three-year periods of observation there was no evidence of a waning in the degree of protection afforded by the pertussis vaccines.

Swabs were taken from 96.4% of all clinical cases, and in 59.8% a bacteriological confirmation was obtained.

Each batch of vaccine gave substantial protection, but the two batches supplied by the Michigan Department of Health gave a considerably greater degree of protection than the others.

Vaccines prepared in this country according to the method used by the Michigan Department of Health are now being tested in similar field trials. An investigation is also being made in which the immunizing properties of vaccines as indicated by laboratory tests are being compared with their prophylactic value in the field.

The Whooping-cough Immunization Committee and the medical officers of health concerned wish to record their gratitude to the many parents who, in the full knowledge that their children would not necessarily receive pertussis vaccine, consented to take part in the investigation. They also wish to thank Messrs. Parke Davis and Co., of Detroit, the Michigan Department of Health, and Messrs. Glaxo Laboratories Ltd. for the free supply of pertussis vaccines, and Messrs. Burroughs Wellcome and Co. for the free supply of "anticatarrhal" vaccine.

REFERENCES

- Anderson, I. M., and Morris, D. (1950). *Lancet*, **1**, 537.
 Bell, J. A. (1941). *Publ. Hlth Rep., Wash.*, **56**, 1535.
 — (1948). *J. Amer. med. Ass.*, **137**, 1276.
 Bradford, W. L., and Slavin, B. (1937). *Amer. J. publ. Hlth*, **27**, 1277.
 Brown, J. H. (1926). *Johns Hopk. Hosp. Bull.*, **38**, 147.
 Byers, R. K., and Moll, F. C. (1948). *Pediatrics*, **1**, 437.
 Cockburn, W. C., and Holt, H. D. (1948). *Mon. Bull. Minist. Hlth, Lond.*, **7**, 156.
 Cruickshank, R., and Knox, R. (1946). *Ibid.*, **5**, 233.
 Doull, J. A., Shibley, G. S., Haskin, G. E., Bancroft, H., McClelland, J. E., and Hoelscher, H. (1939). *Amer. J. Dis. Child.*, **58**, 691.
 Eldering, G., and Kendrick, P. (1938). *J. Bact.*, **35**, 561.
 Felton, H. M., and Willard, C. Y. (1944). *J. Amer. med. Ass.*, **126**, 294.
 Geffen, D. H. (1950). *Med. Offr.*, **83**, 137.
 Hill, A. Bradford, and Knowelden, J. (1950). *British Medical Journal*, **2**, 1.
 Kendrick, P. L. (1942). *Amer. J. publ. Hlth*, **32**, 615.
 — (1943). *Amer. J. Hyg.*, **38**, 193.
 — and Eldering, G. (1939). *Ibid. (Sect. B)*, **29**, 133.
 — Dixon, M. K., and Misner, J. (1947). *Amer. J. publ. Hlth*, **37**, 803.
 — Updyke, E. L., and Eldering, G. (1949). *Ibid.*, **39**, 179.
 Leslie, P. H., and Gardner, A. D. (1931). *J. Hyg., Camb.*, **31**, 423.
 Lewis, J. Tudor (1946). *Med. Offr.*, **76**, 5.
 McCloskey, B. P. (1950). *Lancet*, **1**, 659.
 McFarlan, A. M., Topley, E., and Fisher, M. (1945). *British Medical Journal*, **2**, 205.
 Madsen, T. (1933). *J. Amer. med. Ass.*, **101**, 187.
 Martin, J. K. (1950). *Arch. Dis. Childh.*, **25**, 1.
 Miller, J. J., Saito, T. M., and Silverberg, R. J. (1941). *J. Pediat.*, **19**, 229.
 Pittman, M., and Lieberman, J. E. (1948). *Amer. J. publ. Hlth*, **38**, 15.
 Sauer, L. (1937). *J. Amer. med. Ass.*, **109**, 487.
 Siegel, M., and Goldberger, E. W. (1937). *Ibid.*, **109**, 1088.
 Sohler, R., and Fauchet, S. (1949). *Bull. Acad. nat. Méd., Paris*, **133**, 202.
 Toomey, J. A. (1949). *J. Amer. med. Ass.*, **139**, 448.
 United States Biologics Control Laboratory, National Institutes of Health (1948). "Minimum Requirements for Pertussis Vaccine."

The World Health Organization is helping the Indian Government take preventive action against possible outbreaks of cholera and malaria in the famine-stricken area of Bihar. An appropriation of \$30,000 was made to purchase bleaching powder to sterilize drinking-water as a measure against cholera, and proguanil tablets to prevent malaria. In presenting the Indian request for aid, the W.H.O. regional director for South-east Asia stated that the area affected, with a population of about 20 million people, is normally subject to outbreaks of cholera and malaria, and that the famine conditions that now exist are bound to aggravate the situation.

PROGNOSIS AND TREATMENT OF CARDIAC INFARCTION

A SURVEY OF 200 PATIENTS

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The mortality in untreated series of myocardial infarction has been extensively reviewed in recent publications (Tulloch and Gilchrist, 1950; *Lancet*, 1950). The figures given in different statistics vary between 20 and 40% for the first four weeks following cardiac infarction. About 25% of the patients die either in the seizure or within two months of it, 50% by the end of the first year, 75% by the end of the third year, and 80% by the end of five years (Katz, Mills, and Cisneros, 1949). The average period of survival after the appearance of coronary artery disease, estimated at three and a half years by Levine and Rosenbaum (1941), is now said by McCain, Kline, and Gilson (1950) to be only one and a half years. Cardiac infarction is not a disease of uniform severity, and statistics, however large in number, give only a rough average of the variants encountered in cardiological practice. Although the prognostic significance of the individual symptoms was subjected to painstaking analysis by Rosenbaum and Levine (1941) and by Mintz and Katz (1947), it is rather the grouping of symptoms into clinical features which determines the degree of gravity and the outcome of the disease.

