RELATIONSHIP OF SIGNIFICANCE OF WOUND TO PAIN EXPERIENCED

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• *The frequency of pain severe enough to require a narcotic was studied in 150 male civilian patients and contrasted with similar data from a study of wartime casualties. Efforts were made to have the two groups comparable in essential respects and to make sure that existing differences, such as age and past illness, between the two groups did not influence the results. The group of soldiers had very extensive wounds, were clear mentally, and were not in shock; many had had no morphine at all, yet less than one-fourth said, on being questioned, that they had enough pain to want anything done about it. The percentages of patients desiring narcotics were 32 and 83 for the military and the civilian groups respectively.*

There was no dependable relation between the extent of a pathological wound and the pain experienced. No significant difference was found between the pain of sudden injury and that of chronic illness. The intensity of suffering is largely determined by what the pain means to the patient. This emphasizes the impossibility of appraising, by current experimental techniques at least, the power of analgesic agents in man. It also means that the indiscriminate administration of powerful analgesics to all injured individuals is unsound.

Probably everyone who is accustomed to working with pain of pathological origin has been puzzled by the lack of any obvious correlation of extent of wound with pain reported by the patient. Certainly the degree and duration of pain from any given wound is essentially unpredictable. This was nicely put more than a hundred years ago. On writing of gunshot wounds in the Peninsular War, Guthrie [1] said, "in two persons suffering apparently from the same kind of injury, and with the same detriment, one will writhe with agony, whilst the other will smile with contempt." Also, Dupuytren [2] was quoted in 1836 as saying:

> What a difference there is in the morale of those we treat in civil hospitals and those hit by murderous fire on the field of battle! The military man is accustomed to forgetfulness of self and familiar with the prospect of mutilation. He considers himself happy if he saves his life yet loses an extremity. And, as long as he is assured of security, . . . he faces with courage, even joy, the scalpel of the surgeon. But look at the unfortunate laborer, the farmer, or the artisan, whose work is the only resource of a large family. He is obsessed by fear; misery awaits him. His is a profound sorrow, a dark hopelessness. He accedes only with regret to the insistence of the surgeon. One should not be surprised by the difference in results!

Until recently it had seemed impossible to bring any order into this apparent chaos.

During the compiling of evidence to test the hypothesis that suffering consists of two principal factors, the initial sensation and the reaction to sensation, a possible clarifying situation emerged. It should be mentioned that the hypothesis referred to is more than 60 years old. It goes back to Marshall [3] and to Strong.[4] Factual evidence in support of the interesting speculations of Marshall and Strong has been obtained in the anesthesia laboratory at Massachusetts General Hospital and has recently been summarized.[5] When this evidence is examined as a whole, it carries strong indication that the reaction phase or processing phase is very often of more importance in suffering than is the original sensation. The data to be presented here are in line with this view.

The hypothesis mentioned has been tested as follows: A number of years ago I had an opportunity to study a large group of men recently wounded in battle.[6] Data on these men were collected chiefly on the Anzio Beachhead, where the men studied had been subjected to almost uninterrupted shell fire for weeks. Notable in this group of wounded soldiers was their optimistic, even cheerful, state of mind. It is important to remember that these men were interviewed in a forward area very shortly after having been brought from the battlefield to the field hospital, from an area of desperate anxiety to an area of relative safety. They thought the war was over for them and that they would soon be well enough to be sent home. It is not difficult to understand their relief on being delivered from this area of danger. The battlefield wound marked the end of disaster for them, or so they thought.

The present study was set up to contrast those data with the incidence of pain severe enough to require a narcotic in a series of civilians subjected to surgery. The civilian's surgical operation is viewed as a depressing, calamitous event by most people. Here, then, are two groups of individuals, each with severe tissue trauma. In the one case, there was sudden relief from almost overwhelming anxiety, and the injury was viewed as good fortune; in the other case, the injury was viewed as disaster and was fraught with anxiety. The comparison of interest is the frequency of pain reported in the two situations. The tissue trauma inflicted by the surgeon is, for the categories studied (intrathoracic, intra-abdominal, and bone surgery), far less than that of wounds in the same regions inflicted by high explosive shell fragments (see table); yet, as shown, the pain arising from the surgeon's wounds was far greater than it was from the war wounds. The crucial difference appears to lie in the significance of the two wounds and in the reaction of the patients to each.

