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DA COSTA'S SYNDROME* (OR EFFORT SYNDROME)

BY

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I began this work in January, 1940, and started with an open mind, accepting the conclusion of modern authors (e.g., Paul White, 1937) that the cause and mechanism of "effort syndrome" are unknown. After surveying the English and American literature, after a year's close personal contact with 300 patients, and as the result of certain researches I can no longer hold this opinion. As the story unfolds readers will form their own judgment, but whether they agree with me or disagree, and whether I am right or wrong, are less important than the proper presentation of the facts.

Terminology : Definition : History

Terminology.—It is recognized that no satisfactory name has been given to the condition which has been variously known as "the irritable heart of the soldier" (Da Costa, 1871), "effort syndrome" (Lewis, 1917), "neurocirculatory asthenia" (Oppenheimer *et al.*, 1918a), and "autonomic imbalance" (Kessel and Hyman, 1923). I urge the rejection of all these terms for reasons which will become apparent; nor do I feel morally bound to suggest a substitute, for I believe that the recognition of this syndrome, as such, will die. Further, if it is at times convenient to speak of this group of physical signs and symptoms there can be no better name than Da Costa's syndrome. This not only avoids reference to the heart, to the circulation, to effort, or to false or unproved mechanisms, but it has the unrivalled merit of making Da Costa responsible for its recognition as a distinct clinical entity, and is especially fitting if the syndrome is to become of historical interest only; moreover, it is not just another new name, for the condition always has been Da Costa's syndrome, and might have been called so from the start.

Definition.—Da Costa's syndrome is characterized by a certain group of symptoms which unduly limit the subject's capacity for effort, and by a number of signs depending upon disturbance of the autonomic nervous system, when such symptoms and signs are not due to any known organic disease. The cardinal symptoms are breathlessness, palpitations, fatigue, left thoracic pain, and dizziness; the cardinal signs are those of functional disturbance of the respiratory, vasomotor, muscular, and sudomotor systems. It is admitted that this definition is concerned entirely with the physical side of the picture, but it is from this aspect that the cases have been viewed by the majority of physicians from 1861 to 1941. If it proves nonsensical from the psychological aspect so much the better, for I am defining a view which I believe to be obsolete.

History.—Lack of space forbids the publication of this curious history, and I must refer readers to the classical article of Da Costa (1871) and to those of Wilson (1916), Caughey (1939), and Fraser (1940).

Occurrence

Age.—In soldiers Da Costa's syndrome necessarily occurs at military age, the average being 28.12 years in my series of 200 cases; but 18.6% began in early childhood and 48% in the teens and early twenties. In civilian life Craig and White (1934) found 31.5 years was the average age in their series of 50, and McCullagh (1934) stated that 96 out of a series of 110 cases ranged between 20 and 40 years. Nevertheless Da Costa's syndrome is common in children and may occur in the elderly. Thus in the constitutional group reported by Oppenheimer and Rothschild (1918b, 1918c) the average age of onset was 11.8 years. A similar condition has been investigated in children by numerous observers—e.g., Martius (1899), Bass and Wessler (1913), and Lincoln (1928)—often in association with orthostatic albuminuria, but they failed to link these children with their adult prototypes.

Sex.—It is possible that the curious lack of recognition of Da Costa's syndrome in civilian life is due to the fact that it is commoner in women: the change of sex, plus the lack of khaki uniform, seems to have proved an effective disguise. "Effort syndrome" in the male soldier becomes cardiac, respiratory, or other neurosis in the female civilian. The actual figures are about 3 to 2 in favour of women (White and Jones, 1928; McCullagh, 1934).

Occupation.—Although all occupations are represented (Da Costa, 1871) Table I shows a preponderance of those

TABLE I.—Pre-war Occupation

Author	No. of Cases	Light Work
Hume (1918)	1,000	58.8
Lewis (1917)	543	57
Friedlander and Freyhof (1918)	50	53
Oppenheimer and Rothschild (1918b, 1918c):		
Constitutional group	46	80.4
Cases with good background	39	49
Swan (1921)	58	65.5
Wood (1941)	200	53

employed in light work. The figures of Oppenheimer and Rothschild also show that these patients take up light work because they feel incapable of heavy work—not that clerks, previously fit, break down because untrained to physical effort. Our own E.M.S. histories confirm this.

* The first of three Goulstonian Lectures to the Royal College of Physicians of London, 1941.

I have been unable to get reliable control figures from the War Office, but I am told that the matter is receiving attention.

