A case of abnormal architecture.

Brian Nicholson, B.Sc. and Mark Logan, M.B.

(Answer on page 52)

Just having settled in to your new office at the new Halifax Infirmary, you decide to unpack your things. You notice amid your belongings, a strange brown envelope marked "important", the contents of which is the single radiograph shown as Figure 1.

Q 1: With no other information, can you find the "important" features of this film?

Q 2: Can you give a quick differential with this limited information.

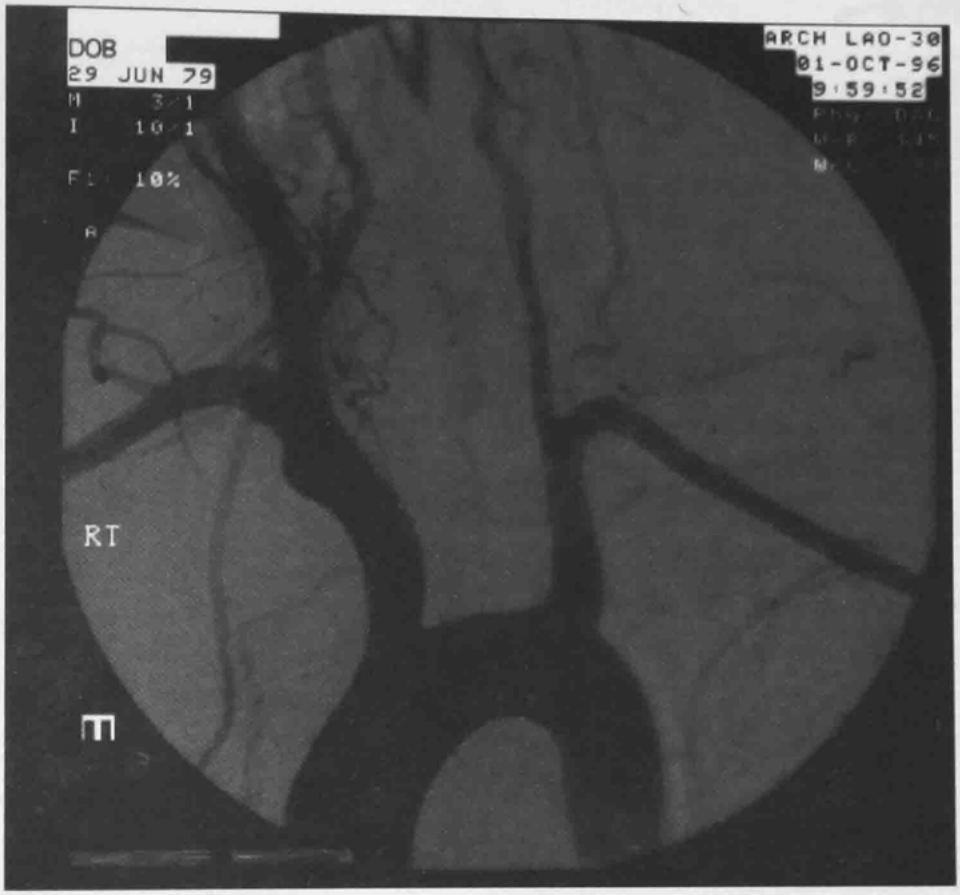


Figure 1.

On closer exam of the envelope you find a small piece of paper inside which reads:

> **"16 yr old female with hx. of L parietal stroke in 1988 and hypertension. Recent medullary infarct with good resolution."**

Q 3: What is your differential now?

Q 4: What is the structure marked "H"?

Q 5: What treatment / intervention would you offer this patient?

Q 6: Are there any other areas of concern that you would like to see radiographically?

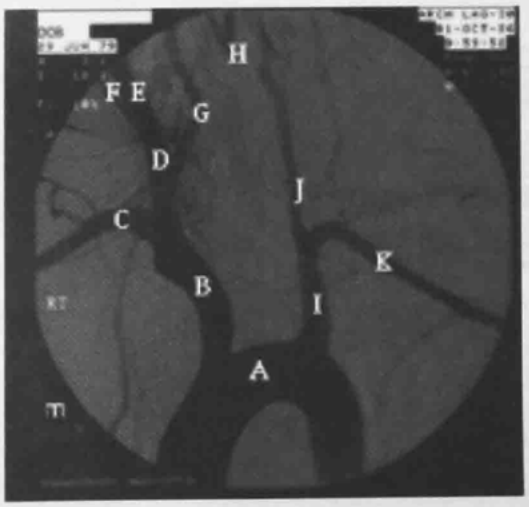
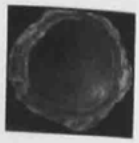


Figure 2: A- aortic arch, B- brachiocephalic trunk, C- R subclavian, D- R common carotid, E- internal carotid, F- external carotid, G- R vertebral, H- ???, I- L subclavian trunk, J- L vertebral artery, K- L subclavian