We were impressed by the fact that in a survey comprising 109 cases of cardiac infarction, mostly untreated by anticoagulants, there were 33—almost one-third—in which shock and cardiac failure were absent and in which prolonged cardiac pain accompanied by conclusive electrocardiographic changes were frequently the only diagnostic features (Papp and Shirley Smith, 1951). All these patients survived the two-months period of close observation. Post-mortem evidence has since proved that these slight coronary attacks correspond to sub-epicardial cardiac infarctions rarely reaching the endocardial surface. Others in our series were unmistakable examples of severe cardiac infarction showing the critical combination of persistent circulatory shock and early congestive heart failure. A middle group of moderate cases could be formed of those in which the ominous symptoms of the severe group appeared only for a short time, in which shock did not outlast the pain, and in which signs of left ventricular failure did not go beyond fleeting basal crepitations.

It seemed worth while, therefore, to investigate separately the prognosis of patients afflicted with slight, moderate, and severe infarctions; to review the complications in the different groups and the ensuing disabilities; and to correlate the clinical and electrocardiographic findings. It was hoped that this study might help to define the treatment of the individual case and lend some precision to prognosis. Patients who had full anticoagulant treatment were considered separately.

Material and Method of Study

From May, 1948, till the end of December, 1950, 200 consecutive cases of cardiac infarction (25 of them treated with anticoagulants) were collected from three different sources—from consultant practice (K.S.S.), from general practice (C.P.), and from Charing Cross Hospital in- and out-patient departments. These were partly recent cases with infarctions less than a fortnight old, and partly older ones which came for control and in which detailed data of the original attack were available. Each case was assessed on the basis of the clinical and electrocardiographic signs exhibited during the attack, and was classified as slight, moderate, or severe. The condition for inclusion in the series was that at least two conclusive electrocardiograms should show the usual serial changes seen in cardiac infarction, except in the case of patients who died within days, when one conclusive cardiogram was accepted as evidence. Patients seen in hospital and general practice came frequently under review, which included clinical, radiological, and cardiographic examinations.

At the end of December, 1950, follow-up letters were sent to the doctors of those patients who had not been seen for three months or more. The questions asked were simple and straightforward, as the many clear answers proved. The patients who were observed during repeated infarctions or who had had previous infarction were assessed for the last one. Those who could not be followed up were included in the two-months period of close observation. Each patient was seen by one of us; most patients were seen by both of us.

Overall Classification: Source, Sex Incidence, Mortality

Severe cardiac infarction formed the largest group; slight cardiac infarctions were rather fewer, and infarc-

tion of moderate grade made up the smallest group (Table I). While almost half of the severe cases were hospital in-patients admitted through the casualty department or Emergency Bed Service, less than one-third of

TABLE I.—Source of Material

	Hospital In-patients	Consultant Practice	General Practice	Hospital Out-patients	Total
Slight cardiac infarction ...	20	27	10	13	70
Moderate cardiac infarction ...	19	15	8	—	42
Severe cardiac infarction ...	40	32	16	—	88
Total ..	79	74	34	13	200

the slight cases were so admitted. All the hospital out-patients who did not become in-patients were slight cases. Patients seen first in consultant and general practice were fairly evenly distributed in the three groups.

Table II, like Table I, comprises the whole series, whether treated or untreated by anticoagulants, and shows the age and sex incidence and total mortality. It furnishes a solid basis for this investigation, for the all-round mortality of the series is 25%. While the mortality of the slight group is only 8.6%, that of the moderate group is 11.9% and that of the severe group 44.3%.

The sex ratio confirmed the well-known preponderance of men over women (4.9:1), though the mortality was about equal—24.7% in men and 26% in women. There was, however, considerable difference in the separate groups: no woman died of slight or moderate cardiac infarction; but in the group of severe cardiac infarction 9 out of 17 women died, whereas 30 out of 71 men died. Thus in severe cardiac infarction, mortality seems to be higher in women (53%) than in men (42%).

TABLE II.—Age and Sex Incidence. Mortality

		30-39		40-49		50-59		60-69		70-79		Total	
		M	F	M	F	M	F	M	F	M	F	M	F
Slight cardiac infarction (70 cases)	Alive	2	—	13	—	20	3	17	7	2	—	54	10
	Dead	—	—	2	—	2	—	1	—	1	—	6	—
Moderate cardiac infarction (42 cases)	Alive	2	—	6	—	11	1	9	3	2	3	30	7
	Dead	—	—	—	—	1	—	4	—	—	—	5	—
Severe cardiac infarction (88 cases)	Alive	—	—	8	—	19	4	11	4	3	—	41	8
	Dead	—	—	3	—	8	3	14	6	5	—	30	9
Total ..												166	34

Proportion of men to women, 4.9:1. Total mortality, 25%. Mortality of slight cardiac infarction, 8.6%. Mortality of moderate cardiac infarction, 11.9%. Mortality of severe cardiac infarction, 44.3%.

TABLE III.—Symptoms of Cardiac Infarction

	Predisposing Conditions	Pre-existent Cardiac Enl.		Previous Infarction	Angina	Infarction Pain Absent	Infarction Pain Present	One Inj. of Mo	Rep. Inj. of Mo	Circulatory Shock		Pulmonary Congestion	Early C.H.F.	Arrhythmia	Pyrexia	E.S.R. 20 mm. + W.B.C. 9,000 +	Electrocardiogram						
		No C.H.F.	C.H.F.							Sl.	Sev.						Ant.	A.w B.B.B. or H.B.	A/L	P.	P.w B.B.B. or H.B.	P/L	A/P
Slight cardiac infarction (70 cases)	33	11	—	6	47	17	53	13	1	11	—	1	—	2	9	5	40	1	13	13	—	3	—
Moderate cardiac infarction (42 cases)	17	3	—	8	21	—	42	21	7	15	2	10	1	4	21	17	22	2	5	9	—	4	—
Severe cardiac infarction (88 cases)	36	15	17	25	44	10	78	43	32	17	51	48	39	21	53	36	31	6	8	18	11	7	—

Enl. = Enlargement; C.H.F. = Congestive heart failure; Mo = morphine; Rep. = Repeated; Sl. = Slight; Sev. = Severe; A. = Anterior; A/L = Antero-lateral; P. = Posterior infarction; P/L = Postero-lateral infarction; A/P = Antero-posterior infarction; B.B.B. = Bundle-branch block; H.B. = Heart-block.

