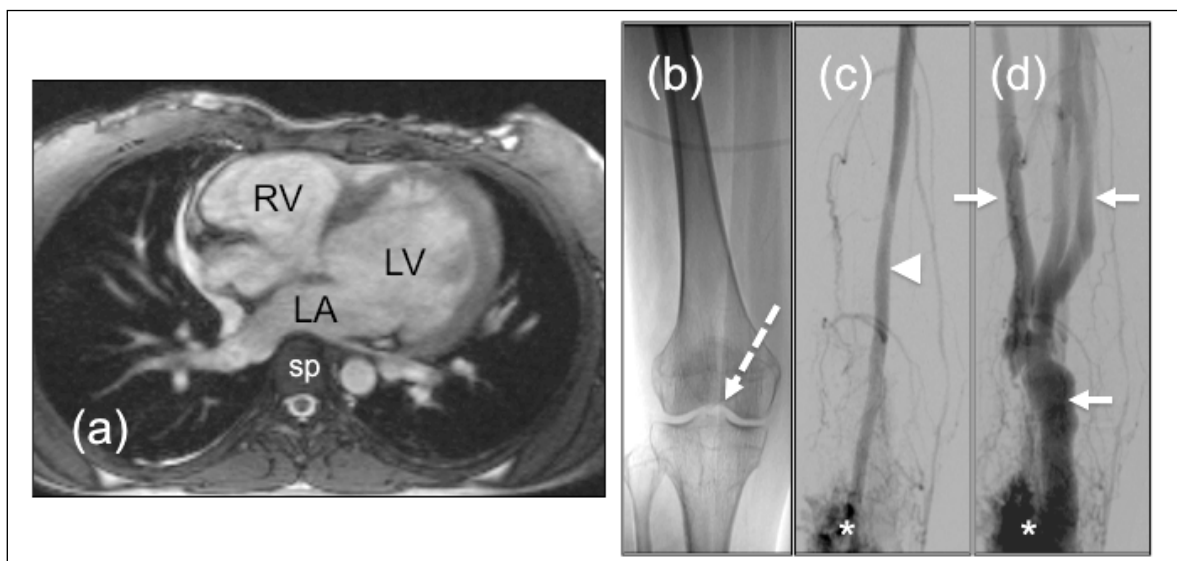
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## Issues of Sexuality In the Elderly

Lynn McNicoll, MD

### CASE 1

A vibrant, robust 75-year-old widower visits his doctor for a routine check-up. As the doctor reviews the patient's pillboxes, he notices a small Tylenol bottle with a large 'V' inscribed on it. The patient explains, "That's for my lady friends in Florida." The perplexed doctor's look evoked further explanation: "My urologist gave me viagra for when I'm in Florida, I have a few lady friends that I visit with." During the summer, the patient lives with his daughter in Rhode Island, which doesn't allow for much privacy. In the winter, he lives alone in his condominium in Florida, giving him plenty of opportunity for sexual intimacy with his lady friends. This healthy and physically active elderly gentleman remains sexually active with the help of medications to treat his mild **erectile dysfunction (ED)**.

### CASE 2

A 94-year-old gentleman has just seen his primary care doctor regarding multiple chronic medical problems - hypertension, coronary artery disease, hypercholesterolemia, osteoporosis, and depression, in addition to coronary artery disease. As the patient is about to leave, he hesitates and asks "What about that blue pill? I have a new lady friend at the assisted living facility and we were thinking about having sex. Can I have that pill for sex?"

Several questions come to mind. He had just informed you that he had had a few bouts of angina with minimal exertion, which resolved with nitroglycerine sublingually, and you had increased his long-acting nitrate. He further informs you that he has not had an erection or erect penis (even during the night) for several years. His coronary artery disease, use of nitrates, and limited functional capacity increase the risk of the medical treatment for ED significantly (increased risk of hypotension and angina), which offers minimal potential benefit (it is unlikely to resulting in a functional erection). You discuss alternatives to erection and orgasm in obtaining sexual intimacy with his new partner.