PrLIPITOR*
ATORVASTATIN CALCIUM



LIPITOR*
(Atorvastatin Calcium)
10 mg, 20 mg and 40 mg tablets

THERAPEUTIC CLASSIFICATION: Lipid Metabolism Regulator

ACTIONS AND CLINICAL PHARMACOLOGY

LIPITOR (atorvastatin calcium) is a synthetic lipid-lowering agent. It is a selective, competitive inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in the biosynthesis of cholesterol.
LIPITOR lowers plasma cholesterol and lipoprotein levels by inhibiting HMG-CoA reductase and cholesterol synthesis in the liver and by increasing the number of hepatic Low Density Lipoprotein (LDL) receptors on the cell-surface for enhanced uptake and catabolism of Low Density Lipoprotein (LDL).
LIPITOR reduces LDL-Cholesterol (LDL-C) and the number of LDL particles, and lowers Very Low Density Lipoprotein-Cholesterol (VLDL-C) and serum triglycerides (TG), as well as the number of apolipoprotein B (apo B) containing particles.
Atorvastatin is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1 to 2 hours. Atorvastatin tablets are 95% to 99% bioavailable compared to solutions.
Mean distribution of atorvastatin is approximately 565 liters. Atorvastatin is ≥98% bound to plasma proteins.
Atorvastatin is extensively metabolized by cytochrome P450 3A4 to ortho- and para-hydroxylated derivatives and various beta-oxidation products. Approximately 70% of circulating inhibitory activity for HMG-Co A reductase is attributed to active metabolites.
Atorvastatin and its metabolites are eliminated by biliary excretion. Less than 2% of a dose of atorvastatin is recovered in urine following oral administration. Mean plasma elimination half-life of atorvastatin in humans is approximately 14 hours, but the half-life of inhibitory activity for HMG-CoA reductase is 20 to 30 hours due to the contribution of longer-lived active metabolites.

INDICATIONS AND CLINICAL USE

LIPITOR (atorvastatin calcium) is indicated as an adjunct to diet, at least equivalent to the American Heart Association (AHA) Step 1 diet, for the reduction of elevated total cholesterol, LDL-C, triglycerides (TG) and apolipoprotein B (apo B) in hyperlipidemic and dyslipidemic conditions, when response to diet and other nonpharmacological measures alone has been inadequate, including:

- Primary hypercholesterolemia (Type IIa),
- Combined (mixed) hyperlipidemia (Type IIb), including familial combined hyperlipidemia, regardless of whether cholesterol or triglycerides are the lipid abnormality of concern, and
- Heterozygous familial hypercholesterolemia.

In clinical trials, LIPITOR (10-80 mg/day) significantly improved lipid profiles in patients with a wide variety of hyperlipidemic and dyslipidemic conditions. In 2 dose-response studies in mildly to moderately hyperlipidemic patients (Fredrickson Types IIa and IIb), LIPITOR reduced the levels of total cholesterol (29-45%), LDL-C (39-60%), apo B (32-50%), TG (19-37%), and increased HDL-C levels (5-9%). Comparable responses were achieved in patients with heterozygous familial hypercholesterolemia, non-familial forms of hypercholesterolemia, combined hyperlipidemia, including familial combined hyperlipidemia and patients with non-insulin dependent diabetes mellitus. In patients with hypertriglyceridemia (TG>350 mg/dL), LIPITOR lowered TG levels by 27-42%.
Limited data is available in homozygous familial hypercholesterolemia (FH). An open-label study with atorvastatin 80 mg/day in homozygote FH patients showed a LDL-C lowering of 30% for patients not on plasmapheresis and of 31% for patients who continued plasmapheresis. A LDL-C lowering of 35% was observed in receptor defective patients and of 19% in receptor negative patients (see PHARMACOLOGY, Clinical Studies).
For more details on efficacy results by pre-defined classification and pooled data by Fredrickson types, see PHARMACOLOGY, Clinical Studies.
Prior to initiating therapy with LIPITOR, secondary causes should be excluded for elevations in plasma lipid levels (e.g. poorly controlled diabetes mellitus, hypothyroidism, nephrotic syndrome, dysproteinemias, obstructive liver disease, and alcoholism), and a lipid profile performed to measure total cholesterol, LDL-C, HDL-C, and TG.
For patients with TG <4.52 mmol/L (<400 mg/dL), LDL-C can be estimated using the following equation:

LDL-C (mmol/L) = total cholesterol - [(0.37 x (TG) + HDL-C)]
LDL-C (mg/dL) = total cholesterol - [(0.2 x (TG) + HDL-C)][1]

For patients with TG levels >4.52 mmol/L (>400 mg/dL), this equation is less accurate and LDL-C concentrations should be determined by ultracentrifugation.

CONTRAINDICATIONS

Hypersensitivity to any component of this medication.
Active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal (see WARNINGS).
Pregnancy and lactation (see PRECAUTIONS).