Race.—Hume (1918) noted a low incidence among the Anzac troops, and from his figures it may be calculated that the ratio of British infantry to the Anzacs, corrected for the difference in total numbers, was as 7:2.5. Brooks (1924) states that fully 66% of his patients were Jews, especially Russian Jews; next he places the Italians, then the Irish, then Americans, Scandinavians, and lastly the negroes. I understand that Da Costa's syndrome was as much a problem in the German armies as it was in those of the Allies (Rudolf, 1916). Thus, although no race is immune, the emotional races are more susceptible than the stolid.

Frequency.—According to Lewis (1940) there were about 60,000 cases of "effort syndrome" in the British Forces during the last war, and of these men about 44,000 received pensions. Fraser (1940) gives a figure of about 29,000 invalided from the Army and Navy up to May, 1918, and says they comprised 80% of all cardiovascular disorders. Among civilians Paul White (1937) finds an incidence of 13.7% of 5,000 patients complaining of symptoms referable to the cardiovascular system; he also said that 19.6% of those with "neurocirculatory asthenia" had organic heart disease; and, conversely, that 4.7% of the organic cases had "neurocirculatory asthenia." McCullagh (1934) found that 2.16% of 2,680 admissions to the Cleveland General Medical Clinic had "neurocirculatory asthenia." Colonel Tidy informs me that Da Costa's syndrome is not a military problem so far in this war. There are but two special centres in England and one in Scotland, and we have had only about 700 cases at the largest of these.

Service.—Table II shows the relation of Da Costa's syndrome to the manner of enlistment. Earlier and later groups are compared in order to show the fall in the number of reservists and the rise in the number of conscripts. In the whole group of 200 cases volunteers took first place with an incidence of 30%. This is no accident: volunteers

TABLE II.—Manner of Enlistment

	First 50 Cases	Last 50 Cases	Total Series of 200
	%	%	%
Regulars	10	6	6.5
Reservists	44	4	19.5
Territorials	14	24	19.5
Volunteers	28	24	30
Conscripts	4	42	24.5

include those who wish to avoid conscription in order to exercise more choice in the selection of their duties; those who believe they will be rejected on medical grounds and wish to impress their friends with their moral worth; those who hope that Army life will cure them of their troubles; those who act impulsively in a passing fit of patriotism and withhold information which might bring about their rejection. Of the first hundred patients there were 52 from France; of the second hundred the majority were from training camps in Britain. Only a few had been in action. Since the man who first breaks down on active service did not break down in his training camp, the lower the incidence of active service cases the poorer the material. In this respect our cases compare unfavourably with those reported by Hume (1918).

Symptoms

Table III gives the incidence of major and minor symptoms as recorded by several authors and as found in my series of 200 cases. Nervousness was difficult to assess, for many patients were suspicious if their nervous integrity was doubted, and seemed anxious to retain a cardiac label.

TABLE III.—Symptoms

Symptom	Addis and Kerr (1919) 100 Cases	Craig and White (1934) 50 Cases	Friedlander and Freyhof (1918) 50 Cases	Hume (1918) 1,000 Cases	Parkinson (1916) 40 Cases	Swain (1921) 90 Cases	Wood (1941) 200 Cases
	%	%	%	%	%	%	%
Breathlessness	100	77	80	67.5	97.5	74	93
Palpitations	96	80	74	35.4	65	72	89
Fatigue		68	44		40		88
Sweats	81	20	54		15	34	80
Nervousness	100		44		12.5	55	79
Dizziness	96	36	54	40.3	50	55	78.5
Pain (left chest)	84	64	88	76.8	60	56	78
Headaches		30				52	72.5
Trembling	40	18					65
Sighs		35					62
Flushes	75	10	32				57
Throbs							57
Cramps							57
Paraesthesia					12.5		56
Dry mouth							55
Syncope	46	20	10	9.8		13	34.5
Vomiting or diarrhoea			12			23	26
Insomnia		18				42	18.5
Frequency of micturition							10.5
Anorexia						30	20

The figures show that breathlessness, palpitations, fatigue, sweats, nervousness, dizziness, and left thoracic pain are the most frequent symptoms, occurring in more than three-quarters of the patients. Minor symptoms, comprising headache, trembling or shakiness, sighs, flushes, throbbing, cramps, paraesthesia, and dry mouth, occurred in half to three-quarters of them. Less common were syncope and significant gastro-intestinal symptoms, with an incidence of 34.5 and 26%, respectively. Relatively rare were insomnia, anorexia, and disturbances of the bladder. I failed to obtain the percentage incidence of phobias and nightmares, but they were common. In Barlow's series of 382 cases nightmares occurred in 23% (1920).

