

MEDICAL GRAND ROUNDS

Parkland Memorial Hospital
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ANTICOAGULANT THERAPY IN CORONARY HEART DISEASE

CASE #1: [REDACTED]

A 45-year-old [REDACTED] was admitted on [REDACTED]/62 to the medical service. A week prior to admission he experienced a dull substernal pain radiating to the left shoulder and arm. An electrocardiogram was reported to be normal. The pain recurred daily and was precipitated by exertion. An hour or two prior to admission, he felt dizzy and lost consciousness for a few minutes. On admission the patient looked ill and perspiring. Blood pressure was 110/80; pulse was 90 and regular. The neck veins were flat. The lungs were clear. The heart was not enlarged; A2 was greater than P2. The peripheral pulsations were equal bilaterally. The electrocardiogram revealed an acute anteroseptal myocardial infarction.

The patient was started on heparin 75 mg. and subsequently on 100 mg. every 8 hours subcutaneously. The clotting time varied between 25 min. and 1 hour. On [REDACTED]/62 (the [REDACTED] day) he complained of a right flank pain and tenderness; in the same afternoon he experienced temporary blurring of vision. Urinalysis disclosed 6-10 RBC/hpf, and IVP a nonfunctioning right kidney.

CASE #2: [REDACTED]

A 50-year-old [REDACTED] was admitted from the [REDACTED] on [REDACTED]/63 with the chief complaints of hematuria and precordial pain. In [REDACTED] 1962 and [REDACTED] 1963, the patient was hospitalized with the diagnosis of acute myocardial infarction. He was started on oral anticoagulant therapy and maintained on 3 mg. Liquamar daily. His last prothrombin time was 22/12 sec. (two weeks prior to admission). While en route from [REDACTED] ([REDACTED]/63), he noticed that his urine was red. He stopped his anticoagulant and four days later ([REDACTED]/63) his prothrombin time was 35 sec. (control 12 sec.).

On admission the blood pressure was 120/80. He had bilateral arcus senilis. The lungs were clear and the heart sounds were regular and of good quality. The electrocardiogram revealed a posterior myocardial infarction of undetermined age. The SGOT determinations for 3 consecutive days were normal. From [REDACTED] to [REDACTED] the urine was loaded with red blood cells. On [REDACTED], few red cells were seen on microscopy, at a time when the prothrombin time was 18 sec. (control 12 sec.). On [REDACTED], the patient was restarted on Liquamar and he is doing well at present.

He was started on anticoagulant therapy and maintained on 5 mg. daily. His prothrombin time was maintained around 25 sec. (control 12 sec.).

CASE #3: [REDACTED]

A 65-year-old man was admitted on [REDACTED]/59 with acute pulmonary edema. For the past three weeks, he began experiencing exertional dyspnea and bouts of nocturnal dyspnea. The patient denied chest pain and hemoptysis. In 1952 he developed right facial paralysis, and the diagnosis of systemic hypertension was made. On admission his blood pressure was 180/90; the pulse was irregular and 140/min. He was moderately obese and cyanotic. Inspiratory moist crepitant rales were heard bilaterally over the lung fields. The heart was enlarged but the sounds were obscured by the chest findings.

The electrocardiogram on admission revealed Q waves in II, III, aVF, left axis deviation and ST-T wave changes. The patient was digitalized and adequately treated. He was started on oral anticoagulant therapy (Coumadin). On the second day he complained of precordial chest pain that was exaggerated by deep inspiration; an aortic systolic murmur (grade 2) became audible. The electrocardiogram revealed an elevated ST in leads V₄-V₆. By the fifth day the prothrombin time was 26/12 sec. From [REDACTED] 1959, the patient was asymptomatic. His prothrombin time ranged between 22 and 28 sec. (control 12 sec.). On [REDACTED] 1959, a friction rub became audible; the prothrombin time was 30/12 sec. From [REDACTED] 1959, the patient complained of frequent episodes of chest pain associated with cold sweat and pallor. On [REDACTED] 1959, the blood pressure dropped to 90/60 and heart sounds became distant. The electrocardiogram continued to show marked elevation of ST. Pericardiocentesis was attempted but no pericardial fluid could be obtained. The patient expired a few hours later.