Method and Data

To get at the question of pain in the earlier study, the wounded man was asked several carefully phrased questions, "As you lie there, are you having any pain?" (Care was taken to be sure the patient understood the

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question.) If the answer was "no," that part of the questioning was dropped. If "yes," further inquiry was made: "Is it slight pain, or moderate pain, or severe pain?" There was usually little hesitation in differentiating. Those who said they were having pain of any degree were asked if the pain was great enough so that they wanted something to relieve it. (Incidentally, it very early became apparent that morphine was an unfortunate word to use, and its use was avoided. To the layman, morphine is a frightening word; the wounded men were alarmed by the implication that they were "bad enough" to need this agent.) Only males were considered in both groups. So much for general procedure.

The striking thing about the war wounds and the men involved was their comparative freedom from pain. Although the soldiers chosen for study all had very extensive wounds, only men who were clear mentally, who were not in shock, and who had had no morphine for at least four hours were chosen for study; many had not had any morphine for seven hours or more, and 36 had not had any at all. Excluding those who had had no morphine, the average time since receiving morphine was 6.4 hours. Only one-quarter of the entire group of men, when questioned 7 to 12 hours after being wounded, said they had enough pain to want anything done about it. (The figure is one-third for the three categories studied here: bone, thoracic, and abdominal wounds.) Their statements were made in response to a direct question, which of course reminded them that analgesic agents were available if they wanted them. These severely wounded men did not have a general block of the pain experience, for they complained in a normal manner at rough handling of their wounds, or at inept venipunctures. The same interrogation procedure as described above was followed in the present study of surgical patients.

*Comparison of the Frequency of Pain Severe Enough to Require a Narcotic in Two Situations, War Wounds and Civilian Surgical Wounds**

Circumstance			Trauma to Bones	Intrathoracic Trauma	Intra-Abdominal Trauma	Total %
War wounds	Pain	none	19	15	7	
		slight	12	18	5	
		moderate	7	11	14	
		severe	12	6	24	
	Narcotic wanted	yes	11	10	27	32
		no	39	40	23	68
	No. of patients		50	50	50	
	Age, yr.		24.8±0.9	24.5±0.8	22.7±0.6	
	Time since trauma, hr.		12.5±1.3	9.8±1.0	7.2±0.7	
Civilian surgical wounds	Pain	none	5	5	1	
		slight	14	4	8	
		moderate	17	17	21	
		severe	14	24	20	
	Narcotic wanted	yes	38	42	45	83
		no	12	8	5	17
	No. of patients		50	50	50	
	Age, yr.		45.5±2.3	49.2±2.0	52.6±1.9	
	Time since trauma, hr.		4.4±0.3	3.0±0.3	4.3±0.4	

* Data based on 300 male patients.

If the extent of tissue trauma had any fixed relationship to the pain experience, there was every reason to suppose that those with war wounds would have more pain, both in frequency and in degree, than those who had the lesser wounds of surgery. As shown here, the opposite was the case (see table). The important difference in the two situations seems to be in the interpretation of the wound. In the one case the war wound marked the end of disaster, the victims thought, and was associated with relatively little pain. In the other case, the surgery, although involving much less trauma, spelled disaster for the patient. It was associated with far more pain than were the war wounds. These data support the view that the reaction or processing component of suffering is at least as important, probably more so, than the original sensation. This is not to deny that wounds and pain often go together; but often they do not, as well. Clearly important factors besides trauma to nerve endings have importance here. It has been suggested that the violence of war wounding happily carries with it analgesia. There is no evidence to support such a view in individuals whose central nervous system is undamaged. Such an occurrence, if it existed, would be fascinating indeed. It seems unlikely that a bone cut by the surgeon's chisel or the femur fractured by the family automobile in a crash is any different physically from the femur fractured by a blow from a shell fragment.