WARNINGS

General

The effects of atorvastatin-induced changes in lipoprotein levels, including reduction of serum cholesterol on cardiovascular morbidity or mortality or total mortality have not been established.

Hepatic Effects

In clinical trials, persistent increases in serum transaminases greater than three times the upper limit of normal occurred in <1% of patients who received LIPITOR. When the dosage of LIPITOR was reduced, or when drug treatment was interrupted or discontinued, serum transaminase levels returned to pretreatment levels. The increases were generally not associated with jaundice or other clinical signs or symptoms. Most patients continued treatment with a reduced dose of LIPITOR without clinical sequelae.
Liver function tests should be performed before the initiation of treatment, and periodically thereafter. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients measurements should be repeated promptly and then performed more frequently.
If increases in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) show evidence of progression, particularly if they rise to greater than 3 times the upper limit of normal and are persistent, the dosage should be reduced or the drug discontinued.
LIPITOR should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease. Active liver disease or unexplained transaminase elevations are contraindications to the use of LIPITOR; if such a condition should develop during therapy, the drug should be discontinued.

Muscle Effects

Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatinine phosphokinase (CPK) values to greater than ten times the upper limit of normal, should be considered in any patient with diffuse myalgia, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. LIPITOR therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.
The risk of myopathy during treatment with HMG-CoA reductase inhibitors is increased with concurrent administration of cyclosporine, fibric acid derivatives, erythromycin, niacin (nicotinic acid) or azole antifungals. Although there is no experience to date with the use of LIPITOR given concurrently with these drugs, with the exception of a pharmacokinetic study with erythromycin (see PRECAUTIONS, Drug Interactions), the benefits and risks of such combined therapy should be carefully considered.
Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has also been reported with HMG-CoA reductase inhibitors. LIPITOR therapy should be temporarily withheld or discontinued in any patient with an acute serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis (such as severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures).

PRECAUTIONS

General

Before instituting therapy with LIPITOR (atorvastatin calcium), an attempt should be made to control elevated serum lipoprotein levels with appropriate diet, exercise, and weight reduction in overweight patients, and to treat other underlying medical problems (see INDICATIONS AND CLINICAL USE). Patients should be advised to inform subsequent physicians of the prior use of LIPITOR or any other lipid-lowering agents.

Effect on the Lens

Current long-term data from clinical trials do not indicate an adverse effect of atorvastatin on the human lens.

Effect on Ubiquinone (CoQ_{10}) Levels

Significant decreases in circulating ubiquinone levels in patients treated with atorvastatin and other statins have been observed. The clinical significance of a potential long-term statin-induced deficiency of ubiquinone has not been established. It has been reported that a decrease in myocardial ubiquinone levels could lead to impaired cardiac function in patients with borderline congestive heart failure (see SELECTED BIBLIOGRAPHY).

Effect on Lipoprotein(a)

In some patients, the beneficial effect of lowered total cholesterol and LDL-C levels may be partly blunted by a concomitant increase in Lp(a) levels. Until further experience is obtained, it is suggested, where feasible, that measurements of serum Lp(a) be followed up in patients placed on atorvastatin therapy (see SELECTED BIBLIOGRAPHY).

Hypersensitivity

An apparent hypersensitivity syndrome has been reported with other HMG-CoA reductase inhibitors which has included 1 or more of the following features: anaphylaxis, angioedema, lupus erythematous-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, eosinophilia, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome. Although to date hypersensitivity syndrome has not been described as such, LIPITOR should be discontinued if hypersensitivity is suspected.

Use in Pregnancy

LIPITOR is contraindicated during pregnancy (see CONTRAINDICATIONS).
Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause harm to the fetus when administered to pregnant women.
There are no data on the use of LIPITOR during pregnancy. LIPITOR should be administered to women of child-bearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the patient becomes pregnant while taking LIPITOR, the drug should be discontinued and the patient apprised of the potential risk to the fetus.

Nursing Mothers

In rats, milk concentrations of atorvastatin are similar to those in plasma. It is not known whether this drug is excreted in human milk. Because of the potential for adverse reactions in nursing infants, women taking LIPITOR should not breast-feed (see CONTRAINDICATIONS).

Pediatric Use

Treatment experience in a pediatric population is limited to doses of LIPITOR up to 80 mg/day for 1 year in 8 patients with homozygous familial hypercholesterolemia. No clinical or biochemical abnormalities were reported in these patients.

Geriatric Use

Treatment experience in adults 70 years or older (N=221) with doses of LIPITOR up to 80 mg/day has demonstrated that the safety and effectiveness of atorvastatin in this population was similar to that of patients <70 years of age. Pharmacokinetic evaluation of atorvastatin in subjects over the age of 65 years indicates an increased AUC. As a precautionary measure, the lowest dose should be administered initially (see PHARMACOLOGY, Human Pharmacokinetics; and SELECTED BIBLIOGRAPHY).