Postmortem examination revealed a distended pericardial sac with 500 cc. of unclotted blood and a fibrinous pericarditis involving both layers. Severe coronary arteriosclerosis with multiple occlusions were found together with healing and recent subendocardial infarctions.

CASE #4: [REDACTED]

A 34-year-old [REDACTED] was admitted to the hospital on [REDACTED]/62 with complaints of sudden onset of chest pain associated with dyspnea and profuse sweating. The pain was crushing in character and radiated to the neck and left arm. The pain lasted 20 to 30 minutes and was relieved by nitroglycerin. There was no previous history of angina. His father died at age 50 while asleep.

On admission, the patient was extremely pale and had frequent premature beats. The blood pressure was 110/70. The heart sounds were normal; the lungs were clear. The rest of his physical examination was noncontributory. His serum cholesterol ranged between 310 and 380 mg.%. SGOT was normal. The electrocardiogram revealed prominent T waves in V₂-V₄ which later became symmetrically negative in I, aVL, V₂-V₆.

He was started on anticoagulant therapy and maintained on 5 mg. daily. His prothrombin time was maintained around 25 sec. (control 12 sec.).

On [REDACTED]/62, the patient experienced total hematuria. His prothrombin time was 37/12 sec. The hematuria was controlled by small doses of vitamin K₁. On the third day, the prothrombin time was 14/12 sec. About 10 days prior to this episode, the patient took D-thyroxine and nicotinic acid for his moderate hypercholesterolemia. Subsequent to this bleeding episode, he was restarted on Coumadin and needed 2.5 mg. every other day to achieve the desired prothrombin level.

Table 1

CLINICAL CONDITIONS ASSOCIATED WITH HYPERCOAGULABLE STATE
(Sise, et al.)

1. Venous thrombosis in cancer (mucin-producing cancers)
2. Other conditions:
 - a. Post-myocardial infarction
 - b. Atherosclerosis and coronary heart disease
 - c. Congestive heart failure
 - d. Postoperative state
 - e. Prolonged inactivity
 - f. Pregnancy - Post-partal heart disease

Table 11

THE EFFECT OF ANTICOAGULANT THERAPY IN ACUTE MYOCARDIAL INFARCTION
ON THE MORTALITY RATE AND ON THE THROMBOEMBOLIC COMPLICATIONS

	Anticoagulant			Control		
	No. of Cases	Per cent	T.E. Episodes Per cent	No. of Cases	Per cent	T.E. Episodes Per cent
Peters, et al. (1946)	50	4	2	60	21	16
Griesman, et al. (1948)	75	9	4	100	35	21
Glueck, et al. (1948)	44	20	7	44	45	17
Wright, et al. (1948)	432	15	11	368	24	25
Wright, et al. (1953)	408	7	—	326	13	—
Hilton, et al. (1949)	38	—	18	38	—	32
Tulloch-Gilchrist (1951)	70	23	13	84	40	29
Holton (1950)	174	22	4	256	36	14
Loudon, et al. (1953)	75	25	15	125	41	21
Furman, et al. (1953)	100	18	—	211	32	—
Beaumont, et al. (1953)	71	10	—	96	37	—
Evans (1952)	—	—	—	1000	19	—

Table III

THE VALUE OF ANTICOAGULANT THERAPY IN THE
"GOOD" AND "POOR RISK" PATIENTS

	<u>No. of Cases</u>	<u>Mortality %</u>	<u>Emboli %</u>
I. Russek			
"Good Risk"	285	3.5	0.7
"Poor Risk"	338	70.1	12.4
Total	623	29.6	7.1
II. Burton			
"Good Risk" - Anticoagulant	98	2	6
- Control	58	5	11.5
"Poor Risk" - Anticoagulant	163	19	15
- Control	184	40	24
III. Conrad, et al.			
"Good Risk" - Anticoagulant	59	3.4	3.4
- Control	129	20.9	8.5
"Poor Risk" - Anticoagulant	87	26.4	6.9
- Control	348	56.3	17.5