Prognosis of Untreated Slight Cardiac Infarction

Included in the 69 patients of this group are the 33 cases published as "slight coronary attack" (Papp and Shirley Smith, 1951) which are recognized as slight cardiac infarctions. Cardiac pain in slight cardiac infarction may be long-lasting (up to 12 hours) when it is intermittent, but is less severe than in the moderate or severe group; only 13 asked for relief by injection, and a second injection of morphine was necessary in only one case (Table III). As in the other groups, angina of effort preceded cardiac infarction for months or years in 47 patients, and in 17 of these prolonged infarction pain was absent (Morgan Jones and Wade, 1949; Stein, 1950). Diagnosis here was based on the electrocardiogram only.

Slight shock was observed in 11 and was responsible for lowering of the systolic blood pressure for a short time to 100–110; even in these patients the pulse pressure never fell under 30 mm., while in the others the fall of the blood pressure was irrelevant. Pyrexia for a few days was known to be present in nine, but many patients were seen late. Out of 20 who were seen early enough a raised E.S.R. or white-cell count was present

later of further cardiac infarction, and Case 179, aged 72, died suddenly two years later of probable ventricular fibrillation. Case 188 died in unknown circumstances.

Though 45 patients were active, 35 out of 63 who were alive continued having angina of effort; in nine it was so severe that they were disabled by it. One of these had to be subjected to stellate ganglionectomy four years later.

Predisposing conditions include hypertension, diabetes, obesity, intermittent claudication, and chain smoking. No particularly adverse prognostic significance could be attached to any of these factors singly or in combination, for they were present in similar proportion in the moderate and severe groups. Precipitating causes (Master, 1946) are not listed, for they were rarely instrumental in provoking infarction. Pre-existent cardiac enlargement was slight in all, and mostly was of hypertensive origin. Except in Case 155, slight cardiac infarction did not produce or make worse existing cardiac enlargement. The electrocardiographic changes were described elsewhere; they are of diagnostic but not of prognostic significance. The far-reaching cardiographic restoration in almost two-thirds of the patients is possible because the Q waves of through-and-through

TABLE IV.—*Prognosis of Untreated Slight Cardiac Infarction (69 Cases)*

Last Follow-up (Years):	$\frac{1}{2}$	$\frac{1}{2}$	1	1½	2	2½	3	3½	4	4½	5	Total
No. of cases	13	10	10	6	9	10	2	4	2	2	1	69
Mild	6	3	4	2	3	2	—	1	—	2	—	23
Moderate	1	3	2	—	1	—	1	—	1	—	—	9
Severe	1	1	—	1	1	3	1	1	—	—	—	8
Further infarction	—	—	2	1	1	—	—	1	1	—	—	5
Congestive heart failure	—	—	—	—	—	—	—	—	—	—	—	1
Thrombo-embolic complications	—	1	—	—	—	—	—	1	—	—	—	2
No complaints	5	2	3	2	3	4	—	1	—	—	—	22
Active	6	7	8	4	5	8	—	2	2	2	1	45
Incapacitated	2	2	1	—	2	2	1	1	—	—	—	11
Died	—	1	1	2	1	—	—	1	—	—	—	6
E.C. { Unchanged	7	3	3	2	2	—	—	1	—	1	—	23
Improved	6	4	2	4	4	2	1	3	—	—	—	26
Recovered	—	2	3	—	2	3	1	—	2	—	1	15
Worse	—	1	2	—	1	1	—	—	—	—	—	5

in five. Basal crepitations were found in one for a short time, but none showed congestive heart failure. The ectopic rhythm present during the attack in two disappeared without treatment as soon as the pain subsided. The electrocardiographic location of the ischaemic zone was more often anterior and antero-lateral than posterior. The presence of bundle-branch block or complete heart-block was exceptional; in the only patient in whom right bundle-branch block was found this probably existed before the actual infarction.

No patient out of these 69 died during the two months of close observation, in which the overall mortality rate is said to be 20–40% (Table IV); moreover, none had further infarction or developed congestive heart failure during this time. Cerebral embolism was observed in Case 7, eight months after slight cardiac infarction; he recovered with no disability. Multiple pulmonary infarcts were found on post-mortem examination in Case 155; these were not due to embolism but to severe pulmonary arteriosclerosis. This, in association with coronary arteriosclerosis, was responsible for the congestive heart failure of which he died. On post-mortem examination fibrotic scars were found in the two predicted myocardial areas—one postero-basal, the other antero-septal where the electrocardiogram had shown acute ischaemia three and a half years and one year previously after slight cardiac infarctions. Case 197 died in pulmonary oedema, Cases 187 and 162 died one and one and a half years

infarction are commonly absent. Though the general impression is that fewer of those who made electrocardiographic recovery were disabled by angina, the exceptions are too many for this to be of prognostic value.

Prognosis of Untreated Moderate Cardiac Infarction

This is the smallest of the three groups, with 39 patients; as it is the intermediate one, some overlapping is inevitable with both slight and severe cardiac infarction. These patients, though not critically ill, showed for a short time some of the signs found in severe cardiac infarction (Table III). Infarction pain was present in all, and 28 were in need of morphine, 7 of repeated injections. The incidence of circulatory shock was higher (17) and shock was severe in two, one of whom also developed signs of early congestive heart failure. Pulmonary congestion was present in 10 and was transitory in all except one. Pyrexia and increase in white-cell count and E.S.R. were present in greater proportion than in the previous group.