Renal Insufficiency

Plasma concentrations and LDL-C lowering efficacy of LIPITOR are similar in patients with moderate renal insufficiency compared with patients with normal renal function. In patients with severe renal insufficiency (creatinine clearance <30 mL/min), the lowest dosage should be used and implemented cautiously (see WARNINGS, Muscle Effects).

Endocrine Function

HMG-CoA reductase inhibitors interfere with cholesterol synthesis and as such might theoretically blunt adrenal and/or gonadal steroid production. Clinical studies with atorvastatin and other HMG-CoA reductase inhibitors have suggested that these agents do not reduce plasma cortisol concentration or impair adrenal reserve and do not reduce basal plasma testosterone concentration. However, the effects of HMG-CoA reductase inhibitors on male fertility have not been studied in adequate numbers of patients. The effects, if any, on the pituitary-gonadal axis in premenopausal women are unknown.
Patients treated with atorvastatin who develop clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients receiving other drugs (e.g. ketoconazole, spironolactone or cimetidine) that may decrease the levels of endogenous steroid hormones.

Drug Interactions

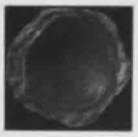
Concomitant Therapy with Other Lipid Metabolism Regulators: Combined drug therapy should be approached with caution as information from controlled studies is limited.

Bile Acid Sequestrants:

Patients with mild to moderate hypercholesterolemia: LDL-C reduction was greater when LIPITOR 10 mg and colestipol 20 g were coadministered (-45%) than when either drug was administered alone (-35% for LIPITOR and -22% for colestipol).
Patients with severe hypercholesterolemia: LDL-C reduction was similar (-53%) when LIPITOR 40 mg and colestipol 20 g were coadministered when compared with that of LIPITOR 80 mg alone. Plasma concentration of atorvastatin was lower (approximately 26%) when LIPITOR 40 mg plus colestipol 20 g were coadministered compared with LIPITOR 40 mg alone.

[1] Friedewald, WT et al. *Clin Chem* 1972; 18(6):499-502.

LIPITOR*
ATORVASTATIN CALCIUM



However, the combination drug therapy was less effective in lowering the triglycerides than LIPITOR monotherapy in both types of hypercholesterolemic patients (see PHARMACOLOGY, Clinical Studies).
When LIPITOR is used concurrently with colestipol or any other resin, an interval of at least 2 hours should be maintained between the two drugs, since the absorption of LIPITOR may be impaired by the resin.
Fibric Acid Derivatives (Gemfibrozil, Fenofibrate, Bezafibrate) and Niacin (Nicotinic Acid): Although there is no experience with the use of LIPITOR given concurrently with fibric acid derivatives and niacin, the benefits and risks of such combined therapy should be carefully considered. The risk of myopathy during treatment with other drugs in this class is increased with concurrent administration (see WARNINGS, Muscle Effects).
Erythromycin: In healthy individuals, plasma concentrations of atorvastatin increased approximately 40% with coadministration of LIPITOR and erythromycin, a known inhibitor of cytochrome P450 3A4 (see WARNINGS, Muscle Effects).
Coumarin Anticoagulants: LIPITOR had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin therapy.
Digoxin: Coadministration of multiple doses of LIPITOR and digoxin increased steady-state plasma digoxin concentrations by approximately 20%. Patients taking digoxin should be monitored closely and appropriately.
Antipyrine: Antipyrine was used as a model for drugs metabolized by the microsomal hepatic enzyme system (cytochrome P-450 system). LIPITOR had no effect on the pharmacokinetics of antipyrine, thus interactions with other drugs metabolized via the same cytochrome isozymes are not expected.
Oral Contraceptives: Coadministration of LIPITOR with an oral contraceptive, containing 1 mg norethindrone and 35 µg ethinyl estradiol, increased plasma concentrations (AUC levels) of norethindrone and ethinyl estradiol by approximately 30% and 20%, respectively. These increases should be considered when selecting an oral contraceptive.
Antacids: Administration of aluminum and magnesium based antacids, such as Maalox® TC Suspension, with LIPITOR decreased plasma concentrations of LIPITOR by approximately 35%. LDL-C reduction was not altered but the triglyceride-lowering effect of LIPITOR may be affected.
Cimetidine: Administration of cimetidine with LIPITOR did not alter plasma concentrations or LDL-C lowering efficacy of LIPITOR, however, the triglyceride-lowering effect of LIPITOR was reduced from 34% to 26%.
Other Concomitant Therapy: Caution should be exercised with concomitant use of immunosuppressive agents and azole antifungals (see WARNINGS, Muscle Effects).
In clinical studies, LIPITOR was used concomitantly with antihypertensive agents and estrogen replacement therapy without evidence of clinically significant adverse interactions. Interaction studies with specific agents have not been conducted.
Cytochrome P-450 Inhibitors: Atorvastatin is metabolized by the microsomal hepatic enzyme system (cytochrome P-450 system) as are most other HMG-CoA reductase inhibitors. While atorvastatin did not interact with antipyrine, it did interact with erythromycin, a known inhibitor of cytochrome P450 3A4. Grapefruit juice has also been shown to inhibit cytochrome P450 3A4. There may be a potential for increased plasma concentrations of HMG-CoA reductase inhibitors upon coadministration with grapefruit juice, and other compounds which affect this enzyme system (see SELECTED BIBLIOGRAPHY).