Although Lewis (1917) states that many of these symptoms are no more than exaggerated manifestations of healthy responses to effort, on questioning 50 normal young men (doctors, medical students, technicians, and soldiers) I found that extreme effort rarely produced more than breathlessness and fatigue. About a quarter noted dizziness, and a quarter mentioned a stitch—but not inframammary pain. Palpitations occurred in 16%; headache, trembling, and throbbing each in 6%; nervousness and sighing not at all; and most of the other symptoms were absent.

In Da Costa's syndrome the chief complaint was palpitation of the heart in 30%, left inframammary pain in 29%, breathlessness in 20%, fatigue in 11%, and dizziness in 10%. In the controls the chief symptom was breathlessness in 80%, fatigue in 12%, palpitation of the heart in 4%, dizziness in 2%, and pain in none.

This comparison throws doubt on the idea that Da Costa's syndrome is produced by the same mechanism as that which determines the symptoms of normal people during extreme effort. Further, some of these symptoms have particular characteristics which are very significant, for they suggest a different interpretation. What is described as breathlessness, for example, is often rapid shallow breathing or a feeling of inability to obtain a satisfying breath; and sweating nearly always refers to the palms of the hands, the soles of the feet, and to the axillae—areas which sweat very little during effort in controls. Again, the symptoms of Da Costa's syndrome are rarely, if ever, confined to exertion. They may occur at any time during the day or night, and they are invariably provoked by emotion.

Now compare the symptoms of Da Costa's syndrome with those produced by some of the unpleasant emotions—e.g., panic, fear, anxiety, and horror. They have been well described by Darwin: "During fright the heart beats quickly and violently, so that it knocks against the ribs;

but it is very doubtful whether it then works more efficiently than usual, for the skin instantly becomes pale, as during incipient faintness." Altered breathing is invariable—it is usually hurried, and as fear increases to terror it becomes laboured. "Under slight fear there is a strong tendency to yawn." Nervousness is taken for granted, for nervousness is fear. "That the skin is much affected under the sense of great fear we see in the marvellous and inexplicable manner in which perspiration exudes from it. This exudation is all the more remarkable as the surface is then cold." After extreme fear there is utter prostration. "One of the best-marked symptoms is the trembling of all the muscles of the body" (Darwin, 1872). Several others may be added: faintness, with or without loss of consciousness, is common, especially in women: weakness of the legs, so that the knees knock together, is familiar to many; worry and headache may be partners; flushes reveal the shame, embarrassment, or anger we are striving to hide; the tongue is said to cleave to the roof of the mouth in moments of great fear; one may be "sick with apprehension"; frequency of micturition, or diarrhoea, may disturb the candidate for an examination or the soldier before he goes over the top.

Signs

Although examination reveals no evidence of organic disease it is very helpful as a means of checking the validity of the patient's complaints, for signs of disturbance of the autonomic nervous system are almost invariable (Table IV).

TABLE IV.—Signs

Sign	Wood 1941 (200 cases)	Friedlander & Freyhof 1918 (50 cases)	Hume 1918 (1,000 cases)	Swann 1921 (90 cases)	McCullagh 1934 (37 cases)
General:	%	%	%	%	%
1. Facies	31				
2. Nervousness	48				
Cardiovascular:					
3. Cold blue hands	44.5				54
4. Flushes	36.5				86
5. Resting pulse > 90 per minute	28				
5. Standing pulse > 100 per minute	35				
6. Overaction of heart or great vessels	44	50			
6. Blood pressure > 150/90	27				
7. Deceleration time > 2 minutes	33				
Respiratory:					
8. Frequent sighs	32				
9. Hyperpnoea or tachypnoea	21.5				
10. Breath-holding < 30 seconds	76				
Sudomotor:					
11. Visible sweat on palms	67				92
11. Sweat trickling from axillae	35				
Skeletal and Muscular:					
12. Tremor or shakiness	26.5	96		76.7	86
13. Poor physical development	41	40		77.5	
13. Asthenic posture	+				
14. Hyperalgesia in area of left thoracic pain	+		26.8		

All of them may be found in recognized forms of psychoneurosis, and may be seen in normal persons under the influence of certain emotions. On the other hand, nervousness, cold blue clammy hands, and sighs are independent of effort both in patients and in controls.