Two patients died during the first two months and four developed thrombo-embolic complications. Five had further cardiac infarctions, and in four congestive heart failure appeared in contrast to one in the slight group. Cardiac infarction, thrombo-embolic complications, and congestive heart failure, singly or in combination, were the causes of death in three cases in the

TABLE V.—Prognosis of Untreated Moderate Cardiac Infarction (39 Cases)

Last Follow-up (Years):	$\frac{1}{2}$	$\frac{1}{2}$	1	1½	2	2½	3	3½	4	4½	7-8	Total
No. of cases	7	5	5	7	2	1	3	3	2	2	2	39
Angina { Mild	—	1	2	—	—	—	1	—	1	—	—	9
{ Moderate	2	1	—	3	—	—	—	—	—	—	—	6
{ Severe	—	1	1	—	—	—	—	—	—	—	1	4
Further infarction	1	—	—	—	1	—	1	1	—	1	—	5
Congestive heart failure	—	1	—	—	2	1	—	—	—	—	—	4
Thrombo-embolic compli- cations	1	—	—	1	—	—	—	1	1	—	—	4
No complaints	3	2	2	4	—	—	1	—	1	—	—	14
Active	3	2	3	6	—	—	2	2	2	1	2	25
Incapacitated	1	1	1	—	—	1	1	—	—	1	—	6
Died	2	—	—	—	2	—	—	1	—	—	—	5
E.C. { Unchanged	4	3	2	3	1	—	1	1	1	1	—	17
{ Improved	2	2	3	4	—	1	1	1	1	—	2	17
{ Worse	1	—	—	—	1	—	1	1	—	1	—	5

late follow-up series (Table V). The proportion of angina is similar to that in the previous group, but it was mostly slight and produced incapacity in two only. No electrocardiogram reverted to normal, though in less than half the signs of actual infarction have disappeared. Thus the immediate prognosis in this group is not much worse than in the previous one, though the clinical and electrocardiographic signs are more severe.

Prognosis of Untreated Severe Cardiac Infarction

The dominant and grave symptom (Table III) was circulatory shock, which was present in 68 of the 88 patients in the severe group; it was mostly severe and outlasted the pain by hours or days. Basal congestion developed in more than half and progressed often to basal consolidation, which prolonged the period of pyrexia and was partly responsible for the high white-cell count and E.S.R. in 36. Shock when severe prevents the development of pyrexia. More than one-third of the patients had pre-existent cardiac enlargement due to either hypertensive or ischaemic heart disease, and half of these were in failure when they developed recent cardiac infarction. The earliest signs of congestive heart failure after severe cardiac infarction were high pulse rate, gallop rhythm, and pulmonary congestion.

Out of 39 who showed early signs of left ventricular failure 21 died within two months and a further 12 within three years (Table VI). The longest survival period among the five who are still alive is three and a half years. Those who in addition to early left ventricular failure developed right ventricular failure died within weeks or months; a similar experience was recorded also by Selzer (1948). An exception was Case 140, in whom subtotal thyroidectomy was performed during irreducible right heart failure, six months after the second cardiac infarction. He is alive and active after three years. The combination of circulatory shock and congestive heart failure was particularly critical. Cardiac infarction was silent in

five cases in which it arose during gross congestive heart failure; the pain-equivalent here was paroxysmal dyspnoea.

Persistent arrhythmia, whether auricular fibrillation, flutter, ectopic rhythms, or salvos of ventricular extrasystoles, is of serious prognostic significance, and no patient who developed persistent auricular fibrillation during the acute stage survived. In our experience the electrocardiographic location of the ischaemic area was diagnostic of severe infarction only when the record showed antero-posterior infarction (Roesler and Dressler, 1947) or when posterior infarction was associated with bundle-branch block or heart-block (Table III). The latter, if transitory, may not be of grave significance; all five patients in whom it ushered in cardiac infarction but disappeared after few hours or days survived the two-months period, and three are known to be still alive. The infarction was "silent" in them and syncope was here the pain-equivalent (Papp, 1951).

Severe cardiac infarction leaves indelible traces in the electrocardiogram. In only 3 out of 67 did the signs of actual infarction disappear, but even in these the record remained abnormal (Table VI). The fact that 50% of these patients had congestive heart failure is in agreement with the findings of Mills *et al.* (1949), who also emphasized the frequency of congestive heart failure in those whose electrocardiogram showed gross persistent changes.

Of the 67 patients with untreated severe cardiac infarction 33 died. Two-thirds of the deaths occurred during the first two months and the remaining one-third during the succeeding three years. The disability in 9 out of 34 who survived was due more to congestive heart failure than to angina; in fact, only three were disabled by severe angina, and this is in contrast with the slight and moderate group. Eight were free from complaints though two had cardiac aneurysm. Twenty-two were able to resume normal activity, mostly in sedentary occupations.

TABLE VI.—Prognosis of Untreated Severe Cardiac Infarction (67 Cases)

Last Follow-up (Years):	$\frac{1}{2}$	$\frac{1}{2}$	1	1½	2	2½	3	3½	4	Total
No. of cases	28	5	5	7	7	6	5	3	1	67
Angina { Mild	1	—	1	3	2	3	1	—	—	11
{ Moderate	—	—	—	1	—	—	—	—	1	2
{ Severe	1	1	—	—	—	1	—	—	—	3
Further infarction	10	1	1	3	1	1	1	—	1	19
Cardiac aneurysm	—	1	—	—	—	—	—	—	—	2
Cardiac enlargement	23	3	3	4	2	3	2	1	—	41
Congestive heart failure	21	1	1	4	2	2	1	1	—	33
Thrombo-embolic complications	6	1	—	1	1	—	2	—	—	10
No complaints	2	—	2	—	1	1	1	1	—	8
Active	1	1	3	4	4	4	3	2	—	22
Incapacitated	5	1	—	—	1	1	—	—	1	9
Died	21	3	2	3	2	1	1	—	—	33
E.C. { Signs of infarction	27	5	5	7	7	5	5	2	1	64
{ No signs of infarction	1	—	—	—	—	1	—	1	—	3

Treated Series

One slight, three moderate, and 21 severe cases of cardiac infarction are included in this series (Table VII). Many more were treated, but only those were selected

TABLE VII.—*Result of Anticoagulant Treatment in 25 Cases of Cardiac Infarction (1 Slight, 3 Moderate, 21 Severe)*