Patients with Severe Hypercholesterolemia:

Higher drug dosages (80 mg/day) required for some patients with heterozygous familial hypercholesterolemia or severe hypercholesterolemia are associated with increased plasma levels of atorvastatin. **Caution should be exercised in such patients who are also severely renally impaired, elderly, or are concomitantly being administered digoxin or erythromycin (see WARNINGS, Muscle Effects; and PRECAUTIONS, Drug Interactions).**

Drug/Laboratory Test Interactions

LIPITOR may elevate serum transaminase and creatinine phosphokinase levels (from skeletal muscle). In the differential diagnosis of chest pain in a patient on therapy with LIPITOR, cardiac and noncardiac fractions of these enzymes should be determined.

ADVERSE REACTIONS

LIPITOR is generally well-tolerated. Adverse reactions have usually been mild and transient. In controlled clinical studies (placebo-controlled and active-controlled comparative studies with other lipid lowering agents) involving 2502 patients, <2% of patients were discontinued due to adverse experiences attributable to LIPITOR. Of these 2502 patients, 1721 were treated for at least 6 months and 1253 for 1 year or more.
Adverse experiences occurring at an incidence ≥1% in patients participating in placebo-controlled clinical studies of LIPITOR and reported to be possibly, probably or definitely drug related are shown in Table 1 below:

TABLE 1. Associated Adverse Events Reported in ≥ 1% of Patients in Placebo Controlled Clinical Trials

	Placebo % (n=270)	LIPITOR % (n=1122)
GASTROINTESTINAL		
Constipation	1	1
Diarrhea	1	1
Dyspepsia	2	1
Flatulence	2	1
Nausea	0	1
NERVOUS SYSTEM		
Headache	2	1
MISCELLANEOUS		
Pain	<1	1
Myalgia	1	1
Asthenia	<1	1

The following additional adverse events were reported in clinical trials; not all events listed below have been associated with a causal relationship to LIPITOR therapy: Muscle cramps, myositis, myopathy, paresthesia, peripheral neuropathy, pancreatitis, hepatitis, cholestatic jaundice, anorexia, vomiting, alopecia, pruritus, rash, impotence, hyperglycemia, and hypoglycemia.
Ophthalmologic observations: see PRECAUTIONS.
Laboratory Tests: Increases in serum transaminase levels have been noted in clinical trials (see WARNINGS).

SYMPTOMS AND TREATMENT OF OVERDOSAGE

There is no specific treatment for atorvastatin overdosage. Should an overdose occur, the patient should be treated symptomatically and supportive measures instituted as required. Due to extensive drug binding to plasma proteins, hemodialysis is not expected to significantly enhance atorvastatin clearance.

DOSAGE AND ADMINISTRATION

Patients should be placed on a standard cholesterol-lowering diet [at least equivalent to the American Heart Association (AHA) Step 1 diet] before receiving LIPITOR, and should continue on this diet during treatment with LIPITOR. If appropriate, a program of weight control and physical exercise should be implemented.

Primary Hypercholesterolemia and Combined (Mixed) Hyperlipidemia, Including Familial Combined Hyperlipidemia

The recommended dose of LIPITOR is 10 mg once a day. The majority of patients achieve and maintain target cholesterol levels with LIPITOR 10 mg/day. A significant therapeutic response is evident within 2 weeks, and the maximum response is usually achieved within 2-4 weeks. The response is maintained during chronic therapy. Doses can be given at any time of the day, with or without food, and should preferably be given in the evening. Doses should be individualized according to baseline LDL-C levels, the desired LDL-C target (such as that recommended by the US National Cholesterol Education Program [NCEP] and/or the Canadian Consensus Conference Guidelines), the goal of therapy and the patient's response. Adjustments of dosage, if necessary, should be made at intervals of 4 weeks or more. The recommended dose range for most patients is 10 to 40 mg/day. The maximum dose is 80 mg/day, which may be required in a minority of patients (see section below).

Cholesterol levels should be monitored periodically and consideration should be given to reducing the dosage of LIPITOR if cholesterol falls below the targeted range such as that recommended by guidelines.

