Coagulation Inhibitor Values in Myocardial Infarction Compared to those in Normals.

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We measured antithrombin III (ATIII) activity, protein C antigen (PC), and free and total protein S antigen (PSf, PSt) in 92 samples from the Thrombolysis in Myocardial Infarction Phase II (TIMI II) t-PA trial (76 male, 16 female), prior to therapy, and, for comparison, in samples from 92 blood donors from the Burlington Red Cross (RC) (54 male, 38 female). TIMI participants were chosen to represent the full spectrum of fibrinogenolysis; because of this, there was a greater proportion of patients with extensive fibrinogenolysis in this group than seen in the full cohort, with an average decrease in fibrinogen of 49%. The Mean(SD) age of this group was 57(10). Results presented as Mean(SEM):

Group/Age	n	PC,ug/ml	PSt,ug/ml	PSf,ug/ml	ATIII,%
RC 50-54	35	3.1(0.1)	16.2(0.4)	4.9(0.2)	102(2.1)
RC 55-60	29	3.0(0.1)	16.3(0.4)	5.0(0.4)	103(2.1)
RC 60-69	26	2.8(0.1)	16.6(0.5)	5.2(0.2)	96(2.3)
RC total	90	3.0(0.1)	16.3(0.3)	5.0(0.2)	101(1.3)
TIMI Pre	92	3.8(0.1)	15.2(0.3)	4.3(0.2)	118(1.9)

In the Red Cross groups, there is a trend towards lower PC and ATIII, and higher PS, with age (not significant). Red Cross males had slightly lower PC than females (2.9 vs 3.1 ug/ml) and higher PSf (5.4 vs 4.4 ug/ml). Unexpectedly, the infarction group, when compared to the Red Cross group as a whole, had higher PC values by 26%, higher ATIII by 17%, and lower PSf by 15% (all, P<0.0001 by T test). These results cannot be accounted for by the age or gender distribution of the TIMI group. Further studies are required to determine if these changes are causative, or reflective, of infarction pathophysiology.

PERSISTENCE OF ARTERIAL EVERSION GRAFT PATENCY UP TO 24 HOURS FOLLOWING A ONE HOUR INFUSION OF ARGATROBAN, A SELECTIVE THROMBIN INHIBITOR

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The efficacy of the synthetic thrombin inhibitor, Argatroban, relative to heparin, for the prevention of delayed (24 hrs) arterial thrombosis was studied in a rabbit femoral arterial eversion graft model. A 4-6 mm arterial segment was excised, turned inside-out and reinserted in the left femoral artery. Intravenous infusion of 50 units/kg heparin over 60 min, resulting in a 3-fold prolongation of the activated partial thromboplastin time (aPTT), was associated with arterial patency after 2 hrs in only 5 of 11 animals with persistent patency at 24 hrs in only one animal. Heparin in combination with intravenous aspirin (17 mg/kg) maintained arterial patency in 2 of 6 animals after 24 hrs. Infusion of 100 ug/kg/min Argatroban for 60 min, which resulted in a 3.5-fold prolongation of the aPTT, prevented arterial occlusion within 2 hrs in all 10 rabbits with persistent patency in 7 animals ($p = 0.008$ vs heparin). Combination of Argatroban and aspirin prevented occlusion in 6 of 8 rabbits after 24 hrs. Pathologic examination of the graft revealed that the extent of graft segment thrombosis was significantly less extensive in the Argatroban alone group than heparin alone group ($p = 0.015$). The addition of aspirin had a tendency to further reduce thrombosis ($p = 0.04$).
Conclusion:
A 1 hr i.v. infusion of Argatroban reduces delayed (24 hrs) arterial eversion graft thrombosis more efficiently than heparin.

CRYPTOGENIC STROKE PATIENTS OF ALL AGES SHOULD UNDERGO SALINE CONTRAST ECHOCARDIOGRAPHY

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Approximately 40% of ischemic cerebrovascular accidents cannot be classified as strokes of determined cause and are therefore referred to as cryptogenic strokes. Patent foramen ovale (PFO) has been implicated as a potential source of paradoxical embolism in some patients with cryptogenic stroke. Though previous studies have detected a PFO by agitated saline contrast echocardiography specifically in younger patients with strokes (age < 55 years), the diagnostic utility of this test has not been demonstrated in the stroke population unselected for age. To address this issue, we performed saline contrast echocardiography in a blinded manner in 39 consecutive pts with ischemic stroke (22 females, 17 males; range 24 - 83 years; mean age 58.7±16.0 years). Using NIH Stroke Data Bank criteria, based on presenting clinical syndrome, noninvasive vascular studies, head CT or MRI, and cerebral angiography when indicated, 23 patients (59.0%) were classified as having strokes of determined cause (10 large vessel atherosclerosis, 9 lacunar and 4 cardioembolic). The remaining 16 patients (41.0%) were classified as cryptogenic stroke patients. PFO was detected by the appearance of microbubbles in left heart cavities. Results follow:

	Cryptogenic strokes	Strokes of determined cause	Total
PFO present	7 (43.7%)	1 (4.4%)	8
PFO absent	9 (56.3%)	22 (95.6%)	31
Total	16	23	39

$p < 0.005$, Fisher's Exact test

PFO was found in >40% of cryptogenic stroke patients. Furthermore, in the 16 patients with cryptogenic stroke, PFO was noted with similar frequency in patients ≥ 55 years of age and patients < 55 years of age (3/7 vs. 4/9).

Conclusion: Paradoxical embolism may account for a sizeable number of cryptogenic strokes and can occur at any age. Hence all patients whose stroke subtype is unclear despite standard evaluation should undergo saline contrast echocardiography.

ADDITIVE EFFECT OF ASPIRIN AND CAFFEINE IN THE INHIBITION OF PLATELET THROMBUS FORMATION IN PARTIALLY STENOSED CORONARY ARTERIES IN DOGS

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Patients with coronary artery disease (CAD) have major complications due to periodic acute platelet thrombus formation in their diseased arteries. Aspirin (ASA) is taken for its antiplatelet effect, although platelets inhibited with ASA can be reactivated with elevated epinephrine (E). Caffeine (C) is widely consumed and is an equivocal risk factor in CAD. We studied the interaction of IV ASA and C in our experimental model of cyclic coronary blood flow reduction (CFR's) (EMF probe) due to acute platelet thrombus formation (APTF) in 70% stenosed circumflex coronary arteries in 10 anesthetized dogs (D). We have previously shown that either ASA 5 mg/kg or C 10-15 mg/kg inhibits APTF and CFR's in vivo but this beneficial effect is overcome by infusion of epinephrine (E) 0.2 μg/kg/min for 20 min. Six D, in which C, 15 mg/kg did not abolish CFR's were then given ASA 2.2±0.7 mg/kg. CFR's were abolished and were not renewed by E. In 4 D given ASA, 5 mg/kg first, CFR's were abolished but returned with E. After C, 6.2±1.4 mg/kg was given IV, no CFR's occurred in response to E. We postulate that caffeine may inhibit phosphodiesterase, elevating intra-platelet CAMP levels, while ASA blocks thromboxane A_2 production. This combination of agents is more effective than either agent alone. This demonstrates that an additive in vivo effect occurs at lower doses of both ASA and C to abolish APTF and CFR's than previously observed. It may be that patients with CAD taking ASA and consuming moderate amounts of C containing substances may be less likely to develop APTF, CFR's and ischemia than those on ASA alone.