### MYTHS ABOUT SEXUALITY IN THE OLDER PERSON

As these two cases illustrate, sexuality remains a prominent part of the lives of older persons. Despite evidence to the contrary, many people believe that older adults do not or should not have sexual activity. In fact, if an older person is physically able and has a partner, sexual activity and satisfaction with sex can persist well into the 90s. Sex, physical intimacy, and emotional intimacy are lifelong needs. Often because of physical or functional limitations, sex may be altered to include mutual masturbation, use of mechanical devices, or simply hugging and kissing. Libido and sexual needs decrease with age in both sexes, thus reducing the frequency of sexual experiences; but persons with healthy sex lives as younger adults will be more likely to have healthy sex lives in their golden years. A national study of older persons showed that sexual activity declines

from 73% to 26% among persons aged 57-64 and 75-85, respectively.<sup>1</sup> Physiologically, age affects sexual function by prolonging the excitement phase and requiring a longer period of stimulation in order to achieve orgasm in both men and women. The refractory period between orgasms is also longer in both men and women.<sup>2</sup>

Another myth is that sexual problems are just part of normal aging, with no solutions, so why bother talking to your doctor about it? Physicians are trained to address issues of sexuality in an unbiased, empathetic, and non-judgmental manner. Patients should not feel embarrassed to bring these issues up during their regular appointments. Treatments, medications, or other solutions may be available to improve or solve the problem. Many medications contribute to reducing sexual drive or the ability to have an erection; therefore medication changes can sometimes make dramatic improvements. Such medications include antidepressants (selective serotonin receptor antagonists are most important), narcotics, antihypertensives (in men), alpha-receptor blockers (in men causing ED), and diuretics. (Table 1)<sup>2,3</sup> Except for mirtazepine and wellbutrin, most antidepressants have an impact on libido, and this impact should be discussed.

Many physical conditions exacerbate sexual problems. (Table 2) In addition, many psychological or social factors affect sexuality, including poor body image, feeling less sexy or attractive due to body changes or surgery, feeling less feminine/masculine, fear of

**Table 1 – Medications and their impact on sexuality in older persons**

Medication	Impact
Antihypertensive	Erectile dysfunction, decreased libido
Alpha-blockers	Erectile dysfunction, decreased libido
Narcotics	Erectile dysfunction, decreased libido
Diuretics	Embarrassment with leakage of urine
Alcohol	Erectile dysfunction, decreased ability to reach orgasm
Antipsychotics	Decreased libido and ability to reach an orgasm, priapism
Anticholinergics	Decreased blood flow to penis
Antidepressants:	
SSRI*	Decreased libido, delayed or no orgasm
Tricyclic	Decreased libido and increases
Antidepressants	erectile dysfunction but less than SSRI
Trazodone	Increased libido, anorgasmia, priapism
Citalopram	Decreased libido but less than SSRI
Venlafaxine	Decreased libido but less than SSRI
Mirtazepine	No sexual side effects
Wellbutrin	No sexual side effects and may have a pro-sexual benefit

\*SSRI = Selective Serotonin Receptor Inhibitors

rejection, performance anxiety, and fear of isolation, abandonment, and guilt. These factors interact to negatively impact sexual experiences in older persons. An assessment of sexual disorders should incorporate these possible medical and psychiatric concerns.

## ISSUES RELATED TO MEN

Erectile function is the most important factor in a healthy sexual life in older men. Many chronic diseases contribute to the development of ED, especially chronic, uncontrolled hypertension and diabetes. Obesity, smoking, hypercholesterolemia, heart disease, and lack of physical activity are other risk factors for ED. Surgical treatment for prostate cancer is often a cause of untreatable and irreversible ED. There are mechanical and pharmacological treatment options for ED. Intracavernous injections of alprostadil, a prostaglandin E1 derivative, are one possibility, but often rejected due to the need to insert a needle into the penis. Yohimbe, a natural herbal regimen, has been shown to improve ED, but is NOT recommended due to risks of acute renal failure, seizures, and death. Newer agents, phosphodiesterase V inhibitors, such as, sildenafil, tadalafil, and vardenafil, act peripherally on the penile vascular system to allow improved tumescence and provide significant benefit in the treatment of ED. To take these medications, patients must have some degree of functional and physical endurance, and cannot be on long-acting nitrates. Diabetics are at increased risk for non-arterial ischemic optic neuropathy and visual deficits.<sup>2,3</sup>

## ISSUES RELATED TO WOMEN

Vaginal dryness and dyspareunia (pain with sexual intercourse) are the most important factors in reducing the sexual desire and frequency in women. Menopause also results in a marked decrease in libido, which does not always recover, especially now that few women take hormone replacement therapy. Vaginal lubricants can be an easy effective strategy for reducing vaginal dryness and pain with intercourse. Other risk factors for sexual dysfunction for older women include being unmarried, divorced or widowed; lack of a physically capable partner; past sexual problems; and lower educational level. As women outlive their husbands, lack of a physically

capable partner is becoming more frequent a problem, and women report significantly less sexual activity than men at all age groups.<sup>1</sup>