	During Treatment	Last Follow-up (Years) of 21 Patients Alive at End of Treatment					
		$\frac{1}{2}$	$\frac{1}{2}$	1	$1\frac{1}{2}$	$2\frac{1}{2}$	3
No. of cases	25	3	6	4	5	2	1
Recurrent cardiac pain or angina	4	—	1	3	3	—	—
Further infarction	3	1	—	1	—	—	—
Thrombo-embolism	2	—	—	1	—	—	—
Haemorrhage	5	—	—	—	—	—	—
Cardiac failure	10	1	2	—	—	—	1
Cardiac aneurysm	—	—	—	1	—	—	—
No complaints	11	2	3	1	3	2	1
Active	—	1	2	2	4	1	1
Incapacitated	—	—	1	1	—	—	—
Died	4	1	1	—	—	—	—
E.C. { Signs of infarction	25	3	5	4	4	2	1
{ No signs of infarction	—	—	1	—	1	—	—

in whom treatment was continued for longer than a fortnight, in whom satisfactory prothrombin levels were obtained, and in whom treatment was started within four or five days after infarction. Some were treated with heparin and dicoumarol after the method of Wright, Marple, and Beck (1948), others with heparin alone, and others with "tromexan." When laboratory facilities were not available heparin was preferred. The reason for treatment in the slight and moderate cases was persistence of cardiac pain.

The four patients with slight and moderate infarction are alive; of the 21 severe cases only four died during the period of treatment (Table VII). Death was due to cardiac failure in all, and so was it in a further two who died within two and six months after infarction. Thrombo-embolism occurred in two during treatment; both had pulmonary infarctions, but these were not severe. Both survived, while in the untreated severe group thrombo-embolism occurred in seven during the first three months (peripheral and cerebral in four, pulmonary in three) and was the cause of death in three. Further cardiac infarction was observed in three; in two it occurred before satisfactory prothrombin levels were reached; this also compares favourably with the untreated series. The influence on recurrent cardiac pain after infarction was variable, and the two patients, one of the slight and another of the moderate group, had to be subjected to stellate ganglionectomy a few months later. In five patients haemorrhagic complications occurred and treatment had to be stopped in three after the second week. In another three, these complications occurred during the first few days and treatment had to be abandoned; these cases were regarded as untreated and are not included in this series.

The late follow-up has shown no difference from the untreated series. The absence of severe angina was remarkable, but this only confirms what has been noted in the untreated series of severe cardiac infarction.

Circumstances and Cause of Death (50 Cases)

These were similar in the 6 slight, 5 moderate, and 39 severe cases of cardiac infarction, whether treated or untreated. Post-mortem confirmation was obtained in 11 instances. Sudden death in cardiac pain may occur at any time after infarction and is possibly due to further infarction or to massive embolism (seven cases). Cardiac

rupture may also cause a fatal termination in the first few days (Gans, 1951). Sudden death in unexplained circumstances (two during sleep, two on the road, one on the bedpan) may be due to the causes mentioned (in one instance post-mortem examination showed a recent cardiac infarction). Death in shock and cardiac pain occurred in three cases within hours or days after the beginning of infarction, while most of the nine who also showed signs of congestive heart failure died between the first and fourth weeks.

Congestive heart failure caused death usually at a later stage (18 cases), and was twice associated with pulmonary infarction. Pulmonary infarction was in neither instance due to embolism but to local thrombosis. Peripheral and cerebral embolism were fatal complications in five patients, but in only one was post-mortem confirmation obtained. In two further cases the clinical diagnosis was not substantiated at necropsy: although myocardial infarction with mural thrombosis was found on post-mortem examination, the limb symptoms were due to arteriosclerotic gangrene precipitated by circulatory shock and possibly vasoconstriction (Swan and Henderson, 1951). Unrelated conditions included bronchopneumonia and suicide. In each instance there was post-mortem confirmation of healed cardiac infarction. One patient died in unknown circumstances.

Death in 90% was due to further cardiac infarction, shock, or congestive heart failure. In only 10% could thrombo-embolism be held responsible, and then it was more often due to local thrombosis than to embolic phenomena.

Repeated Cardiac Infarction

More than half of the deaths occurred during or following a first attack of cardiac infarction. Twelve patients died after the second episode, the date of the first cardiac infarction being known in 10. The survival periods from the first attack were two months in one, from one to three years in six, and from seven to eight years in two. In five who succumbed after the third cardiac infarction the survival periods were five months in one, six to seven years in two, and 12 years in two. Follow-up of surviving patients showed comparable results: out of 20 who had repeated attacks, five could be followed up to two years, nine up to four years, five up to seven years, and one up to 20 years after the first attack.

It is not the number of cardiac infarctions but the severity of the single attacks which is of prognostic significance. Patients who had previous infarctions might develop successively small marginal ischaemic areas; the clinical expression of such slow extension of infarction was a recurrence of slight or moderate attacks of cardiac infarction. What is being accomplished in severe cardiac infarction in one stage may be accomplished gradually by repeated cardiac infarctions. Finally, a stage may be reached when the patient is without symptoms or disability for a long time; such a course corresponds to the case of severe cardiac infarction in which suddenly a large coronary artery is occluded. Electrocardiography here is of great prognostic value, as a second infarction in a hitherto unaffected area is of grave significance.

Treatment

The technique of anticoagulant treatment is well known (Wright, 1950). Heparin is given either by intravenous injection through a polythene tube, 5,000–7,500 units four-hourly, or by intramuscular injection 15,000–25,000 units twice a day. The latter method is obviously

to be preferred in general practice; it does not need much laboratory control, and the addition of 1 ml. of 1% procaine makes the injection almost painless (Abrahams, 1950). The cost and the risk of haematoma formation at the place of the injections are its great drawbacks. If laboratory control is available dicoumarol should be given with heparin; if the initial prothrombin time is normal (12–18 seconds) 300 mg. should be given in divided doses the first day, 200 mg. the second day, and 100 mg. the third day. After 48 hours heparin can be discontinued, as a satisfactory prothrombin time will be reached by then. This is 25–40 seconds, with a control around 15–20 seconds, and the aim is to keep the patient on this level during the three to four weeks' treatment. The average maintenance dose of dicoumarol is 50–100 mg. daily; but it can be higher or lower, and has to be worked out for every patient.