Comment on Civilian Data

Age.—An obvious difference between the two groups shown in the table is age. This appears not to be important as far as the present thesis is concerned: 20 civilians fell in the 17-to-30-year age group, similar to the soldiers; 18 (90%) of these civilians had pain severe enough to want a narcotic. Fifty-seven civilians fell in a second 13-year period, age 50 to 63, and had pain severe enough to want a narcotic in 50 (88%) of the cases.

Anesthetic Agents and Time of Interview.—Patients receiving thiopental sodium with nitrous oxide and a muscle relaxant recovered consciousness sooner than those receiving ether and were ready for interview correspondingly earlier. The incidence of those having sufficient pain to want a narcotic is not significantly different in the two groups. The data are as follows: For the patients receiving a muscle relaxant, the interview time averaged 2.9 hours after the completion of the surgery, with 87% having sufficient pain to want a narcotic. For the patients receiving principally ether, the interview time was 4.7 hours after completion of surgery and the percentage wanting a narcotic was 84.

It should be added that 50% of the patients receiving a muscle relaxant had had a narcotic by the time of the interview, whereas 43% of those receiving ether had. Any important difference is questionable. If there is any difference at all, it is doubtless because of the fact that consciousness is recovered earlier when the thiopental muscle-relaxant sequence is used than is the case with ether. Notwithstanding the somewhat greater frequency with which the patients had received a narcotic before the interview in the muscle-relaxant group, 54% of this group of 54 patients, on interview, had pain characterized as severe, 33% had moderate, 7% had slight, and 6% had none. In the ether group, only 31% of a total of 74 patients had pain characterized as severe, 40% had moderate, 20% had slight, and 9% had none. The earlier and possibly more frequent administration of a narcotic to the muscle-relaxant group has not obscured the fact that pain is very frequently present in this group and of a

severe degree, even severer than was true of the ether anesthesia group. The thesis of this study is supported, for the percentages 87 and 84 (see above) of those having pain severe enough to want a narcotic are not different for the two types of anesthesia.

Duration of the Pathological State.—It is only fair to point out that the wounded soldiers have had their disability suddenly thrust upon them. It should also be borne in mind that the soldiers' trauma continues during the ambulance haul over the inevitably rough roads of the battle area until he enters the forward hospital. This rough handling is especially serious in the case of fractures of long bones, for splinting is never perfect. As for the other group, one might suppose that the patient subjected to long illness would be more likely to complain of pain and ask for an analgesic agent sooner than one whose surgery was a sudden necessity; however, this did not prove to be the case. Of the patients subjected to operations associated with long illness, 46 in a random sample (gastrectomy, esophagectomy, aortic graft, "cup" arthroplasty to hip, spinal fusion), 87% wanted a narcotic at the interview. Of the patients not subjected to long illness preceding surgery, 20 in a corresponding random sample (fracture of bone, cholecystectomy, appendectomy, lithotomy), 90% wanted a narcotic. Thus, long duration of the disability does not appear to be a factor.

Pathological Pain Versus Experimental Pain

It may be remarked that the data presented here, confirming as they do the unrelatedness of the extent of a pathological wound and the pain experienced, cast further doubt on the usefulness of experimental pain in man for the purposes to which it has so far usually been put[7] and, conversely, support the use of pain of pathological origin for work in this field. Some discussion of this point is indicated, for the data presented here strongly support the importance of the reaction component of suffering (see above), and this lies at the heart of the controversy on experimental versus pathological pain.

There are many ingenious methods of producing pain for experimental purposes: electric shocks to teeth, pricks of the skin, ischemia of muscles, heat to the forehead, and so on. All of these methods have one thing in common, and that is the assumption that the more nerve endings are traumatized, the more the pain experienced. Scores of such studies have been made, and often these even deal with complex minutiae of the situation.