The signs present are roughly proportional in number to the severity of the case, as judged by the Army category recommended on discharge from hospital (Table V). The ratio in the right-hand column illustrates this best, and is so computed because the choice between Categories C and E may depend upon the national importance of the patient's civil occupation. There were 165 cases in this series, and 87% had three or more signs. In a series of 50 controls (young doctors, medical students, and healthy soldiers) only 1 showed three signs, and only 3 showed two signs; there were 22 with a single sign and 24 with none.

TABLE V.—Significance of Clinical Signs (165 Cases)

Signs	Cases	Category Returned			Ratio A1 : C + E
		A1 Full Duty	C Light Duty	E Totally Unfit	
0-2	21	16	5	0	3:1
3-4	37	13	15	9	1:2
5-6	48	13	20	15	1:3
7-8	31	6	15	10	1:4
9-10	20	0	10	10	0:20
11-14	8	0	0	8	0:8

Diagnosis*

Da Costa's syndrome is often diagnosed as rheumatic carditis, toxic myocarditis, weak or tired heart, cardiac strain, anaemia, V.D.H., thyrotoxicosis, pulmonary tuberculosis, pleurisy, influenza, angina pectoris, or malingering. There is little excuse for these errors: the family history gives a clue in over 50%; the patient's history is diagnostic in about 75% (Lecture III); there are about twenty characteristic symptoms, and some fourteen characteristic signs. Da Costa's syndrome is a positive diagnosis, not a negative one.

It is often said that the symptoms of "effort syndrome" are indistinguishable from those of early organic heart disease; that on the history it is impossible to say that the case is not one of mitral stenosis. During the last year I have examined 100 recruits with early organic heart disease. There were 80 with rheumatic heart disease (various combinations of aortic and mitral disease), 18 with congenital heart disease of various kinds, 1 with auricular fibrillation of unknown origin, and 1 with paroxysmal supraventricular tachycardia. Symptoms occurred in 21, and in 13 of these the characteristic features of Da Costa's syndrome were present. The lack of any relation between the symptoms and the size of the heart (Table VI) supported

TABLE VI.—Relation of Symptoms to Size of Heart in Conscripts with Uncomplicated Organic Heart Disease

Degree of Cardiac Enlargement (as judged on X-ray Screen)	No. of Cases	Symptoms			
		None	Like those of Da Costa's Syndrome	Probably Cardiac	Total with Symptoms
None	32	24	7	1	8
Slight	39	31	3	5	8
Moderate	23	20	2	1	3
Considerable	6	4	1	1	2

the view that the symptoms were not of cardiac origin. Only 8% had symptoms which appeared to be referable to the heart itself. The remaining 79 cases were symptom-free, and 59 of these patients were known to be capable of exerting themselves to the full, either in their work or in sport. It is concluded that inactive early organic disease rarely produces symptoms, and should not be confused with Da Costa's syndrome.

Mechanism of Somatic Manifestations: Left Inframammary Pain

A complete review of the English and American literature, from the heated discussion in the *British Medical Journal* of 1858 (C. Coote; Inman; Fuller) to the latest remark by Spillane (1940), reveals the astonishing fact that not only the cause but also the site of origin of left inframammary pain is unknown. The best description of it is that by Fuller (1858) as it occurred in himself; details have been added by Baker (1930). There have been, and still are, four main views as to its origin: that it is cardiac (Martyn, 1864; Cowan and Ritchie, 1935; Bourne and Wittkower, 1940); that it is referred from faulty function of muscles or ligaments about the spine (H. Coote, 1858)—

* The section under this heading will be dealt with more fully in the *Proceedings of the Royal Society of Medicine*.

a theory made plausible by the experimental work of Kellgren (1940); that it is a myalgia, resulting from fatigue of accessory muscles of respiration (Inman, 1858; Broadbent, 1875; Briscoe, 1920, 1927); that it is imaginary (Schnur, 1939).

I have made some observations on the source of inframammary pain. By stimulating interspinal ligaments with 6% saline Lewis and Kellgren (1939) have shown that it is not possible to distinguish visceral from somatic pain by its character. The special features of left inframammary pain do not therefore determine its origin. I have confirmed this fact in four subjects who were unable to distinguish between spontaneous pain, induced local pain, and induced referred pain.

