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INJURY AND INTERNAL DISEASE

BY

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When a person alleges that a disease was brought on by injury truth may reside in one or other of the following:

TABLE I

- (a) Injury may cause disease.
- (b) Injury may precipitate disease.
- (c) Injury may aggravate disease.
- (d) Disease may promote injury (Ewing's "traumatic determinism").
- (e) Injury may reveal disease.
- (f) The association may be a pure coincidence.
- (g) In post-traumatic debility and invalidism sundry maladies and degenerations may be installed.

In an assessment of any case certain minimal data must be forthcoming—namely:

TABLE II

- (a) An authentic and tested statement of particulars of the injury.
- (b) A full record of clinical chronology covering the pre-accident period, the injury, and the post-traumatic period.
- (c) Accurate observation of all clinical phenomena, identification of the disease beyond all doubt, and a knowledge of the morbid processes at work.

With this framework we can first turn to the literature, and at once a few generalizations stand out:

TABLE III

- (a) There is hardly any internal disease which has not by someone somewhere been attributed to injury.
- (b) A very great deal of plagiarism and uncritical acceptance of authority has taken place.
- (c) There is often a hopeless conflict of opinion between pathologists and clinicians.
- (d) Many flimsy pieces of evidence have been copied from book to book for years.

Cancer

The first internal malady worthy of study is cancer, and here we are faced with conflicts of opinion. Briefly, three views can be found in the literature on the subject of injury causing cancer—namely: (1) Such an event is opposed to all known principles, but it may occasionally happen. (2) It not only may occasionally happen but in certain types of cancer it frequently does happen. (3) Wherever truth may lie between propositions 1 and 2, here, at least, is an authentic and well-tested case, or series of cases, without comment.

The main leaders of proposition 1 have been Phelps (1910), who, however, excluded sarcoma from his survey;

Stephens (1928); Knox (1929), whose paper was an incisive and hostile counterblast to the writings of Coley; Mock and Ellis (1926); and more especially Ewing (1926, 1928).

As is well known, the chief exponent of proposition 2—namely, that injury is often associated causally with cancer—has always been Coley, who began his observations more than forty years ago. When Knox suggested that the protocols of Coley and others were nothing but a parcel of anecdotes and vague impressions Coley (1929) replied with the obvious retort that many authors make too great an effort to discredit the direct statements of intelligent patients. It is a fact that Coley's cases are always minutely described, and one often has a feeling that scepticism about his conclusions would be the very antithesis of science.

Class 3—namely, cases of post-traumatic cancer described by clinicians without comment—cause little difficulty. They are very scarce in medical literature as a whole. Among the best examples are those of Levy (1927) (sarcoma), Wainwright (1928) (carcinoma), Paul (1929) (rodent ulcer), Wells and Cannon (1930) (carcinoma of lung), Halper (1931) (sarcoma), Halper (1932) (sarcoma), Shaw (1935) (sarcoma), Willan (1930-1) (sarcoma).

The whole literature on cerebral tumour allegedly following injury was carefully reviewed by Marburg in 1934. The only possible conclusion from this typical pre-anschluß Viennese monograph is that head injury is extremely rare and unimportant as a cause of cerebral tumour. Parker and Kernohan (1931) found in a series of 431 cases of glioma of the brain that 58 (13.4%) reported injury as a cause. In a series of 431 patients without tumours of the brain there was a history of injury to the head in 45 (10.4%). In 200 normal persons 71 (35.5%) reported injury to the head. On further examining the 58 the history could be disregarded in all but 21—i.e., 5%.

Lastly, in the matter of comparative pathology it is very notable that Volume XCIII, 1931, of *Annals of Surgery*, which was devoted to an international study of cancer, contained little or nothing about acute traumatic malignancy. Slye (1931) recorded observation on seemingly very quarrelsome mice. Of 14,000 necropsies on these animals, 1,301 showed indisputable neoplastic growths. Of the 1,301, 51 arose under observation at the sites of recorded gross trauma sustained in fighting. Slye thought little of this, but believed more in heredity and gave good reasons.

Organic Nervous Disease

We can now pass to a consideration of organic nervous disease, exclusive of epilepsy and mental disorder, which will be dealt with later.

Here again three types of views are discernible in the very extensive literature—namely: (a) Trauma plays no part at all in the installation of organic nervous disease. (b) In certain cases trauma is the decisive precipitating factor. (c) Wherever truth may lie between *a* and *b*, here is a thought-provoking case.

The great authority of Kinnier Wilson (1923) stands behind proposition *a*. Addressing the American Medical Association at San Francisco in 1923, he expressed himself as hostile to the notion that trauma might initiate morbid neurological processes, especially progressive lesions. He denounced suggestions of the existence of traumatic cerebral tumour, but grudgingly admitted that a few cases of disseminated sclerosis and a very few cases of tabes and dementia paralytica might seem to be initiated by trauma. Very similar views have been expressed by Crouzon (1931), Jelliffe (1935), and many others of less standing.