Examination of the pain arising in injury or disease indicates that this basic assumption of many experimentalists does not hold true. Presumably one of the reasons for studying experimental pain is to learn something about pain of pathological origin, its cause, its mechanism, and its therapy. In view of the findings presented here, it seems that experimental pain in man as employed so far has little to offer in the appraisal of the analgesic power of these agents. There are, clearly, basic differences between pain of experimental origin and pain from pathological sources. This fact has not been given the attention it deserves. The lesser wounds of civilian surgery have more pain associated with them than do the greater wounds of warfare. It is evident that there is also a qualitative difference here (for some wounds are painless). This appears to be determined by the significance of the wound.

There is an abundance of evidence to indicate that experimental pain methods in man do not work as well as has been thought for the appraisal of analgesic agents. Experimental pain in man certainly has other established uses, as, for example, in determining the anatomy of the pain apparatus. The most carefully presented and fully studied experimental pain method is that of Hardy, Wolff, and Goodell.[8] Some 15 groups of investigators have now been unable to confirm many of their observations,[7] particularly as their work relates to analgesic agents. In the second place, experimental pain in man might have wider usefulness if it could be possible to separate it from the reaction phase. The evidence against this having been done (for experimental pain) to date has been summarized elsewhere.[7] This is not intended to imply that it will never be done.

It is important to make the following point clear: What is said relates to man and not to animals. There is much reason to believe that the situation is different in the two species. Unlike the situation with experimental pain in man, in animals the effect of powerful analgesic agents on experimental pain leads in many hands to reproducible results. As pointed out before,[5] presumably all pain is serious and significant to an animal, to the extent that experimental pain never is to man. Thus the reaction of the animal to experimental pain is likely to be the same as for pathological pain; the two are not differentiable to the animal. This makes experimental pain in an animal comparable to pathological pain in man, if reaction to the original sensation is as important as it seems to be in the pain experience.

General Observations

The data accumulated here indicate something more than the limited usefulness of experimental pain in man; namely, they indicate that some factor other than the extent or degree of wounding is of principal importance in the pain experienced. It has seemed profitable to search for this other factor or factors. From the evidence presented above, it seems reasonable to conclude that reaction to the original pain sensation is a very important factor in suffering. There may be other important factors that merit examination. In any case, the nature of this reaction and the factors that influence it are poorly understood and need study. It is not inconceivable that ingeniously devised experiments that utilize pain of both pathological and experimental origin may be useful not only as mentioned but also in investigation of the influence of fatigue, adaptation, and focus of attention on the pain experience. Work in such a direction is now in progress in the anesthesia laboratory at Massachusetts General Hospital.

The dangers of conclusion based upon causality are well known. It has been shown, however, that, in a situation where the anxiety level is high, as in civil

surgery, wound pain of sufficient degree to require narcotics is far more common than it is in a situation where desperate anxiety (fear of sudden death on the battlefield) has been replaced by a far lesser worry (a wound). It can be pointed out that this finding is in accord with several other types of observations. Malmo and Shagass,[9] in a study of the effects of experimentally induced thermal pain in normal subjects and in pathologically anxious patients, found when they studied striated muscle activity such as finger movements and neck muscle potentials that the greater the degree of anxiety as reflected in the muscular activity, the greater the frequency with which pain was signaled. The differences are statistically reliable. Their data also show that the more severe the anxiety, the greater the overreaction to painful stimuli. Their findings corroborate earlier observations of Chapman, Finesinger, Jones, and Cobb[10] that the threshold values of thermal pain stimulation are higher in controls than in psychoneurotic patients (half of whom were suffering from anxiety) as far as motor reaction to pain is concerned. These findings, which deal with experimental pain, appear to have an analogue in the clinical findings, reported in the present study, that pathological pain was encountered far more frequently in a situation filled with anxiety than in one in which tremendous anxiety has been greatly lessened. Observations complementing these are those of Hill, Kornetsky, Flanary, and Wikler[11] and Hill, Belleville, and Wikler,[12] in which they appear to show in an interesting experimental situation that morphine relieves anxiety and hence, they believe, relieves pain. In our findings, when there was more anxiety, more pain appeared. In the two circumstances there seems to be an important relationship between pain and anxiety. In our situation, when anxiety was present, the incidence of pain increased; in the Lexington group, when anxiety was relieved, pain was relieved. Since such different approaches lead to the same conclusion, it seems unlikely that a false attribution to causality could explain all of these observations.