There are three good reasons why the pain is not imaginary: its character and behaviour are too uniform; medical colleagues who have suffered from it are good witnesses of its reality; and although it may be abolished by certain injections, presently to be described, I have never succeeded in having any effect upon it by injections through the same skin puncture but into the wrong structure. Schnur's (1939) work is not in disagreement, for his success in relieving pain by trivial injections admittedly depended upon strong counter-suggestion, and any pain may be removed from consciousness by such a method; even major operations have been performed successfully and painlessly under hypnosis.

Is the Pain Local or Referred?

Granting, then, that the pain has a bodily foundation, we have next to consider whether it is local or referred. Lemaire (1926) first showed that pain referred from viscus could be abolished by anaesthetizing the skin in the area where it was felt. His work was confirmed by Weiss and Davis (1928), Rudolf and Smith (1930), and Morley (1931). On the other hand, Woollard, Roberts, and Carmichael (1932) were unable to influence, by cutaneous anaesthesia, the shoulder-tip pain produced by pinching the proximal end of the divided phrenic nerve in 9 cases of phrenic avulsion. The evidence is therefore conflicting, and the controversy is not yet settled.

When pain is referred from some muscular or ligamentous lesion it is not relieved by skin anaesthesia or by nerve-block, according to experiments made by Kellgren (1938). On the other hand, my own observations suggest that it may be so relieved.

Experiment 1.—0.3 c.cm. of 6% saline was injected into the third right interspinal ligament after anaesthetizing the superficial tissues. Considerable pain was referred to an area just above the right nipple. The skin in this region was quickly anaesthetized with 2% novocain, with prompt relief. Owing to the transient nature of pain produced in this way I could not be sure that it would not have passed away as quickly without interference. A second injection of 0.3 c.cm. of 6% saline was therefore given into the same interspinal ligament, but only a trivial and very fleeting pain developed anteriorly, which vanished almost as soon as it was noticed.

Experiment 2.—0.15 c.cm. of 6% saline was injected into the fourth right interspinal ligament. Pain was referred to an area just below and external to the right nipple. It was described as severe and pressing in character. Cutaneous anaesthesia afforded immediate relief. Double the dose of saline was then injected into the same interspinal ligament, but no pain whatever developed anteriorly.

It seems, therefore, that pain referred from viscus or from ligament may or may not be relieved by cutaneous anaesthesia. The effect may depend upon the intensity of the stimulus.

I am certain that cutaneous anaesthesia does not influence the local pain produced by injecting saline into intercostal muscle. Four experiments were made, and as they were all alike I will describe only one.

Experiment 3.—An area of skin measuring about 30 sq. cm., rounded in shape, in the left submammary region, was anaesthetized with 2% novocain until a pin-prick could not be felt. Only 0.1 c.cm. of 6% saline was then introduced, through the middle of the anaesthetic area of skin, into the intercostal muscle. Severe pain resulted, maximum beneath the centre of the anaesthetic area, and spreading diffusely outwards all round. Local tenderness was associated.

I am also certain that spontaneous local pain resulting from injury to ligament is uninfluenced by cutaneous anaesthesia.

Experiment 4.—Advantage was taken of a case of dislocation of the second left costo-chondral junction. There was considerable local pain and tenderness. The skin covering the painful region was anaesthetized to pin-prick, but no relief was afforded.

Bearing these facts in mind, I investigated the effect of cutaneous anaesthesia on five cases of Da Costa's syndrome in which there was left inframammary pain. Confluent cutaneous wheals and pallor were produced in a rounded area 6 to 7 cm. in diameter, immediately over the tender spot, by the intradermal injection of 2% novocain with adrenaline, until the skin was proved anaesthetic to pin-prick. The pain and tenderness were uninfluenced in every case. This suggests, but does not prove, that the pain is local.

I have found no evidence in the literature relating to the effect of intramuscular novocain on referred pain. Although there is no reason to suppose that it would have any effect the point is too important to leave unchecked.

Experiment 5.—0.3 c.cm. of 6% saline was injected into the fifth left interspinal ligament. A sharp pain, indistinguishable from the spontaneous variety, developed below the left nipple. 5 c.cm. of 0.5% novocain was at once injected into the intercostal muscle at the site of maximum pain, where there was a local tender spot. Relief was not obtained, and the pain lasted another four minutes.

Experiment 6.—This patient complained of spontaneous pain in the third left intercostal space between the sternum and the nipple line. There was tenderness in the third interspinal space at the time of the experiment, but no pain anteriorly. 0.15 c.cm. of 6% saline was injected into the third left interspinal ligament, and pain was referred to the fourth intercostal space anteriorly—one space lower than the site of his spontaneous pain. There was an associated tender spot. Into this 5 c.cm. of 0.5% novocain was injected intramuscularly, but there was no relief. As the pain was rather severe and persistent, 2 c.cm. of 0.5% novocain was injected into the stimulated interspinal ligament, with immediate effect.