Many medical conditions also contribute to a reduced desire for sex, including urinary incontinence, osteoarthritis (due to pain with intercourse), and changes in body mass and shape.<sup>4</sup> Up to 50% of breast cancer patients report significant sexual problems due to alteration of self-image and self-confidence.<sup>5</sup> A study assessing the sexual healthcare needs of older women reported that they had concerns similar to younger women, but were less likely to discuss these concerns. They were, however, willing to address their concerns if brought up by a physician - an important message to primary care physicians.<sup>6</sup> Phosphodiesterase inhibitors have not been shown to be of benefit except as an antidote to the sexual side effects of selective serotonin reuptake inhibitors.<sup>3</sup>

## CONCLUSION

Other issues include sexuality among nursing home residents, especially those with dementia; another difficult issue is sexual activity between unmarried couples in the nursing home. In addition, sexually inappropriate behavior and sexual disinhibition in persons with dementia should not be confused with the normal sexual needs of a older adults.

In summary, sexuality remains an important part of quality of life in older persons. However, due to physical and functional limitations, sexual activity may be adapted to incorporate more intimacy and a wider sexual repertoire to include erotic literature, sexual lubricants, and self-stimulation. Physicians should be open to discussing these issues with their elderly patients, and be open to initiating such conversations, being sensitive to the comfort level of the patient.

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## Disclosure of Financial Interests

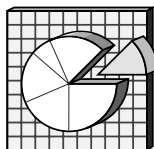
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**Table 2: Medical conditions affecting sexuality in older persons**

Medical Condition	Impact
Osteoarthritis or other	Pain with intercourse joint problems
Stroke	Poor coordination and contractures
Parkinson's Disease	Poor coordination
Surgery for breast cancer	Self image and confidence
Surgery for prostate cancer	Causes incontinence and impotence
Pelvic surgeries	Causes incontinence or impotence
Incontinence (urinary or fecal)	Embarrassment
Chronic foley catheter	Inhibits intimacy and obstruction
Chronic pain syndromes	Inhibits libido
Depression	Decreases libido
Vision and hearing loss	Reduces the stimuli for sexual excitement
Heart and lung disease	Reduces the ability to perform during intercourse
Diabetes mellitus	Causes ED and reduces orgasm



## Mental Health Among Children With Special Health Care Needs In Rhode Island

*Hyun (Hanna) Kim, PhD, Samara Viner-Brown, MS, and Deborah Garneau, MA*

**Children with special health care needs (CSHCN)** are defined as "...those who have or are at increased risk for a chronic physical, developmental, behavioral, or emotional condition and who also require health and related services of a type or amount beyond that required by children generally."<sup>1</sup> In Rhode Island, 17.2% of children younger than 18 years, or 41,783 children, were estimated to have a special health care need in 2005-2006.<sup>2</sup> The prevalence of CSHCN in Rhode Island was higher than the nation as a whole (13.9%).<sup>2</sup>

CSHCN, in general, have higher levels of unmet needs for routine and specialty care and are less likely to have a comprehensive medical home, compared with the general pediatric population.<sup>3</sup> Moreover, CSHCN with mental health problems are even more likely than CSHCN without mental health problems to experience diminished health and quality of life and to have problems accessing and receiving needed care.<sup>4</sup>

The objectives of this study are to 1) estimate the prevalence of mental health problems among CSHCN in Rhode Island and 2) assess disparities in the Federal Maternal and Child Health Bureau's core outcomes between CSHCN with mental health problems and CSHCN without mental health problems.

### METHODS

Data from the 2005/06 National Survey of Children with Special Health Care Needs (NS-CSHCN) were analyzed to examine mental health problems among CSHCN in Rhode Island. The NS-CSHCN is a random digit dial telephone survey administered in all 50 states and the District of Columbia to assess the prevalence and impact of special health care needs. Parents or guardians of CSHCN aged 0-17 years responded to the survey. In Rhode Island, the interviews were completed for 850 CSHCN with an overall response rate of 54.4%. The detailed information on the survey is presented elsewhere.<sup>2</sup>

CSHCN are defined as having a mental health problem if their parents reported that their

child has at least one of the following: 1) any difficulty with behavior problems such as acting-out, fighting, bullying, or arguing; 2) mental retardation or developmental delay; or 3) depression, anxiety, an eating disorder, or other emotional problems. The mental health problems in this study are therefore defined as having **emotional, behavioral, or developmental (EBD)** problems. Since some of the screeners for EBD problems were not asked for children <2 years of age in the survey, this study analyzed the data only for children  $\geq 2$  years.