Table IV

INDICATIONS FOR LONG-TERM ANTICOAGULANT THERAPY

1. Myocardial infarction under age of 55
2. After two infarctions at any age
3. Severe angina of less than 24 months' duration
4. Recurrent embolization
5. Thrombophlebitis or thromboembolic disease
6. Familial hypercholesterolemia and myocardial infarction

CONTRAINDICATIONS FOR ANTICOAGULANT THERAPY

1. In an uncooperative or indifferent patient
2. Chronic alcoholism and/or hepatic disease
3. Renal insufficiency
4. Blood dyscrasia (hemorrhagic tendency)
5. Ulcerative lesions of the GI tract
6. Severe debility and cachexia
7. Inadequate laboratory facilities

Table V

	<u>Generic Name</u>	<u>Trade Name</u>	<u>Usual Initial Dose</u>	<u>Usual Maintenance Dose</u>
<u>Coumarin</u>				
	1. Bishydroxycoumarin	Dicumarol	300-600	25-100
	2. Ethyl biscoumacetate	Tromexan	900-1200	600+
	3. Warfarin	Coumadin	40-60	5-10
<u>Indandione</u>				
	1. Phenindione	Danilone Hedulin	200-400	50-100
	2. Diphenadione	Dyraxin	20-50	3-5

Table VI

PROTHROMBIN RESPONSE AND DISAPPEARANCE RATE OF VARIOUS HYPOPROTHROMBINEMIC AGENTS AFTER ONE INTRAVENOUS DOSE IN MAN
(Weiner, et al.)

		Half-Life	<u>Day of Prothrombin</u>		Rate of Metabolism
			Peak	Recovery	
Tromexan	1650 mg.	2.5 hours	1	2	25% per hour
Phenylindanedione	350 mg.	6.5 hours	2	4	10% per hour
Dicumarol	400 mg.	32 hours	2-3	5	25% per day
Warfarin	65 mg.	90 hours	2-3	5-6	17% per day

Table VII

	<u>Prothrombin</u>	<u>Factor VII</u>	<u>Factor IX</u>	<u>Factor X</u>
Quick Test	—	+	—	—
"P-P" Test	+	+	—	—
Thrombotest	+	+	+	+

HYPERCOAGULABILITY AND BLOOD COAGULATION

11. McDonald, J. L., "Hypercoagulability, thrombosis and arteriosclerosis in hemophilia," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
12. Campbell, J. L., and J. L. McDonald, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
13. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
14. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
15. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
16. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
17. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
18. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
19. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).
20. McDonald, J. L., and others, "The hypercoagulability in hemophilia (factor VIII deficiency) in relation to the hypercoagulability in other diseases," *Am. J. Med. Sci.*, **195**, 1-10 (1953).

REFERENCES

1. Shapiro, E.: Reasons for the unsettled state of the anticoagulant controversy. *Dis. Chest* 35:95, 1962 (Jan.).

THROMBOGENIC THEORY

2. Plotz, M.: *Coronary Heart Disease: Angina Pectoris, Myocardial Infarction*. Hoeber-Harper, New York, 1957, p. 71.
3. Groen, J., and Van der Heide, R.: Atherosclerosis and coronary thrombosis. *Medicine* 38:1, 1959.
4. Duguid, J.: Diet and coronary disease. *Lancet* 1:891, 1954.
5. Duguid, J.: Thrombosis as a factor in the pathogenesis of aortic atherosclerosis. *J. Path. & Bact.* 60:57, 1948.
6. Duguid, J.: Mural thrombosis in arteries. *Brit. Med. Bull.* 11:36, 1955.
7. Woolf, N., and Crawford, T.: Fatty streaks in the aortic intima studied by an immuno-histochemical technique. *J. Path. & Bact.* 80:405, 1960.
8. Gore, I., and Stone, F.: Editorial: Atherosclerosis and thrombosis. *Circulation* 25:753, 1962 (May).
9. Gore, I., and Larkey, B.: Functional activity of aortic mucopolysaccharides. *J. Lab. & Clin. Med.* 56:839, 1960.
10. Kirk, J.: Anticoagulant activity of human arterial mucopolysaccharides. *Circulation* 20:975, 1959.