Dubos[13] has summarized the evidence to show that the etiology of most diseases has several components. It is now clear that those two strong characters, Pasteur and Koch, pressed too narrowly for their "doctrine of specific etiology" (a given microbe for a given disease) and that there is something to be said for the reserve Pidoux and Virchow showed during what might be called the overestablishment of the doctrine of specificity of cause of disease. It is now known that in nearly all infectious and metabolic diseases physiological and environmental factors enter to determine the disease process. The human body is full of latent infectious organisms that act in disease processes only under special physiological or environmental conditions. In the work presented here, we can pursue this view of nonspecificity even further and apply it not to a disease but to a symptom of disease. A wound is not alone the cause of pain; the significance of the wound may be the paramount factor in determining the production of pain. Hardy, Wolff, and Goodell[14] in attempting to generalize concerning the pain experience have said, "The adequate stimulus for pain sensation is the damaging of tissue." From the data given in this present study, this is clearly not the case: great tissue damage can be produced without pain being experienced. Neither the wounding nor the wound is at times an adequate stimulus for pain.

Summary and Conclusions

In a situation in which a wound has great advantage and means escape from overpowering anxiety and fear of death on the battlefield (war wounds terminating military service), extensive wounds are associated with comparatively little pain. In a situation in which the wound connotes disaster (major surgery in civil life), lesser wounds are associated with far more pain than in the former situation. The essential difference appears to be in the difference in anxiety level in the two cases, in the attitude of the patient, and in his reaction to his wound. The findings reported here support the 60-year-old concept of the importance in suffering of the reaction component as opposed to the original pain sensation.

In experimental pain it might seem possible to control the "reaction or processing component" of suffering and, therefore, to measure the action of analgesic agents on the "original sensation." Since many different and widely separated groups of careful investigators have failed to confirm this, it appears reasonable to conclude that analgesic agents have in the experimental situation relatively little effect upon original sensation but very great effect upon the reaction component, since with pain of pathological origin when the reaction is apparently great, consistent and reproducible effects of analgesic agents can be demonstrated. Thus analgesic agents appear to have their principal action on the reaction component.

Extent of wound bears only a slight relationship, if any (often none at all), to the pain experienced. This fact fails to support the relevance of experimental pain work to the pathological pain experience. The concept underlying all experimental pain methods, that the more severe the stimuli to nerve endings, the more the pain, does not hold for pathological pain. Thus the usefulness of experimental pain methods in man for the purposes to which they have often been put (evaluation of the analgesic power of narcotic agents) is questionable. Just as the doctrine of specific etiology of disease falls short, so also is the relationship not precise between cause and a symptom of disease (injury) as far as a wound and resulting pain are concerned. The level of anxiety is important in considering the production of pain. The unfortunate and common practice of administering powerful analgesic agents to all injured individuals is clearly unsound. A considerable number of such patients may not have pain. In others alteration of mood, as for example relief of anxiety, can have beneficial effect. In short, even a great wound is not necessarily an "adequate stimulus for pain."