Six core outcomes, developed by the **Maternal and Child Health Bureau (MCHB)** to measure progress toward implementing community-based systems of services for CSHCN, were used to assess disparities between CSHCN with EBD problems and CSHCN without EBD problems. These six core outcomes are used as National Performance Measures for all state Title V programs, and Rhode Island must monitor its progress in achieving them. Each core outcome was disaggregated into its essential elements and these elements were then translated into measurable criteria using items contained in the survey.<sup>4</sup> Each of these outcomes and their elements were assessed by mental health status using the chi-square test. Unless noted, all estimates were weighted to reflect the noninstitutionalized population of children 2-17 years of age in Rhode Island.

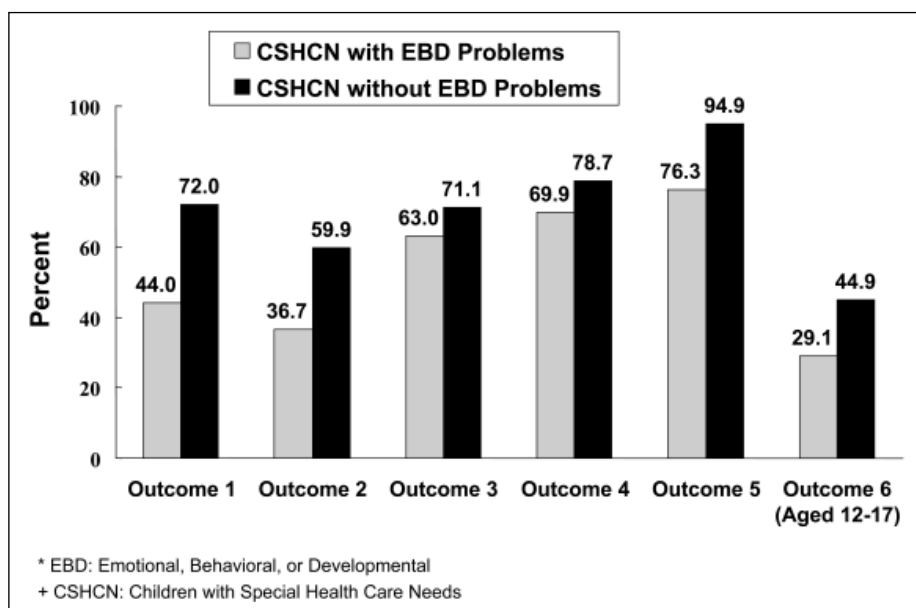


Figure 1. Disparities in Core Outcome Measures by Emotional, Behavioral, or Developmental (EBD) Status among Children with Special Health Care Needs (CSHCN) aged 2-17 years, Rhode Island, 2005/06.



Table 1. Proportion of CSHCN (Aged 2–17) with Emotional, Behavioral, or Developmental (EBD) Problems by Selected Characteristics, Rhode Island, 2005/06

	n*	%	P-Value
<b>Overall</b>	<b>828</b>	<b>40.9</b>	
<b>Age (in year)</b>			
2–5	118	24.4	.0010
6–11	317	41.6	
12–17	393	45.9	
<b>Sex</b>			
Male	529	45.7	.0030
Female	298	33.2	
<b>Ethnicity</b>			
Non-Hispanic	718	39.2	.0307
Hispanic	105	53.4	
<b>Race</b>			
White only	687	38.6	.0795
Black only+	38	45.9	
Other++	92	54.0	
<b>Mother's Education</b>			
< High School	45	59.7	.0114
High School	129	46.5	
> High School	653	36.2	
<b>Poverty Status</b>			
< 200% FPL	245	53.0	.0000
200% - <400% FPL	259	36.0	
At or above 400% FPL	242	28.2	
<b>Insurance Type</b>			
Private	516	28.9	.0000
Public	184	57.5	
Both Private & Public	93	50.7	

† Sample size is too small to produce reliable estimate.

++ Other category includes Asian, American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, and multiple races.

\* n is unweighted sample size with non-missing data.

## RESULTS

Overall, 40.9% of CSHCN aged 2–17 years in Rhode Island have EBD problems. (Table 1) The proportions of EBD problems were higher among teens (45.9%), male children (45.7%), Hispanic children (53.4%), children whose mothers have < high school education (59.7%), children living in households with incomes < 200% federal poverty levels (53.0%), and children who have public insurance (57.5%) compared to their counterparts.