Experiment 7.—0.3 c.cm. of 6% saline was injected into the fourth right interspinal ligament of one of my colleagues. Moderate pain developed below the right nipple, but seemed to be passing off just before the intramuscular novocain was given. A further 0.3 c.cm. of saline was therefore injected into the same interspinal ligament, and pain was at once referred to the same site as before, despite the presence of 5 c.cm. of 0.5% novocain in the intercostal muscle at the site of the tenderness.

It is concluded from these experiments that intramuscular novocain has no effect upon pain referred from ligament. I think it may be assumed that it has no effect on any referred pain. On the other hand, it is well known that local intramuscular injections of novocain abolish the local pains of such lesions as fibrositis.

The effect of injecting 2 c.cm. of 2% or 5 c.cm. of 0.5% novocain into the intercostal muscle at the site of tenderness was observed in 11 patients complaining of left inframammary pain. Distress was sometimes experienced as the needle penetrated the superficial intercostal fascia. Both pain and tenderness were promptly abolished in all cases. Skin anaesthesia was never obtained, locally or over the area supplied by the intercostal nerve, proving that the latter was not blocked. The above experiments indicate that left inframammary pain is local.

Pain felt at or near the inferior angle of the left scapula was investigated in two cases; in both, the posterior pain was accentuated by pressing upon the anterior tender spot, but the anterior pain was not influenced by pressing on the posterior tender spot. In the first case 2 c.cm. of 2% novocain was injected into the intercostal muscle at the site of the anterior tender spot with complete relief of both anterior and posterior pain and tenderness. Pressure upon the anterior tender spot no longer produced pain behind. In the second case the skin over the posterior tender spot was anaesthetized with 2% novocain, whereupon the pain shifted an inch or so lower down. The new area was then anaesthetized, and the pain was abolished. Pressure upon the anterior tender spot no longer induced posterior pain. It is concluded that this posterior pain was referred from the anterior lesion. This confirms the observations made by Parkinson (1919), who found that pain at or near the inferior angle of the left scapula never preceded left mammary pain, but that it came either at the same time or subsequently. The lack of any association in the mind of the patient between the angle of the left scapula and the heart was shown by Schnur (1939), and is therefore further evidence that inframammary pain has a somatic foundation.

Cause of Inframammary Pain

The cause of the pain is more elusive than its site of origin. Its association with neurosis is incontestable (Broadbent, 1875; Kellogg and White, 1932; Schnur, 1939). But it is not enough to dismiss it as neurotic: it is still pertinent to ask, What is the mechanism of its expression? If the problem is one of psychosomatic medicine, it is no less a problem.

Sir Charlton Briscoe (1920, 1927) studied the behaviour of the respiratory muscles for many years, and revived the theory that inframammary pain might be due to fatigue of the muscles involved in exaggerated thoracic breathing, mentioning especially the scalenus anticus and the triangularis sterni. He designed a spring belt, to be worn round the chest, in order to inhibit thoracic and encourage diaphragmatic breathing. Unfortunately he failed to distinguish left inframammary pain from angina pectoris, and his findings were discredited on this account.

Although ignorant of his work at the time, and having been led to the conclusion that the pain was coming from muscle or related structures in the chest wall, I investigated the method of respiration in 150 cases of Da Costa's syndrome by means of x rays. During routine screening I picked out those in which diaphragmatic movement was very good (14 cases) and those in which it was very poor (14 cases), and found that of the former group 4 had pain, compared with all 14 in the latter. As this difference seemed significant the investigation was elaborated.

The diaphragmatic excursion was measured from its position at the end of quiet expiration to that on full inspiration (the total movement from complete expiration to complete inspiration was usually normal, the diaphragm assuming a position of rest near its limit of full inspiration in those with poor phrenic movement but retaining its power of complete expiration), and the expansion of the lower and upper thorax was measured with a tape measure at the level of the ninth costal cartilage and at the highest possible level under the arm respectively. The presence or absence of pain was unknown until the examination had been completed and the results recorded. Table VII confirms the original observation, and shows that pain is associated not only with poor phrenic movement but also with poor thoracic expansion.