HYPERCOAGULABLE STATE IN MYOCARDIAL INFARCTION

11. McDonald, L.: Blood coagulation, thrombosis and atherosclerosis in ischemic heart disease. *Proc. Roy. Soc. Med.* 53:35, 1960.
12. Cooperberg, A., and Teitelbaum, J.: The concentration of antihemophilic globulin (AHG) in patients with coronary artery disease. *Ann. Int. Med.* 54:899, 1961.
13. Rosenthal, R., and Weaver, J.: Acceleration of blood coagulation in acute myocardial infarction as demonstrated by the heparin clotting time; effect of dicumarol therapy. *Circulation* 6:257, 1952 (Aug.).
14. Beaumont, J., Chevalier, H., and Lenegre, J.: Studies on spontaneous variations in blood coagulability immediately following myocardial infarction. *Am. Heart J.* 45:756, 1953.
15. Ennis, G.: Blood coagulation following myocardial infarction. *Circulation* 18:716, 1958.

16. Sise, H., Moschos, C., and Becker, R.: On the nature of hypercoagulability. *Am. J. Med.* 33:667, 1962.

ANTICOAGULANT THERAPY IN MYOCARDIAL INFARCTION

A. SHORT-TERM

17. Solandt, D., Nassin, R., and Best, C.: Production and prevention of cardiac mural thrombosis in dogs. *Lancet* 2:592, 1939.
18. Russek, H., Zohman, B., Doerner, A., Russek, A., and White, L.: Indications for bishydroxycoumarin (Dicumarol) in acute myocardial infarction. *Circulation* 5:707, 1952 (May).
19. Russek, H., and Zohman, B.: "Selective" versus "routine" use of anticoagulants in acute myocardial infarction. *J.A.M.A.* 156:1130, 1954 (Nov. 20).
20. Russek, H.: Hazards in the treatment of acute myocardial infarction. *Am. J. Med. Sci.* 232:403, 1956 (Oct.).
21. Schnur, S.: The current dispute concerning anticoagulants in acute myocardial infarction. *J.A.M.A.* 156:1127, 1954 (Nov. 20).
22. Russek, H.: Present status of anticoagulant therapy in acute myocardial infarction. *Dis. Chest* 43:541, 1963 (May).
23. Hilden, T., Raaschou, F., Iversen, K., and Schwartz, M.: Anticoagulants in acute myocardial infarction. *Lancet* 2:327, 1961 (Aug. 12).
24. Harvald, B., Hilden, T., and Lund, E.: Long-term anticoagulant therapy after myocardial infarction. *Lancet* 2:626, 1962 (Sept. 29).
25. Evans, W.: Anticoagulant therapy in coronary occlusion. *Proc. Roy. Soc. Med.* 47:318, 1954.
26. Honey, G., and Truelove, S.: Prognostic factors in myocardial infarction. *Lancet* 1:1155, 1957.
27. Wright, I., Marple, C., and Beck, D.: Myocardial infarction. Its clinical manifestations and treatment with anticoagulants. New York, Grune and Stratton, Inc., 1954.
28. Wright, I.S., Beck, D.F., and Marple, C.D.: Myocardial infarction and its treatment with anticoagulants: A summary of the findings for 1031 cases. *Mod. Concepts Cardiovasc. Dis.* 23:208, 1954 (Jan.).
29. Burton, C.: Anticoagulant therapy of recent cardiac infarction. *Canad. Med. Assn. J.* 70:404, 1954.
30. Wright, I.: The use of anticoagulants in coronary heart disease; progress and problems, 1960. *Circulation* 22:608, 1960 (Oct.).

31. Conrad, F., and Rothermick, N.: A clinicopathological study of acute myocardial infarction and the role of anticoagulant therapy. *Arch. Int. Med.* 103:421, 1959 (March).
32. Anticoagulant treatment for coronary thrombosis. *Lancet* 1:1148, 1963 (May 25).
33. Holten, C.: Evaluation of anticoagulant therapy for myocardial infarction. *Lancet* 2:1386, 1962 (Dec. 29).
34. Master, A., Weiser, F., and Rabin, R.: The emergency treatment of the complications of acute coronary artery occlusion. *Dis. Chest* 42:457, 1962 (Nov.).
35. Reznik, W.: Preinfarction angina. An interpretation. *Mod. Concepts Cardiovasc. Dis.* 31:757, 1962 (Nov.).