The following reductions in total cholesterol and LDL-C levels have been observed in 2 dose-response studies, and may serve as a guide to treatment of patients with mild to moderate hypercholesterolemia:

TABLE 2. Dose-Response in Patients With Mild to Moderate Hypercholesterolemia (Mean Percent Change from Baseline)[a]

Lipid Parameter	LIPITOR Dose (mg/day)			
	10 (N=22)	20 (N=20)	40 (N=21)	80 (N=23)
Total-C: 7.1 mmol/L[b] (273 mg/dL)[b]	-29	-33	-37	-45
LDL-C: 4.9 mmol/L[b] (190 mg/dL)[b]	-39	-43	-50	-60

[a] Results are pooled from 2 dose-response studies
[b] Mean baseline values

Severe Hypercholesterolemia

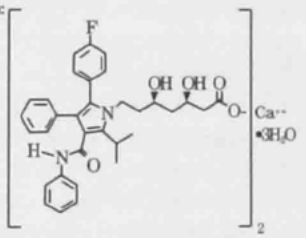
In patients with severe hypercholesterolemia, including heterozygous familial hypercholesterolemia, higher dosages (up to 80 mg/day) may be required (see WARNINGS, Muscle Effects and PRECAUTIONS, Drug Interactions).

Concomitant Therapy
See PRECAUTIONS, Drug Interactions.
Dosage in Patients With Renal Insufficiency
See PRECAUTIONS.

PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Atorvastatin calcium
Chemical Name: [R-(R*,R*)]-2-(4-fluorophenyl)-β, δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino) carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate
Empirical Formula: $(C_{33}H_{34}FN_2O_5)_2Ca \cdot 3H_2O$
Molecular Weight: 1209.42
Structural Formula:



Description: Atorvastatin calcium is a white to off-white crystalline powder that is practically insoluble in aqueous solutions of pH 4 and below. Atorvastatin calcium is very slightly soluble in distilled water, pH 7.4 phosphate buffer and acetonitrile, slightly soluble in ethanol, and freely soluble in methanol.

Tablet Composition: Each tablet contains either 10 mg, 20 mg or 40 mg atorvastatin as the active ingredient. Each tablet also contains the following non-medicinal ingredients: calcium carbonate, candelilla wax, croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, hydroxypropyl methylcellulose, polyethylene glycol, talc, titanium dioxide, polysorbate 80 and simethicone emulsion.
Stability and Storage Recommendations: Store at controlled room temperature 15 to 25°C.

AVAILABILITY OF DOSAGE FORMS

LIPITOR (atorvastatin calcium) is available in dosage strengths of 10 mg, 20 mg and 40 mg atorvastatin per tablet.
10 mg: White, elliptical, film-coated tablet, coded "10" on one side and "PD 155" on the other. Available in bottles of 90 tablets.
20 mg: White, elliptical, film-coated tablet, coded "20" on one side and "PD 156" on the other. Available in bottles of 90 tablets.
40 mg: White, elliptical, film-coated tablet, coded "40" on one side and "PD 157" on the other. Available in bottles of 90 tablets.

1. LIPITOR (atorvastatin calcium) Product Monograph, Parke-Davis Div., Warner-Lambert Canada Inc., February 1997. 2. Dart A, Jerums G et al. A multicentre, double-blind, 1-year study comparing the safety and efficacy of once-daily atorvastatin with that of simvastatin patients with hypercholesterolemia. *Am J Cardiol* 1997; in press. 3. Bertolini S, Bitollo Bon G, et al. The efficacy and safety of atorvastatin compared to pravastatin in patients with hypercholesterolemia. *Atherosclerosis* 1997; in press. 4. Davidson MM, McKenny JM, Stein EA, et al. Long term efficacy and safety of atorvastatin compared to lovastatin in hypercholesterolemic patients. *Am J Cardiol* 1997; in press. 5. Heinonen TM et al. Atorvastatin, a new HMG-CoA reductase inhibitor as monotherapy and combined with colestipol. *J Cardiovasc Pharmacol Therapeut* 1996; 1(2):117-22. 8. Parke-Davis 1997 catalogue and ODB Formulary 1996.

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Answer: Takayasu's Arteritis

Takayasu's Arteritis (TA) is an acute periarteritis that most commonly presents in young or adolescent females. This inflammatory disease has historically been seen most commonly in an Asian population but recent studies have shown that more cases are presenting around the world. In North America, the estimate of incidence is 2.6 per million persons per year (1). TA tends to affect both the proximal aorta and its branches (2) but involvement of the abdominal aorta and its branches has also been studied (3).

Among the varied signs and symptoms that TA can present with include fever, sweating, arthralgia, myalgia, cough, hemoptysis, pleural effusion, elevated ESR, and leg ulcers (4). More characteristic symptoms of TA involve a history of TIAs, stroke, cool extremities, headaches, dizziness, amaurosis fugax or diplopia (2). Even vague signs, such as intra-abdominal pain or unexplained hypertension may be important clues to mesenteric or renal artery stenosis. Physical signs (incidence percentages in patients with TA shown in parenthesis) like vascular bruits (80%), claudication (70%), aortic regurgitation (20%), carotodynia (30%) and diminished or absent pulses (60%) can often be elicited from patients with TA (1).