To see whether extremes would yield more convincing results, I noted those cases in which the sum of the left and right phrenic excursion measured 4 cm. or less, and

TABLE VII

	No. of Cases	Respiratory Movement		
		Diaphragm (Left + Right)	Lower Thoracic	Upper Thoracic
Pain absent or trivial ..	53	cm. 5.66	cm. 4.84	cm. 4.2
Pain moderate or severe ..	47	4.65	3.3	3.5
Average	100	5.18	4.1	3.87

those with a lower thoracic expansion of 2 cm. or less (the upper thoracic expansion was very rarely diminished alone). Of 43 cases with these poor measurements, 66% had significant pain and 14% had none; whereas of 57 patients with measurements exceeding these limits, only 14% had significant pain, while 60% had none. Table VIII

TABLE VIII

	No. of Cases	Significant Pain	Pain Trivial or Absent
Relatively good breathers (diaphragmatic movement > 5 cm.; lower thoracic expansion > 3 cm.; upper thoracic expansion > 2.5 cm.)	40	12.5%	87.5%
Bad phrenic movement: 4 cm. or less (normal thoracic expansion)	25	72	28
Bad thoracic expansion: lower measurement 2 cm. or less (normal phrenic movement)	16	75	25
Bad phrenic + bad costal movement	10	90	10

gives a more detailed analysis, and is even more convincing. When both diaphragmatic and lower thoracic movements were at fault 90% had pain; but only 12.5% had pain when both of these movements were good.

Muscular Strain

It is concluded that there is some association between left thoracic pain and poor diaphragmatic or lower thoracic movement. Since very few patients had pain while these measurements were being made, pain is unlikely to have been responsible for the functional disturbance of the respiratory muscles. It is therefore suggested that functional disturbance of the respiratory muscles may be a factor in pain production. It has already been noted that the diaphragm fails to relax properly, approaching its limit on inspiration but falling far short of it on expiration—a fact which suggests that the respiratory muscles are in a state of tonic contraction. These muscles, so often poorly developed, might well become fatigued or strained, especially when called upon to do increased work, as on effort or as a result of emotion. Douglas and I reproduced the pain, in 8 out of 19 cases in which it was the leading symptom, by asking the patient to breathe vigorously for a few minutes.

This hypothesis does not, however, explain why the pain is left-sided. I was unable to confirm C. Coote's (1858) suggestion that it was associated with the common type of scoliosis with concavity to the left. Two other reasons, however, suggest themselves: (1) the pain is actually bilateral in 25%, and there are often odd pains in other sites, but the patient focuses his attention on the pain which he believes to be coming from his heart; (2) the heart itself, bumping with undue vigour against the chest wall, may act as a traumatic factor. The first suggestion has the support of psychiatric studies; the second would explain why lying on the left side so often aggravates the pain—a posture which rests the thoracic muscles of respiration on that side at the expense of the diaphragm (Webb, Forster, and Gilbert, 1921; Butler and Dana, 1928), but

which increases the impact of the heart against the chest wall.

There is another group of cases in which left thoracic pain is obviously the result of muscular strain. There were 6 such cases out of a series of 36 patients who complained of severe pain. In these instances pain was the initial symptom, the onset being sudden and dramatic, and occurring when the patient had no thought of heart disease. A good and common example of the kind of effort responsible for these lesions is cranking an engine; another is lifting a heavy weight. Various muscles may be affected, but after testing the effect of vigorous contraction of individual muscles on the pain I believe that the attachments of pectoralis major and minor, of the external oblique, and of the upper slip of the rectus abdominis, to the fifth rib, are especially susceptible. When the pectorals are to blame pain may be referred to the left arm. Some of these patients volunteered that they felt something snap in their chests.

To sum up, left inframammary pain arises in local muscular or fibrous tissue; it may be due to fatigue or strain of respiratory muscles in cases with respiratory neurosis; to strain of certain muscular attachments involved in such actions as cranking a lorry or lifting a heavy weight; to incessant minimum trauma from the overacting heart of cardiac neurosis; it is predisposed to by poor physique in Da Costa's syndrome; it is maintained and exaggerated by the belief that it arises in the heart. Several of these factors may operate together.

(Lectures II and III will appear in our next two issues. The complete list of references will be appended to the third lecture.)