ANTICOAGULANT THERAPY IN MYOCARDIAL INFARCTION

B. LONG-TERM

36. Ensor, R., and Peters, R.: Long term anticoagulant therapy in coronary disease. *J.A.M.A.* 169:914, 1959 (Feb. 28).
37. Borchgrevink, C. F.: Long-term anticoagulant therapy in angina pectoris and myocardial infarction. A clinical trial of intensive versus moderate treatment. *Acta Med. Scand.* 168(Suppl. 359):1-52, 1960.
38. Myers, J., and Bauer, F.: Anticoagulant therapy in the relatively young male with myocardial infarction. *Ann. Int. Med.* 55:760, 1961 (Nov.).
39. Thomes, B., Scallen, R., and Savage, R.: The prophylactic value of long term anticoagulant therapy. *Circulation* 21:354, 1960 (March).
40. Owren, P.: Indications for anticoagulant therapy. *New Eng. J. Med.* 268:1173, 1228, 1963.
41. Long-term anticoagulants after cardiac infarction. *Lancet* 1:718, 1959 (April 4).
42. Thomes, B.: Long term anticoagulant therapy. *Minnesota Med.* 45:995, 1962 (Oct.).
43. Thomes, A., Schallen, R., and Savage, I.: Value of long-term anticoagulant therapy in coronary disease. *J.A.M.A.* 176:181, 1961 (April 22).
44. Suzman, M., Ruskin, H., and Goldberg, B.: An evaluation of the effect of continuous long-term anticoagulant therapy on the prognosis of myocardial infarction: a report of 82 cases. *Circulation* 12:338, 1955 (Sept.).
45. Nichol, S., Phillips, W., Casten, G.: Virtue of prompt anticoagulant therapy in impending myocardial infarction: Experiences with 318 patients during a 10-year period. *Ann. Int. Med.* 50:1158, 1959.

46. Cole, D., Singian, E., and Katz, L.: The long-term prognosis following myocardial infarction and some factors which affect it. *Circulation* 9:321, 1954 (March).
47. Nichol, E. S., Keyes, J. N., Borg, J. F., Coogan, T. J., Boehrer, J. J., Mullins, W. L., Scott, T., Page, R., Griffith, G. C., and Massie, E.: Long-term anticoagulant therapy in coronary atherosclerosis. *Am. Heart J.* 55:142, 1958 (Jan.).
48. Manchester, B.: The value of continuous (1 to 10 years) long-term anticoagulant therapy. *Ann. Int. Med.* 47:1202, 1957.
49. Manchester, B.: Problems in the management of long-term anticoagulant therapy in coronary heart disease. *Prog. Cardiovasc. Dis.* 6:272, 1963 (Nov.).
50. Bjerkelund, C.: Therapeutic level in long term anticoagulant therapy after myocardial infarction. *Am. J. Cardiol.* 11:158, 1963.
51. Levy, R.: A critique of certain measures presently employed in managing patients with cardiac infarction. *Am. Heart J.* 64:1, 1962 (July).
52. Seaman, A.: An overview of anticoagulant therapy for coronary artery disease. *Am. J. Med.* 33:717, 1962.
53. McMichael, J.: Long term anticoagulant therapy. *Brit. Med. J.* 1:970, 1959 (April 11).
54. Hilden, T.: Anticoagulant therapy in acute myocardial infarction. (Letter to the Editor) *J.A.M.A.* 183:903, 1963 (March 9).