The disease presentation of TA typically comes in two distinct stages. In the "pre-pulseless" (early) or systemic phase, TA usually presents with the vague constitutional symptoms. This is a contrast from the obliterative or "pulseless" (late) stage where the diagnosis is usually made and the patient shows ischemic and inflammatory changes in their vasculature (5). There are no specific Human Lymphocyte Antigen markers that directly correlate with TA in the North American population (6). ESR is the only consistently elevated lab result seen in active forms of TA.

Diagnosis is generally confirmed by arteriography (especially digital subtraction angiography) as is shown in Figure 1. Now both CT and MRI are being used to show luminal narrowing and mural thickening to support the arteriographic findings of afflicted vessels (7, 8). The five year survival rate has been reported to be over 90% (2).

A differential diagnosis could include the following pathologies: 1) chronic aortitis with involvement of the common carotid artery, 2) giant cell arteritis, 3) ankylosing spondylitis, 4) congenital absence of left common carotid, 5) arterial occlusion/ embolism, 6) thromboangitis obliterans (Buerger's Disease).

Treatment usually involves the use of glucocorticoids (with 60% remission rate). Additional benefits are gained with the administration of cytotoxic agents in those who have relapse of their disease on glucocorticoids (2). Surgical treatment with bypass of significantly stenosed vessels (9) and transluminal balloon angioplasty in those with aortic obstruction (3) has been shown to be protective in the development of stroke or other thromboembolic events.

Returning to this case, the mysterious y-shaped object seen at the top of the angiogram is the bifurcation of the obliterated left common carotid. It is interesting to note the smoothness of the arch. Most initial impressions of the film tend to favor a congenital absence of the great vessel to explain the anomaly. However, the appearance of the bifurcation leads to the diagnosis of TA.

Although TA predominantly affects the aorta, upper extremity vessels and the cerebral blood supply involvement of the abdominal aorta is not uncommon (4). Examination of the renal arteries, the superior mesenteric artery and the femoral-iliac system should be undertaken, especially in the case of this patient who has a history of hypertension.

In truth, this patient did have TA involving her right renal artery that was successfully treated with balloon angioplasty at age 9. There has been no relapse of stenosis in this vessel since then. The patient had a well developed collateral blood supply through the Circle of Willis and no attempts to bypass the carotid stenosis were being considered at the time of the investigation.

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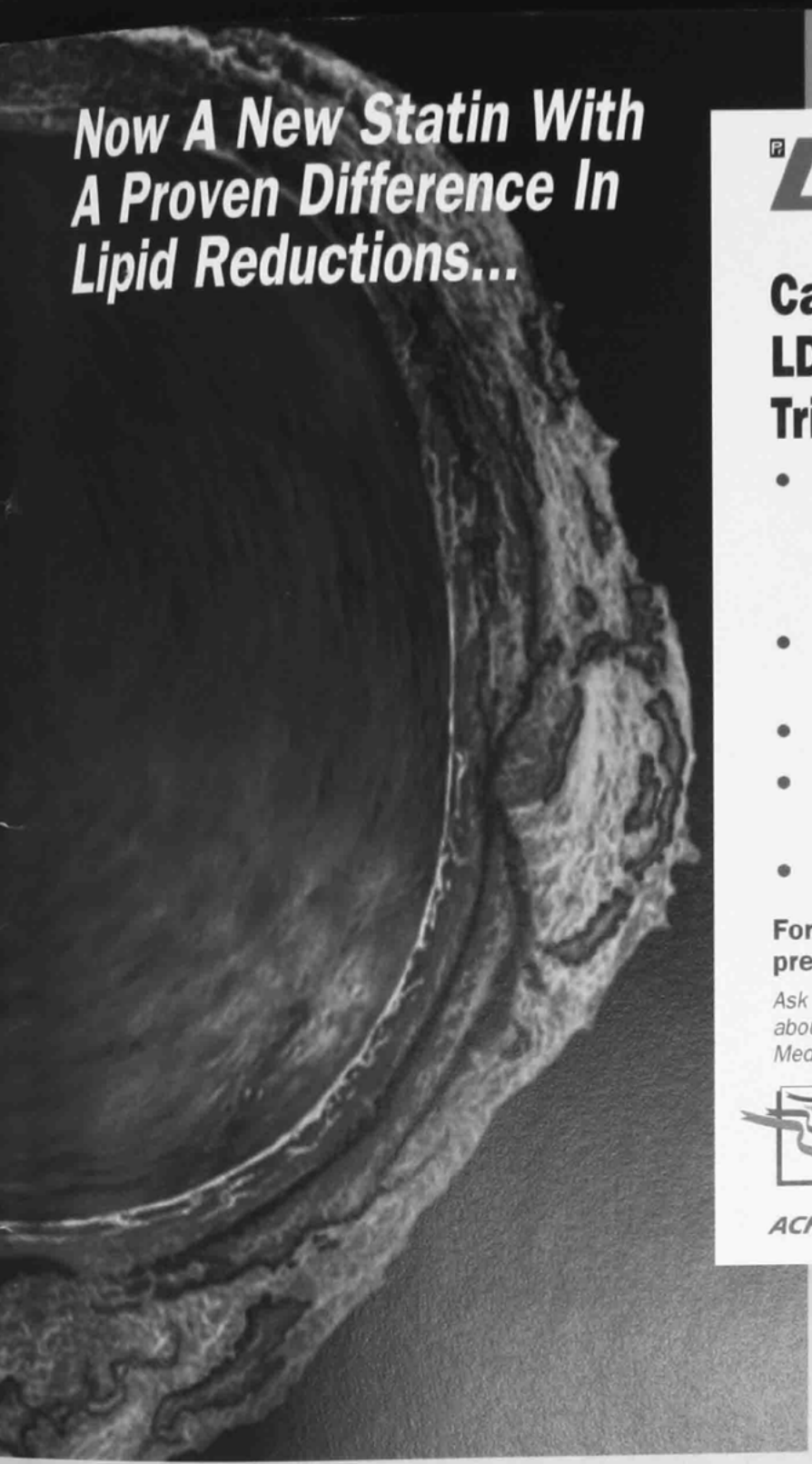