Compared with CSHCN without EBD problems, CSHCN with EBD problems had significantly lower rates of meeting all of the six core outcomes. (Table 2) Less than half of families of CSHCN with EBD problems (44.0%) reported that they were partners in decision-making at all levels and were satisfied with the services they received, compared with 72.0% of families of CSHCN without EBD problems (Core Outcome 1). Only 36.7% of CSHCN with EBD problems reported they received coordinated, ongoing, comprehensive care within a medical home, compared with 59.9% of CSHCN without EBD problems (Core Outcome 2). Less than two-thirds (63.0%) of CSHCN with EBD problems reported that they had adequate private and/or public insurance to pay for the services they needed, compared with

71.1% of CSHCN without EBD problems (Core Outcome 3). Fewer CSHCN with EBD problems (69.9%) than CSHCN without EBD problems (78.7%) were screened early and continuously for special health care needs (Core Outcome 4). Significantly fewer families of CSHCN with EBD problems (76.3%) than families of CSHCN without EBD problems (94.9%) reported that community-based services were organized so families could use them easily (Core Outcome 5). Lastly, only 29.1% of youth (aged 12–17 years) with special health care needs who have EBD problems and 44.9% of youth with special health care needs who do not have EBD problems reported they received the services necessary to make transitions to all aspects of adult life, including adult health care, work, and independence (Core Outcome 6). (Figure 1)

## DISCUSSION

The results indicate that a substantial proportion of CSHCN in Rhode Island has EBD problems and the EBD problems are disproportionately high among certain groups of CSHCN (such as teens, males, Hispanics, children whose mothers have low education, children living in low income families and children who have public insurance). Our results also demon-

strate that these children are at increased risk for not meeting all of the MCHB core outcome measures, which means EBD problems appear to be barriers to obtaining family-centered, coordinated, and community-based care. To improve emotional, behavioral, and cognitive development of children, early diagnosis and effective interventions are necessary, especially for children living in socio-economically disadvantaged families. The Office of Special Healthcare Needs at the Rhode Island Department of Health has initiated such programs to strengthen the coordination between pediatric primary and specialty care while developing a common language among parents and professionals and schools concerning emotional behavioral health. In early 2008, the Department of Health partnered with Bradley Hospital and Hasbro, Inc. to develop and disseminate the Rhode Island Parents' Guide to Children's Mental Health that assists children and their families find answers about mental healthcare and enable them to better access and use the children's mental healthcare system in Rhode Island. Based on the disparities highlighted in this analysis, the Office of Special Healthcare Needs plans to collaborate with Rhode Island Parent Information Network and Parent Support Network to address the coordination between medical and behavioral health.

Table 2. Proportion of CSHCN (Aged 2-17) Who Met the Core Outcomes by Emotional, Behavioral, or Developmental (EBD) Status, Rhode Island, 2005/06

Core Outcome and Element	CSHCN with EBD Problems	CSHCN without EBD Problems	P-Value
	%	%	
<b>Core Outcome 1: Families of CSHCN are partners in decision-making at all levels and are satisfied with the services they receive</b>			
1.1 Doctors usually or always make the family feel like a partner	85.9	92.6	.0129
1.2 Family is very satisfied with services received	46.2	74.5	.0000
<b>Proportion meeting Core Outcome 1</b>	<b>44.0</b>	<b>72.0</b>	<b>.0000</b>
<b>Core Outcome 2: CSHCN receive coordinated, ongoing, comprehensive care within a medical home</b>			
2.1 The child has a usual source of care	93.5	95.0	.4308
2.1a The child has a usual source for sick care	94.6	95.5	.6129
2.1b The child has a usual source of preventive care	98.1	99.2	.1820
2.2 The child has a personal doctor or nurse	96.0	98.7	.0363
2.3 The child has no problems obtaining referrals when needed	86.5	92.5	.1525
2.4 The child receives effective care coordination	49.2	73.3	.0000
2.4a Family usually or always gets sufficient help coordinating care, if needed	62.0	84.3	.0000
2.4b Family is very satisfied with doctors' communication with each other	58.4	76.6	.0001
2.4c Family is very satisfied with doctors' communication with other programs	55.3	69.2	.0408
2.5 The child receives family-centered care	63.1	73.7	.0096
2.5a Doctors usually or always spend enough time	81.1	84.8	.2662
2.5b Doctors usually or always listen carefully	88.8	93.1	.1302
2.5c Doctors are usually or always sensitive to values and customs	87.8	93.0	.0412
2.5d Doctors usually or always provide needed information	75.3	90.0	.0000
2.5e Doctors usually or always make the family feel like a partner	85.9	92.6	.0129
2.5f An interpreter is usually or always available when needed†	79.7	77.8	.9255
<b>Proportion meeting Core Outcome 2</b>	<b>36.7</b>	<b>59.9</b>	<b>.0000</b>
<b>Core Outcome 3: Families of CSHCN have adequate private and/or public insurance to pay for the services they need</b>			
3.1 The child has public or private insurance at time of interview	98.6	98.6	.9822
3.2 The child has no gaps in coverage during the year before the interview	91.0	95.4	.0584
3.3 Insurance usually or always meets the child's needs	90.5	94.5	.0727
3.4 Costs not covered by insurance are usually or always reasonable	74.1	78.5	.2068
3.5 Insurance usually or always permits child to see needed providers	91.8	97.1	.0080
<b>Proportion meeting Core Outcome 3</b>	<b>63.0</b>	<b>71.1</b>	<b>.0432</b>
<b>Core Outcome 4: Children are screened early and continuously for special health care needs</b>			
4.1 Child has received routine preventive medical care in past year	80.0	86.6	.0645
4.2 Child has received routine preventive dental care in past year	80.2	86.1	.0971
<b>Proportion meeting Core Outcome 4</b>	<b>69.9</b>	<b>78.7</b>	<b>.0318</b>
<b>Core Outcome 5: Community-based services are organized so families can use them easily</b>			
5.1 Child's family has experienced no difficulties using services	76.3	94.9	.0000
<b>Proportion meeting Core Outcome 5</b>	<b>76.3</b>	<b>94.9</b>	<b>.0000</b>
<b>Core Outcome 6: Youth with SHCN receive the services necessary to make transitions to all aspects of adult life, including adult health care, work, and independence (Youth aged 12-17)</b>			
6.1 The child receives anticipatory guidance in the transition to adulthood	29.6	41.5	.0759
6.1a Doctors have discussed shift to adult provider, if necessary	30.3	51.1	.0513
6.1b Doctors have discussed future health care needs, if necessary	57.8	69.8	.0829
6.1c Doctors have discussed future insurance needs, if necessary	21.5	28.0	.3235
6.2 The child has usually or always been encouraged to take responsibility for his or her health care needs	72.2	86.4	.0038
<b>Proportion meeting Core Outcome 6</b>	<b>29.1</b>	<b>44.9</b>	<b>.0107</b>