EFFECTS OF ANTICOAGULANTS (Besides Effects on Clotting Mechanism)

55. Gilbert, N., and Nalefski, L.: The effect of heparin and Dicumarol in increasing the coronary flow volume. *J. Lab. & Clin. Med.* 34:797, 1949.
56. Meyer, J.: Localized changes in properties of the blood and effects of anticoagulant drugs in experimental cerebral infarction. *New Eng. J. Med.* 258:151, 1958.
57. Schuller, E.: Donnees Recentes sur le traitement anticoagulant. *Presse Med.* 71:9, 1963.
58. Alexander, B.: Anticoagulant therapy with coumarin congeners. Action and guidelines. *Am. J. Med.* 33:679, 1962.
59. Weiner, M., Brodie, B., and Burns, J.: A comparative study of hypoprothrombinemic agent. The physiologic disposition and chemical pharmacology of coumarin and indanedione compounds. *Intern. Conf. on Thrombosis and Embolism*. B. Schwabe & Co., Basel, 1955, pp. 181-193.
60. Newcomb, T.: Current concepts in therapy. *New Eng. J. Med.* 280:545, 1959 (March 12).

61. Alexander, B., and Wessler, S.: A guide to anticoagulant therapy. *Circulation* 24:123, 1961 (July).
62. Murray, D., Jaques, L., Perrett, T., and Best, C.: Heparin and the thrombosis of veins following surgery. *Surgery* 2:163, 1937.
63. Wishart, J., and Chapman, C.: Dicumarol therapy in congestive heart failure. *New Eng. J. Med.* 239:701, 1948 (Nov. 4).
64. Anderson, G., and Hull, E.: The effect of dicumarol upon the mortality and incidence of thromboembolic complications in congestive heart failure. *Am. Heart J.* 39:697, 1950 (May).
65. Proctor Harvey, W., and Finch, C.: Dicumarol prophylaxis of thromboembolic disease in congestive heart failure. *New Eng. J. Med.* 242:208, 1950 (Feb. 9).
66. Levinson, D., and Griffith, G.: Evaluation of anticoagulant therapy in congestive heart failure. *Circulation* 4:416, 1951 (Sept.).
67. Glueck, H., Hyder, H., and Wasserman, P.: The prevention of thromboembolic complications in myocardial infarction by anticoagulant therapy. A clinical-pathologic study. *Circulation* 13:884, 1956 (June).
68. Hermann, R., Davis, J., and Holden, W.: Pulmonary embolism. A clinical and pathologic study with emphasis on the effect of prophylactic therapy with anticoagulants. *Am. J. Surg.* 102:19, 1961 (July).
69. Minales-Lopez, B., Carrillo, P., Toledo, F., and McCook, G.: Long-term anticoagulant therapy in the treatment of intermittent claudication. *Angiology* 8:534, 1957 (Dec.).

TESTS USED IN FOLLOW-UP MANAGEMENT

70. Boyles, P., and Nichol, S.: Coagulation defects induced by long-term anticoagulant therapy. *J. Am. Geriatric Soc.* 8:419, 1960 (June).
71. Matthews, J. M., and Walker, W.: Control of anticoagulant therapy. A trial of thrombotest. *Lancet* 2:1159, 1959 (Dec. 26).
72. Allington, M. J.: Thrombotest method for the control of anticoagulant therapy. *Lancet* 1:224, 1960 (Jan. 23).
73. Lempert, H., and Poller, L.: Evaluation of thrombotest in the control of anticoagulant therapy. *Lancet* 2:1115, 1960 (Nov. 19).
74. Moore, C., and Beeler, M.: Thrombotest versus one-stage prothrombin time determination. *New Eng. J. Med.* 264:681, 1961 (April 6).
75. Rager, C.: Place du temps de Quick et du thrombotest d'Owren dans les surveillances du traitement anticoagulant aise longs cours. *Arch. mal coeur* 56:695, 1963 (June).