Tromexan is safer than dicoumarol since it has no lag action, and the prothrombin time returns to normal within 24 hours, should complications make its discontinuance necessary. Furthermore, a satisfactory prothrombin time can be reached within 24 hours and therefore the addition of heparin may not be necessary. The dose is 1,200 mg. the first day, 900 mg. the second day, 600 mg. the third day. The maintenance dose is 150–600 mg.; in our experience a stable prothrombin time is more difficult to obtain with tromexan than with dicoumarol. About 75–80% of the patients can be stabilized on a satisfactory prothrombin level, and, in these, thrice-weekly prothrombin estimations during the first fortnight and twice weekly thereafter will suffice. The rest of the patients are unstable reactors in whom the prothrombin time shows wide variations; in spite of daily laboratory control they may develop haemorrhagic complications, and should be referred to hospital or treated with heparin.

A daily examination of the patients for subcutaneous or oral haematomas, and the inspection of every urine specimen for haematuria, are essential, as haemorrhages may affect vital regions and be difficult to control. If they occur in patients on heparin, 5–10 ml. of protamine sulphate should be injected intravenously and treatment be discontinued until the clotting time becomes normal (4–7 minutes). Treatment thereafter should be continued under laboratory control and heparin should be temporarily discontinued if the clotting time exceeds 20 minutes. If the patient is being treated with tromexan or dicoumarol a prothrombin time of 50 seconds (with a control time of 15–20 seconds) is the danger signal. If the patient is on tromexan, its discontinuance for one day will lower the prothrombin time to near or below the maintenance level; if on dicoumarol, 60–70 mg. of vitamin K intravenously, followed by a second dose four hours later, may avert haemorrhage. In the presence of haemorrhage repeated transfusions with fresh whole blood may be necessary.

In general practice choice of the drug depends on the laboratory control available. With reasonable laboratory control tromexan is safer than dicoumarol. With no laboratory control intramuscular heparin is the only alternative, though it is much more unpleasant for the patient and not altogether devoid of danger. Hepatic or renal disease, ulcerated surfaces, pregnancy, and haemorrhagic tendency are absolute contraindications for both.

Additional treatment includes penicillin, digitalis, quinidine, oxygen, and analgesics. If pyrexia persists for more than three to four days it is com-

monly due to infection of the congested lung bases, and penicillin treatment should not be delayed. Cardiac failure is better treated with intramuscular ouabaine injections (0.25–0.5 mg. daily) than with digitalis, though in the presence of shock the effect of both is unsatisfactory. Extrasystolic arrhythmia requires quinidine, 5 gr. (0.32 g.) three or four times a day, to reduce the danger of ventricular fibrillation. An oxygen tent may be life-saving when shock persists or when cyanosis and engorgement of the neck veins indicate right-sided heart failure. Recurrent cardiac pain should be treated with morphine if severe; if it is moderate, "nepenthe," 20 min. (1.2 ml.), or pethidine, 100 mg. by injection or by mouth, may suffice and have less unpleasant side-effects. Sedation by "sodium amytal," 2 gr. (0.13 g.) three times a day, is less depressing than by phenobarbitone.

Absolute rest in bed should be continued for four to six weeks in severe cardiac infarction; if failure exists after this period nothing is gained by prolonging the complete rest. The patient should be treated as a cardiac invalid and be allowed the amount of exercise compatible with his reduced cardiac reserve. In contrast, in slight and moderate cardiac infarction complete immobility in bed is not only unnecessary but may be harmful. To prevent pulmonary congestion and phlebothrombosis these patients should have respiratory exercises, should move their legs, and should be allowed to use the commode as soon as pyrexia has subsided. After two to three weeks they are allowed up by gradual stages provided the E.S.R. has become normal.

Discussion

The results of this investigation confirm the statement made by many others that anticoagulant treatment considerably reduces the mortality of cardiac infarction. Thus the suggestion that it should be used in all cases of coronary thrombosis (Wright *et al.*, 1948) and that it "should be considered for every sufferer of myocardial infarction" (Tulloch and Gilchrist, 1950) is based on good evidence. Furthermore, preventive treatment of impending cardiac infarction has been advocated by Wood (1950) in patients who have prolonged attacks of angina at rest; to these cases can be added patients who have increasingly severe angina of effort of less than a fortnight's duration, for in our experience many of these have either already sustained cardiac infarction or are in danger of it. The limitation of hospital accommodation, the non-existent laboratory facilities in general practice, and the cost of intramuscular heparin treatment as advocated by Abrahams (1950) (about £60–£70 for three to four weeks) make a selection of cases imperative.

Our investigations have shown that the mortality of untreated cases of slight and moderate cardiac infarction during the first two months of close observation is less than 2% (Tables IV and V) and that the incidence of thrombo-embolic complications is negligible. Thus over half of the patients with cardiac infarction seen in general, consultant, and hospital practice will be at no disadvantage through having conservative treatment. In moderate cardiac infarction, where the clinical symptoms may be equivocal, the electrocardiographic signs may tilt the balance for or against anticoagulant treatment, while the risks attending the use of anticoagulants have to be remembered.

There is the same gradation in severity in cardiac infarction as there is from angina to cardiac infarction

(Freedberg *et al.*, 1948); in fact, there is no strict dividing-line between these two conditions, which are differentiated more for didactic than for pathological reasons. The first attack of angina may be the clinical expression of cardiac infarction and, conversely, severe coronary arteriosclerosis may be symptomless until it produces fatal cardiac infarction (Cassidy, 1946). The successive evolution of slight and moderate cardiac infarction is often similar to ordinary angina of effort, and in fact many of these patients are severely disabled by angina though their electrocardiogram may have reverted to normal.

Slight cardiac infarction may be only an episode in the clinical history of slowly progressing coronary narrowing which favours development of collateral circulation (Blumgart *et al.*, 1950). In contrast, the sudden occlusion of a large coronary artery in a heart previously unprepared by the development of collateral circulation produces severe cardiac damage; but once the patient is over the critical period and does not develop congestive heart failure, he may eventually become able to lead a comparatively normal life. These are only the two extreme types of the disease, and their combination is frequent. Nevertheless they justify a variation of therapeutic approach to cardiac infarction according to the severity, even when the symptoms in the individual patient vary if long enough observed (Boas, 1951).