<sup>†</sup> Sample size is too small to produce reliable estimate

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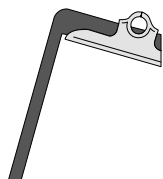
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## Internet Prescribing and the Physician Patient Relationship

*Jeannine Jeha and Robert S. Crausman MD*

In 1997, a young pharmacist who had gone on to medical school graduated from Jefferson Medical College in Philadelphia, PA. In 2000, he was licensed to practice medicine in the state of Rhode Island; in 2001 he earned Board Certification in Emergency Medicine. Several years later, he entered into an agreement with Rx Partners, an Internet pharmacy that employed physicians to approve prescriptions for patients who completed online questionnaires along with their medication requests via a website, conveniently named SpeedyRxDrugs.com. Rx Partners would then fill the prescription and mail it to the patient. Available medications included several controlled substances.

In 2007 a complaint was filed with the RI Board of Medical Licensure and Discipline. After an investigation, it was determined that this Internet prescribing violated the provisions of Rhode Island General Law 5-37 and constituted unprofessional conduct in the practice of medicine. The physician was sanctioned with a formal Reprimand and required to complete a Board approved personalized ethics curriculum.

This was not the first Rhode Island physician to be sanctioned for illegitimate Internet prescribing. In 2001 another more senior physician had been sanctioned with 3 years Probation.

Illicit online prescribing is not a problem unique to our State. It is an international problem that has grown exponentially with the Internet. "Rogue" online pharmacies operate through websites and provide customers with prescription medications. Prescriptions are written or approved by licensed physicians based upon perfunctory online questionnaires completed by so-called patients. Safeguards intrinsic to the physician-patient relationship are nonexistent. There have been numerous documented instances of patient harm, including death.

Unfortunately, the lure of easy money coupled with the increasing demands of medical practice has attracted physicians nationwide. Physicians are generally paid between \$2 and \$50 per prescription. For example, one physician was paid approximately \$250,000 over a 7-month period before having to surrender his medical license to the Texas Medical Board. This physician was also sentenced to 3 years in federal prison for his role in the medication-related death of an 18-year-old man.

According to the Federation of State Medical Boards more than 150 physicians were disciplined nationally between 1999 and 2006 for unprofessional conduct relating to Internet pre-

scribing. The FSMB through its clearinghouse on Internet prescribing conducts investigations by purchasing prescription medications online. Since 2000 more than 90% of submitted online questionnaires have been approved despite containing fictitious information or physical data that would contraindicate prescription. There are approximately 1400 rogue pharmacy websites with many selling controlled substances.

Advancing Internet technology has revolutionized many aspects of medical practice through legitimate telemedicine. However, with regard to Internet prescribing this technology has advanced well ahead of effective regulation by State and Federal authorities.