COMPLICATIONS OF ANTICOAGULANT THERAPY

76. Jaques, L.: Spontaneous hemorrhage with anticoagulants. *Circulation* 25:130, 1962 (Jan.).
77. Michaels, M.: Bleeding from occult tumors during anticoagulant therapy. *Circulation* 25:804, 1962 (May).
78. Fuller, J. A.: Experiences with long-term anticoagulant treatment. *Lancet* 2:489, 1959 (Oct. 3).
79. Dickerson, J., and Morrison, F.: Cardiac tamponade with anticoagulant treatment of myocardial infarction. *J.A.M.A.* 174:1939, 1960 (Dec. 10).
80. Grosogeat, Y., and Maurice, P.: Pericardite aigue primitive avec "tamponade" mortelle: role aggravant du traitement anticoagulant. *Arch. mal coeur* 54:985, 1961 (Sept.).
81. Messinger, W., and Emmanuel, G.: Recognition and treatment of hemopericardium and hemorrhagic pericarditis by pericardiotomy. *Arch. Int. Med.* 103:613, 1959 (April).
82. Wessler, S., Zoll, P., and Schlesinger, M.: The pathogenesis of spontaneous cardiac rupture. *Circulation* 6:334, 1952.
83. Aarseth, S., and Lange, H.: The influence of anticoagulant therapy on the occurrence of cardiac rupture and hemopericardium (81 of them cardiac ruptures). *Am. Heart J.* 56:250, 1958.
84. Lange, H., and Aarseth, S.: The influence of anticoagulant therapy on the occurrence of cardiac rupture and hemopericardium following heart infarction. A controlled study of a selected treated group based on 1044 autopsies. *Am. Heart. J.* 56:257, 1958.
85. Smith, W.: "Postcardiotomy syndrome", anticoagulants and hemopericardium. *Lancet* 1:750, 1961 (April 8).
86. Watson, R., and Pierson, R.: Effect of anticoagulant therapy upon aspirin-induced gastrointestinal bleeding.
87. Owens, J., Neely, W., and Owen, W.: Effect of sodium dextrothyroxine in patients receiving anticoagulants. *New Eng. J. Med.* 266:76, 1962 (Jan. 11).
88. Magid, E.: Tolerance to anticoagulants during antibiotic therapy. *Scand. J. Clin. & Lab. Invest.* 14:565, 1962.
89. Weiner, M., and Dayton, P.: Effect of barbiturates on coumarin activity. *Circulation* 20:783, 1959.
90. Beamish, R., and McCreath, N.: Intestinal obstruction complicating anticoagulant therapy. *Lancet* 2:390, 1961 (Aug. 19).

91. Hafner, C., Cranley, J., Krause, R., and Strasser, E.: Anticoagulant ileus. J.A.M.A. 182:947, 1962 (Dec. 1).
92. Kipen, C.: Gangrene of the breast. A complication of anticoagulant therapy: report of two cases. New Eng. J. Med. 265:638, 1961 (Sept. 28).
93. Audier, M., Galinier, L., Ruf, G., and Serradimigni, A.: Les dangers des traitements anticoagulants. Presse Med. 70:1093, 1962 (May 5).
94. Duron, L., and Vander Veer, J.: Recurrent myocardial infarction after cessation of anticoagulant therapy. Am. Heart J. 60:6, 1960 (July).
95. Sise, H., Gauthier, J., and Becker, R.: Risk of interrupting long-term anticoagulant treatment. Circulation 20:771, 1959.
96. Rustad, H., and Myhre, E.: Surgery during anticoagulant treatment. The risk of increased bleeding in patients on oral anticoagulant treatment. Acta Med. Scand. 173:115, 1963 (Jan.).
97. Behrman, S., and Wright, I.: Dental surgery during continuous anticoagulant therapy. J.A.M.A. 175:483, 1961 (Feb. 11).

of the patient's condition, and the patient was discharged from the hospital. The patient was subsequently readmitted to the hospital for a second episode of bleeding. The patient is now being treated with a low-dose regimen of ASA.

The patient's condition improved after the second episode of bleeding. The patient was subsequently readmitted to the hospital for a third episode of bleeding. The patient is now being treated with a low-dose regimen of ASA.

CASE #2: A 35-year-old male with juvenile hemophilia A. The patient had a long history of bleeding episodes, with the most recent episode occurring in 1960. The patient was treated with a low-dose regimen of ASA, and the bleeding episodes stopped. The patient is now being treated with a low-dose regimen of ASA.

ASA was restarted 11/6/60 with no further bleeding. The patient was treated with a low-dose regimen of ASA, and the bleeding episodes stopped. The patient is now being treated with a low-dose regimen of ASA.

Prothrombin times during periods of melena varied from 64 to 72 seconds. The platelet count was 600,000. The hemoglobin fell from 15.0 to 10.0 g/dl. The patient is now being treated with a low-dose regimen of ASA.