CEREBRAL SYMPTOMS OCCURRING DURING SULPHAPYRIDINE TREAT- MENT OF MENINGOCOCCAL MENINGITIS

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The value of sulphapyridine in the treatment of meningococcal meningitis is established beyond doubt. According to our own experience as well as the large number of papers published on the subject, rapid improvement of the clinical picture and an uneventful recovery can be confidently forecast provided that the dosage is adequate and the patient not hopelessly overwhelmed by an acute meningococcal septicaemia. Moreover, the drug is generally accepted as having a large margin of safety, and such common toxic manifestations as occur during treatment are usually more unpleasant than dangerous. Of the more serious complications, the possibility of an acute haemolytic anaemia, or anuria following obstruction of the renal tubules by sulphapyridine crystals, should be borne in mind. Fortunately both conditions are very uncommon, and neither has been observed in our own series of cases. Agranulocytosis is a well-recognized sequel of prolonged treatment with sulphapyridine, but as in meningococcal meningitis large doses are usually given over short periods the possibility of this complication need not be considered seriously.

The 5 cases described below are chosen from 70 cases treated at this hospital since the beginning of 1940. Their clinical history suggests that heavy doses of sulphapyridine may give rise to cerebral symptoms closely simulating those of acute meningitis, which may therefore be erroneously ascribed to the infection itself. As this type of toxic reaction may lead to death unless administration of the drug is promptly discontinued, it is unnecessary to stress the importance of recognizing it at the earliest possible moment.

Case I

A boy aged 14 was taken ill suddenly, with headache and vomiting, in the morning of February 12, 1940. By the evening he was in a semiconscious state, and a lumbar puncture performed at home showed purulent cerebrospinal fluid. He was given four injections of 2 c.cm. of sodium sulphapyridine (10 grains) at four-hourly intervals during the night.

He was admitted to hospital in the morning of the 13th in a semicomatose state. He was very irritable, and showed intense head retraction and spasm of the hamstrings. There was a profuse petechial rash on the trunk. The cerebrospinal fluid was under increased pressure, was turbid, and contained numerous pus cells and meningococci. Sodium sulphapyridine 3 c.cm. was given intramuscularly on admission, and was continued every three hours. On the 14th there was a slight improvement, but the cerebrospinal fluid was still turbid and under increased pressure. On the 15th the fluid became clearer, but the boy was still restless and confused. The dosage of sulphapyridine was now reduced to four-hourly injections of 3 c.cm. Although on the 16th the cerebrospinal fluid was clear and under normal pressure, his general condition, restlessness, and confusion became steadily worse, and he died at 9 p.m.

Case II

A male baby aged 20 months was taken ill on March 23, 1940, with abdominal pain and vomiting. He was admitted to a general hospital on April 1, but no signs suggestive of meningitis were found during the first four days. On the 5th photophobia and head retraction were observed and Kernig's sign became positive. A lumbar puncture was performed and some turbid fluid containing meningococci was withdrawn. He was given $7\frac{1}{2}$ grains (one tablet) of sulphapyridine and transferred to this hospital.

On admission the presence of pus cells and meningococci in the cerebrospinal fluid was confirmed. The child was drowsy and showed the characteristic signs of meningitis—well-marked head retraction, positive Kernig's sign, and intense photophobia. There was no rash. Sodium sulphapyridine 2 c.cm. was injected intramuscularly, and 1.4 c.cm. was given every four hours. On the 6th there was no change in his condition. The cerebrospinal fluid, however, was under normal pressure and was much clearer than on the previous day. During the next two days the fluid became clear, but there was no corresponding improvement in the clinical signs. The child was still very drowsy, and head retraction was pronounced. On the 9th the dose of sodium sulphapyridine was increased to 3 c.cm. six-hourly. The cerebrospinal fluid was still clear and under normal pressure, but head retraction and drowsiness remained. On the 13th the dose of sulphapyridine was reduced to 3 c.cm. twelve-hourly. Next morning slight improvement was noticed, but the patient's condition deteriorated later in the day, and he died during the night.

Case III

A girl aged 7 was admitted to hospital on July 14, 1940, twenty-four hours after the onset of her illness. She was drowsy but not unconscious, and resisted examination. Neck rigidity and spasm of the hamstring muscles were well marked, but no petechial haemorrhages were seen. The cerebrospinal fluid was turbid and under increased pressure; microscopic examination showed numerous pus cells and meningococci.

As she was unable to take sulphapyridine by mouth the drug had to be given by intramuscular injection. Sodium sulphapyridine 3 c.cm. was administered immediately, and the injections were repeated three-hourly throughout the next forty-eight hours. Next day she was still confused and restless, and the cerebrospinal fluid was turbid, although no longer under increased pressure. On the 16th the dosage of sulphapyridine was reduced to 2 c.cm. six-hourly. Although