The diagnosis of severe cardiac infarction can nearly always be made within 24 hours. Prolonged continuous pain requiring repeated injections of morphine is the first sign; if circulatory shock is delayed, a mounting pulse rate and a falling pulse pressure (25 mm. or under) herald its approach. All the other signs which make up the clinical picture of severe myocardial infarction are the secondary effects of circulatory shock associated later with left ventricular failure. They are in order of appearance basal crepitations, increase of the pulse rate, and gallop rhythm.

The influence of circulatory shock on the myocardium favours cardiac failure by extension of the infarcted area (Corday *et al.*, 1949); left ventricular failure increases circulatory embarrassment in the lungs and may cause pulmonary oedema or pulmonary consolidation, or both. Thus pulmonary infarction during the first few days following cardiac infarction is only exceptionally of embolic origin, as infarction of the right ventricular wall, and therefore formation of mural thrombosis in the right ventricle, is rare. If shock of cardiac origin could be effectively treated, anticoagulant treatment would be of secondary importance. As the results of treatment of shock are uncertain (Schwartz, 1947; Corday *et al.*, 1949; Epstein and Relman, 1949) one aims to reduce the thrombogenic effect of slowing of the circulation (Macfarlane, 1950) by prolonging the clotting-time (heparin) or by reducing the prothrombin level (coumarin drugs) of the blood.

In our experience real embolic complications amount to no more than 15% (Shirley Smith, 1950); thrombo-embolic complications or peripheral ischaemia may occur so soon after cardiac infarction that they cannot be prevented in spite of effective anticoagulant treatment. The risk of phlebothrombosis of the legs—the embolic source of pulmonary infarction—can be reduced by anticoagulant treatment though not abolished.

In about 15% of cases increasingly severe premonitory pain may herald the infarction for days or weeks, the electrocardiogram remaining unchanged until finally the infarction develops. These cases therefore begin as myo-

cardial ischaemia and develop into slight cardiac infarctions; yet they may progress into severe ones. The aim, then, is the prevention of impending cardiac infarction, and results in these cases are being published separately (Shirley Smith and Papp, 1951).

Summary

Two hundred consecutive cases of cardiac infarction, 175 treated on conservative lines and 25 treated with anticoagulants, were collected from consultant, general, and hospital practice and divided into three groups—slight, moderate, and severe. The prognostic significance of each of these groups was investigated separately and the clinical and electrocardiographic findings were correlated. The ages of the patients ranged from 34 to 75 years, the sex ratio was five men to one woman; the total mortality was 25%, being about equal in the sexes.

All the 69 patients with untreated slight cardiac infarction were alive at the end of two months; six men died six months to four years later (8.6%), but there were no deaths among the women. Disability for the patients' usual occupation was due to angina in 11 cases; only one had congestive heart failure three and a half years later. Normal activity was resumed in 45. Cardiographic restoration occurred in almost two-thirds of the patients irrespective of the presence of angina.

Out of 39 untreated cases of moderate cardiac infarction two died during the first two months and a further three two to three years later (12.8%). No female patient died. Four had thrombo-embolism, but only one had it during the first two months. Five had further cardiac infarction. Incapacity in four was due to congestive heart failure, in two to angina. Normal activity was resumed in 25. No cardiogram reverted to normal, though in 17 the signs of infarction have disappeared.

Out of 67 patients with untreated severe cardiac infarction 33 died (50%); two-thirds of the deaths occurred during the first two months, and the mortality in women was higher than in men. Congestive heart failure, present in 33 cases, appeared early in 21. Further infarction took place in 19, in 10 of these within two months; thrombo-embolism occurred in 10, in six of these within two months. Out of 34 who survived nine were incapacitated, mostly by congestive heart failure. Normal activity in sedentary occupation was resumed in 22. The cardiogram remained abnormal in all, and signs of infarction persisted in 64.

Twenty-five cases (1 slight, 3 moderate, and 21 severe) were treated with anticoagulants. Only four out of the 21 with severe infarction died during the first month, and two a few months later (21.6%). Thrombo-embolism was seen in only two while under treatment, and both recovered. Early cardiac failure was observed in 10, of whom six recovered. The value of anticoagulant treatment in severe cardiac infarction is confirmed. In contrast, this treatment is unnecessary in slight and moderate cardiac infarction, where the early mortality is less than 2%. In such patients, who are fundamentally sufferers from angina, cardiac infarction may be no more than an episode which does not produce permanent cardiac damage.

More than half of the deaths occurred during or following first cardiac infarction. Death in 45 (90% of the 50 who died) was due to further cardiac infarction, shock, or congestive heart failure; only in five was thrombo-embolism the cause, and then local thrombosis was more often responsible than embolism. The success of anticoagulant treatment is therefore due much less to prevention of embolism than to reduction of the thrombogenic effect of circulatory shock on the myocardium, lungs, and peripheral circulation.

The choice of anticoagulant depends on the ready availability of laboratory control. The indications for additional treatment with penicillin, ouabaine, quinidine, oxygen, and analgesics are discussed.