To guide practicing physicians the Board articulated a position statement on Internet prescribing and the physician-patient relationship in 2007. "It is inappropriate to prescribe medications via the Internet or similar venue without an appropriate physician/patient relationship that would typically include: 1) patient history, 2) physical and/or mental health assessment, 3) legitimate records kept, 4) licensed and trained practitioners, 5) elements of informed consent wherever appropriate and reasonable, and 6) AMA/AOA code of ethics followed."

### REFERENCES

- Federation of State Medical Boards. Intensifying the fight against 'rogue' Internet pharmacies in State of the States, physician regulation 2007.
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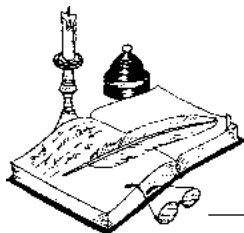
*Jeannine Jeha, a student at Northeastern University, was an intern at the RI Department of Health.*

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The authors have no financial interests to disclose.

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# Physician's Lexicon

## From Telepathy To Telekinesis

**The English writer, Frederic Myers [1843 – 1901]**, was seeking a word to define communication between two minds by means other than the customary sensory channels. Finding none, he invented the word, 'telepathy' literally, feeling from afar. Two Greek roots were employed: *telo-*, meaning far off, distant; and *patho-*, meaning feeling or disease. [Pathologists have managed to confine its use to disease-states solely as in pathogen, pathology and pathos. The word, telepathy, could easily have meant, diseases from afar.]

Medicine has employed the *tel-* prefix in a variety of terms: telephone, telangiectasia, telomere, telephase, teledendron, telemetry, telencephalon, telalgia and recently, teleradiography. And in general usage, such additional words as

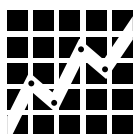
telethon, television, telephoto, telekinesia, teletype and televangelism.

An earlier Greek word, *telos*, conveys a slightly different sense, that of ultimate destiny rather than mere distance. Thus the *telos* of an acorn is the oak tree and the ultimate *telos* of the blastomere is the newborn infant. The medical term teleology incorporates this meaning when it describes the ultimate purposes and destinies within the world of nature. The class of bony fish, called the teleosts, represents another example of the Greek prefix denoting ultimate destiny, in this case, evolutionary destiny. And the son of Odysseus and Penelope was named Telemachus, meaning fighting from afar [an understandable adolescent acting-out given the tendency of Odysseus to stay away from his home for decades at a time.]

The Romans, a more earthy ethnic group, also employed a *tell-* prefix [named after Tellus, goddess of the earth], denoting anything pertaining to the earth. Thus, geologic words such as tellurian, telluride and the element, tellurium are formed.

Yet another Latin word, *tela*, may be easily confused with the root terms and derivative medical terms listed above. A *tela* signifies a web or netlike structure, as in *tela choroidea* or *tela conjunctiva*.

— STANLEY M. ARONSON, MD



RHODE ISLAND DEPARTMENT OF HEALTH  
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## VITAL STATISTICS

EDITED BY COLLEEN FONTANA, STATE REGISTRAR

### Rhode Island Monthly Vital Statistics Report Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	October 2007	12 Months Ending with October 2007		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	239	2,749	257.0	3,809.0
Malignant Neoplasms	202	2,243	209.7	5,767.5
Cerebrovascular Diseases	27	386	36.1	612.0
Injuries (Accidents/Suicide/Homicide)	53	552	51.6	8,625.5
COPD	29	415	38.8	285.0

Vital Events	Reporting Period		
	April 2008	12 Months Ending with April 2008	
	Number	Number	Rates
Live Births	857	12,912	12.1*
Deaths	825	10,094	9.5*
Infant Deaths	(3)	(84)	6.5#
Neonatal Deaths	(2)	(61)	4.7#
Marriages	348	6,692	6.3*
Divorces	268	3,053	2.9*
Induced Terminations	371	5,020	388.8#
Spontaneous Fetal Deaths	52	857	66.4#
Under 20 weeks gestation	(47)	(781)	60.5#
20+ weeks gestation	(5)	(76)	5.9#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,067,610

(c) Years of Potential Life Lost (YPLL)

**Note:** Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

\* Rates per 1,000 estimated population

# Rates per 1,000 live births

### NINETY YEARS AGO, OCTOBER 1918

The Rhode Island Medical Society suspended publication of the journal from October 1918 through December 1919, when three key staff members went to serve in the War.