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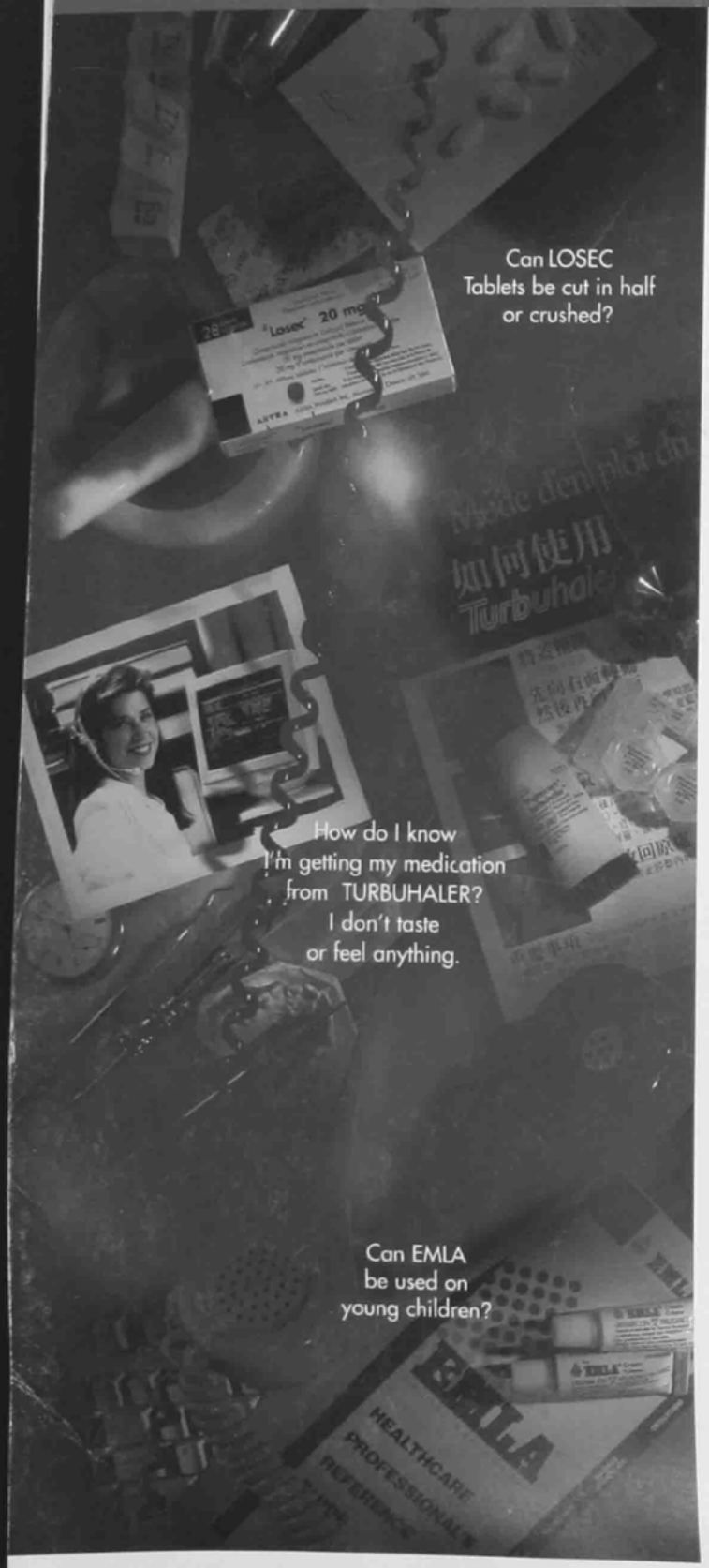

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