REFERENCES

- Abrahams, D. G. (1950). *British Medical Journal*, **2**, 1418.
- Blumgart, H. L., Zoll, P. M., Freedberg, A. S., and Gilligan, D. R. (1950). *Circulation*, **1**, 10.
- Boas, E. P. (1951). *Amer. Heart J.*, **41**, 323.
- Cassidy, M. (1946). *Lancet*, **2**, 587.
- Corday, E., Bergman, H. C., Schwartz, L. L., Spritzler, R. J., and Prinzmetal, M. (1949). *Amer. Heart J.*, **37**, 560.
- Epstein, F. H., and Relman, A. S. (1949). *New Engl. J. Med.*, **241**, 889.
- Freedberg, A. S., Blumgart, H. L., Zoll, P. M., and Schlesinger, M. J. (1948). *J. Amer. med. Ass.*, **138**, 107.
- Gans, R. H. (1951). *Amer. Heart J.*, **41**, 332.
- Jones, A. Morgan, and Wade, E. J. (1949). *Brit. Heart J.*, **11**, 411.
- Katz, L. N., Mills, G. Y., and Cisneros, F. (1949). *Arch. intern. Med.*, **84**, 305.
- Lancet*, 1950, **1**, 28.
- Levine, S. A., and Rosenbaum, F. F. (1941). *Arch. intern. Med.*, **68**, 1215.
- McCain, F. H., Kline, E. M., and Gilson, J. S. (1950). *Amer. Heart J.*, **39**, 263.
- Macfarlane, R. G. (1950). *Brit. Heart J.*, **12**, 427.
- Master, A. M. (1946). *N.Y. Med.*, **2** (No. 9), 19.
- Mills, G. Y., Simon, A. J., Cisneros, F., and Katz, L. N. (1949). *Arch. intern. Med.*, **84**, 632.
- Mintz, S. S., and Katz, L. N. (1947). *Ibid.*, **80**, 205.
- Papp, C. (1951). *Brit. Heart J.* In press.
- and Smith, K. Shirley (1951). *Ibid.*, **13**, 17.
- Roesler, H., and Dressler, W. (1947). *Amer. Heart J.*, **34**, 817.
- Rosenbaum, F. F., and Levine, S. A. (1941). *Arch. intern. Med.*, **68**, 913.
- Schwartz, W. B. (1947). *Amer. Heart J.*, **33**, 169.
- Selzer, A. (1948). *Amer. J. med. Sci.*, **216**, 172.
- Smith, K. Shirley (1950). *Brit. Heart J.*, **12**, 428.
- and Papp, C. (1951). *Ibid.* In press.
- Stein, I. (1950). *Amer. Heart J.*, **40**, 325.
- Swan, W. G. A., and Henderson, C. B. (1951). *Brit. Heart J.*, **13**, 68.
- Tulloch, J. A., and Gilchrist, A. R. (1950). *British Medical Journal*, **2**, 965.
- Wood, P. (1950). *Diseases of the Heart and Circulation*. London.
- Wright, I. S. (1950). *Circulation*, **2**, 929.
- Marple, C. D., and Beck, D. F. (1948). *Amer. Heart J.*, **36**, 801.

ISOLATION OF SALMONELLAE FROM FAECES OF DOMESTIC ANIMALS

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The importance of salmonellae as causes of disease in man and animals is recognized. Most outbreaks of food-poisoning in man caused by these organisms are thought to follow the consumption of food directly or indirectly associated with infection of animals (Topley and Wilson, 1946). Salmonella infection among domestic animals is also of economic importance to the agricultural industry and is associated with serious disease problems, particularly among young animals.

A considerable amount of evidence has accumulated from studies of clinical salmonella infection to indicate the species most commonly affected and the types of salmonellae that have been isolated from them. Less time has been devoted to the study of animals that are latently infected with salmonellae. The work carried out on this subject has been confined mainly to the examination of such material as mesenteric lymph nodes. Since the bacteria in these nodes may be constantly confined to them, this potential source of food-poisoning would be removed with the viscera after slaughter. Of more importance from the public health and agricultural

points of view are animals that are symptomless faecal excretors of salmonellae. During their life such animals may give rise to disease in susceptible animals and may contaminate milk, eggs, and other food products, and after slaughter their carcasses and those of other animals may become contaminated with salmonellae.

The purpose of this paper is to report on the isolation of salmonellae from the faeces of cattle, sheep, horses, pigs, goats, chickens, turkeys, ducks, and geese. Faecal specimens were examined from adult healthy commercial stock, from animals suffering from diseases other than primary salmonella infection, and, where possible, from animals exhibited at agricultural shows. The third group was included in order to determine the effect of hygiene and general management on the incidence of salmonellae in the faeces of healthy animals.

Techniques

Several methods of isolation and preliminary identification of salmonellae from faecal specimens were tested. The method finally adopted was as follows.

A sample of faeces about the size of a hazel nut was inoculated into selenite F medium (Leifson, 1936) and into tetrathionate broth* (Rolfe, 1946). These enrichment media were incubated at 37° C. for 18 to 24 hours and plated on to Hynes's (1942) modification of Leifson's desoxycholate-citrate agar with the addition of 1% sucrose and 1% salicin (D.C.S.S.) as described by Haines, Elliot, and Tomlinson (1947). Tetrathionate broth was always used within three days of its preparation. The inoculated D.C.S.S. plates were incubated at 37° C. for 48 hours. The plates were then inspected and suspicious non-fermenting colonies were marked and tested for indole and urease production by the rapid test described by Williams Smith and Chave (1949).

Colonies negative to this test were then streaked on to a modification of the D.C.S.S. medium, the sucrose, salicin, and lactose being replaced by 1% dulcitol (D.C.D.). The plates were incubated for 24 hours at 37° C. One plate of this medium was sufficient for six to eight strains. The object of this procedure was to obtain pure cultures for further examination and to ascertain whether the cultures fermented dulcitol. Colonies on the D.C.D. medium that either fermented dulcitol and/or agglutinated with polyvalent O serum were transferred into plain Craigie tubes to induce motility and then subcultured on to moist agar slopes. The resulting cultures were studied serologically by means of antisera obtained either from the Standards Laboratory, London, or were prepared by one of us (A. B.). Organisms giving positive slide-agglutination reactions were submitted to a full tube test and their biochemical characteristics were also determined. Where necessary, final identification of cultures were made at the Salmonella Reference Laboratory, Colindale.

In the early part of the work specimens were plated directly on to D.C.S.S. medium as well as being inoculated into enrichment media. The results showed that there was no advantage from direct plating, and, because of the extra labour involved, it was discontinued. When a salmonella was isolated by one or both of the enrichment methods the original faecal specimen was plated direct on to D.C.S.S. medium. Sometimes the initial examination of suspicious colonies for indole and urease production was replaced by slide-agglutination tests with polyvalent O serum. When this was done the

*Medium A with brilliant green omitted.