### FIFTY YEARS AGO, OCTOBER 1958

An Editorial, "Whose Hoop is Being Twisted?" argued against any extension of Social Security legislation to encompass health care. "The medical profession of Rhode Island does not oppose the Social Security Act *per se*. It does have misgivings about its operation, and it does criticize the continuous efforts of certain political groups to change the concept of the program into one of state socialism." The editorial praised private-sector voluntary insurance: "...there is nothing wrong with the extraordinary development of voluntary health insurance in this country in the past decade...it is one of the brightest achievements in a society that is saturated with the false sense of security by political and social planners." In Rhode Island, Blue Cross and Physicians Services enrolled 66,000 of the 80,000 residents over age 65; another 7200 were covered under the state's public assistance program ("which Rhode Island doctors greatly subsidize"); and 1500 were inmates of state institutions. The Editorial presumed that some of the remainder had bought other insurance.

The Honorable Thomas B. Curtis, Missouri, House of Representatives, had entered "Socialized Medicine in Great Britain - A Ten-Year Appraisal," into the Congressional Record; and the Journal reprinted the entry. The entry had originally appeared in the *Shreveport Times* ("Britain's 10-Year Flop in Free Medical Care," which in turn had drawn upon an article in the *London Economist* that focused on the costs of Britain's system.

### TWENTY-FIVE YEARS AGO, OCTOBER 1983

In an Editorial, "Debunking the Dioxin Scare," the Journal reprinted the review from *St. Louis Metropolitan Medicine*, a publication of the St. Louis Metropolitan Medical Society). Monsanto Corporation was based in St. Louis. The St. Louis Society, the American Medical Association, and Monsanto had all argued that dioxin posed no cancer risk. The editorial continued: "...the only long-term health problem linked to dioxin in the numerous studies is an acne-like condition (chloracne) in some workers." The conclusion: "It is time that the scare [cancer] be laid to rest."

Howard R. Cohen, MD, Allan M. Deutsch, MD, Michael J. Ryvicker, MD, and Sanford L. Schatz, MD, contributed "Radiographic Case of the Month." They used computed tomography to show "anterior dislocation of the meniscus of the TIMJ with reduction in opening of the mouth" in a 33 year-old woman.

Robert D. Coli, MD, in "The Diagnostic Information System: A New Tool for Accurate Medical Decision-Making," commented: "Looking for the solution without understanding the problem is working in the dark."

Maurice M. Albala, MD, George Meissner, MD, Thomas Wachtel, MD, and David Williams, MD, contributed "Clinicopathological Case Report" from Rhode Island Hospital. A 62 year-old man with diabetes was admitted with "severe weakness and persistent cough." The diagnosis: anatomic Hodgkin's disease, lymphocyte-depletion type; secondary neoplastic neuromyopathy; secondary aspiration pneumonitis, organizing and old.

Donald C. Williams and Bruce C. Kelly, PhD, from the Rhode Island Department of Health discussed "Differences in Hospital Use by Residence, The RI Experience in 1980." State residents used an average 1,095.9 days per 1000 population; urban residents used more (Woonsocket was highest, at 1,443.9). More people in the Blackstone Valley had tonsillectomies; more women in Scituate, West Warwick, Johnston, East Greenwich and Coventry had abdominal hysterectomies; more people in Newport County had disc surgeries.

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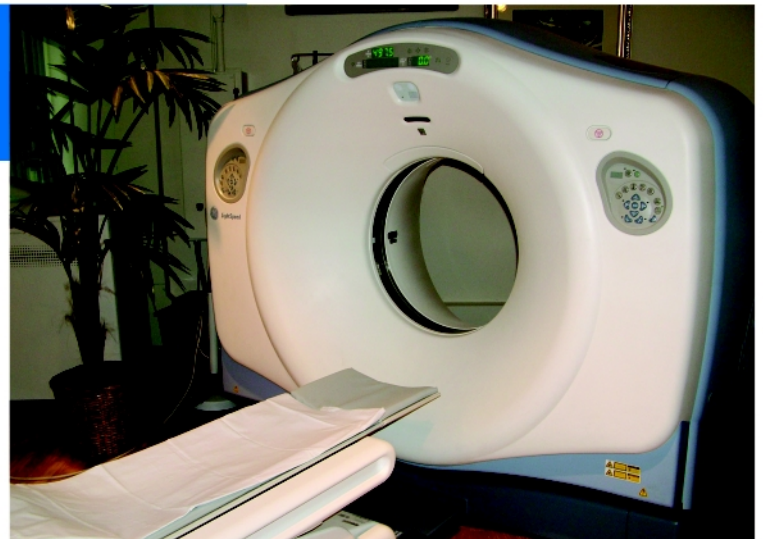
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