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"ATHLETIC PSEUDONEPHRITIS"—ALTERATION OF URINE SEDIMENT BY ATHLETIC COMPETITION

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• *Urine specimens were obtained from 47 football players who had passed complete physical examinations and denied renal disease. Each submitted at least one normal specimen together with additional specimens before and after games or strenuous practice.*

Each day was scored as to the severity of the required exertions, and this score was found to be roughly proportionate to the frequency of abnormalities in the urine. On no day did every member of the squad submit a completely normal specimen. In addition to protein, the more unusual types of formed elements appeared in 27 of the 424 urine specimens examined; these included red blood cell casts in 10, epithelial casts in 7, broad casts in 3, and white blood cell casts in 3. During the study, gross hematuria appeared in one subject. In every instance, the abnormalities disappeared when the daily exercise was made less severe.

These findings explained the spontaneous recovery of an athlete whose history of gross hematuria, which is given in some detail, had raised the suspicion of acute glomerulonephritis.

My interest in urinary sediment changes after exercise resulted from seeing a young male who entered the student health service of the University of Pennsylvania on Sept. 6, 1955, complaining of a sore throat of eight days' duration and tea-colored urine of six hours' duration.

Report of a Case

An 18-year-old male was referred from the preseason football training camp, where he had reported two days after developing a severe sore throat at home on Aug. 30. At camp, the initial therapy by the team physician consisted of gargles, acetylsalicylic acid, and fluids. As the student was not febrile nor more than slightly annoyed by his symptoms, he was allowed to enter into the full training program. No subjective improvement had occurred by Sept. 3, and 600,000 units of procaine penicillin G were given intramuscularly on that and the following day. After an active scrimmage on Sept. 5, the man noticed that his urine had become the color of "strong tea." A second specimen obtained three hours later was again that color, and he was sent to the Hospital of the University of Pennsylvania for admission. On entry he denied the presence of headache, backache, or the reception of unusual trauma to the back or abdomen. He also denied previous hematuria, previous renal disease, contact with poison ivy, and recent insect bites. The family history was negative for renal disease.

The physical examination showed a healthy young male in no distress, with blood pressure of 140/90 mm. Hg. The oropharynx was reddened and speckled with white exudates. Bilateral cervical lymphadenopathy was present. There was no costovertebral angle tenderness, and the remainder of the examination gave normal results. The hemoglobin level was 12.1 gm. per 100 cc., and the white blood cell count was 6,900 per cubic millimeter, with a normal differential. The urine had a specific gravity of 1.030 and was acid in reaction; it contained a trace of protein, innumerable red and white blood cells, and occasional granular and white blood cell casts. Diagnosis of acute glomerular nephritis was made, and the patient was placed on therapy with bed rest, acetylsalicylic acid, and 600,000 units of procaine penicillin G intramuscularly every six hours.

The subsequent clinical course and laboratory studies did not substantiate the diagnosis. Blood pressure remained well within the normal limits, averaging 120/75 mm. Hg. The temperature did not rise above 98.6 F (37 C) orally. His fluid output remained well above oliguric levels, averaging 1,150 cc. every 24 hours. Throat culture did not reveal the presence of hemolytic streptococci; antihyaluronidase and antistreptolysin titers were in an intermediate range but were felt to be too low for acute glomerular nephritis. Further urine specimens were free of albumin and showed progressive disappearance of casts and red blood cells until the third hospital day. On that day the urine contained a sudden shower of red blood cell casts, considered identical with those seen in acute glomerular nephritis. Over the next 24 hours these disappeared entirely, and urinary examinations showed normal results for the remainder of his 10-day hospitalization.

By the 10th day the sore throat and cervical lymphadenopathy had disappeared; the hemoglobin level was reported at 14.3 gm. per 100 cc. After a staff conference it was concluded that the clinical picture was probably that of "football hematuria" with associated pharyngitis, even though red blood cell casts had occurred in the urine for one day. With that diagnosis the patient was discharged. During a two-week period of observation at home, both physical examinations and urinalyses daily failed to reveal the presence of disease. At the end of that time he was allowed to return to active participation in football. Through three months of follow-up, he has shown no clinical evidence of nephritis. Results of the urinalyses have been included in the study presented below. These were usually normal but on occasion demonstrated the abnormalities found in the urinalyses of his fellow teammates. His gross hematuria has not recurred.

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