There is a very rich seam of literature in support of proposition *b*—namely, that trauma may in certain cases initiate organic nervous disease. Harris (1933) quotes what he calls the “astounding difference” in the views given on the traumatic factor in progressive muscular atrophy in the second and the fourth editions of Price’s *Textbook of Medicine*, and points out the fallacies of condemning the possibilities of trauma. He quotes his own cases in great detail, and these support proposition *b*. Harris sums up his personal experience as follows: “My own view is that when symptoms develop directly after an injury in a previously healthy individual we have no right whatever to assume that the injury has no causal connexion with the development of the disease.” Very similar views were expressed by Hinds-Howell (1932) and Garland (1938).

Coming to proposition *c*—namely, simply recorded cases—we find the following: Jelliffe (1935) reported one case (not seen by him) of alleged traumatic amyotrophic lateral sclerosis together with some learned comments on contradictions and evasions by neurologists. The bulk of his paper is a summary recapitulation of 90 similar cases from the literature with comment such as “doubtful” or “too remote,” but no substantial discussion. In another further study of alleged traumatic amyotrophic lateral sclerosis Waggoner and Löwenberg (1939) published a remarkable case of a patient exhibiting *both* amyotrophic lateral sclerosis due to natural causes and a traumatic syndrome resembling amyotrophic lateral sclerosis. Elkington (1936) examined and reported on 41 cases of meningitis serosa circumscripta. He believed trauma to be the cause in 9. As for progressive muscular atrophy, Sutton (1938) recorded one case on rather attenuated evidence, and Walker (1938) mentioned four cases, in only one of which the traumatic cause was accepted without question by the party liable to pay compensation. Turner (1939) made a very careful survey and concluded that trauma might initiate progressive muscular atrophy in a certain small proportion of cases.

There are on record any number of cases of Parkinsonism allegedly due to trauma, and among the best examples are: Pommé and Liégeois (1931), following head injury; Ramond (1935), following concussion; Weinberg (1939), 2 cases following electric shock; Patrick and Levy (1922), general review; Grimberg (1934), head injury; Kulkov (1932), head injury; Bruetsch and De Armond (1935), head injury; Faure-Beaulieu (1932), peripheral injury; Naville and de Morsier (1932), review of 42 cases

following peripheral injury; Hodgson (1937), peripheral gunshot wound; Walker (1937), peripheral industrial accident.

There is one other disease which I have always thought nervous rather than “rheumatic.” I mean chorea. In 1934 I found myself in possession of minute notes of 200 cases of chorea, personally observed. In these 200 I found 26 definitely initiated by physical injury such as a scald, lacerated scalp, injuries in a fire, severe caning, dog-bite, etc. (Walker, 1935).

Myocardial and Pericardial Lesions

A very learned monograph on myocardial and pericardial lesions alleged to follow non-penetrating trauma was written by Warburg of Copenhagen in 1938. It is very interesting to peruse the reviews of this little book. In England the *Lancet* (October 22, 1938) was friendly, non-committal, and uninformative, while the *British Medical Journal* (November 12, 1938) was hostile, critical, and sceptical about Warburg’s conclusions. On the other hand, the *Journal of the American Medical Association* (November 12, 1938) willingly accepted Warburg’s conclusions that blunt non-penetrating trauma to the chest may indeed install myocardial disease. The subject has been reviewed in modern fashion by Barber (1940), whose notes and references set out a clear exposition. Case records especially worthy of study (in addition to those quoted by Barber) are those of Kahn and Kahn (1929); Kahn (1930); Levison (1927); and Elkin (1935). The case which is reported by Priest (1939) is an especially interesting and curious one. The paper by Hay and Jones (1927) purporting to show the installation of auricular fibrillation by trauma met with severe criticism in that many cardiologists in effect insisted that the cases did not fulfil the requirements laid down at the beginning of this paper (Table II).

The best recent review of coronary disease and angina following strain or inordinate exertion is that of Boas (1939), who showed the relationship clearly in an admirably careful survey of 14 cases.

Mental After-effects of Head Injury

A consideration of the mental after-effects include a review of the literature on traumatic epilepsy, late traumatic apoplexy, psychosis, and chronic subdural haemorrhage. These are here considered in turn:

Of traumatic epilepsy Stevenson (1931) wrote:

“The term ‘traumatic epilepsy’ should be limited to cases of epilepsy resulting from injury to the brain or its membranes. The term ‘Jacksonian epilepsy’ should be applied only to localized fits of cortical origin. . . . Traumatic epilepsy may develop as late as ten years or more after severe injury of the head, but usually there has been in the interval vertigo, paroxysmal headache, or other premonitory symptoms. Epilepsy following superficial wounds of the head is most often psychogenetic in origin. . . . The fits in traumatic epilepsy are, in most cases, clinically the same as in idiopathic epilepsy. Both major and minor attacks occur. Vertigo and mental deterioration are both more common in traumatic epilepsy than in idiopathic.”

Similar observations can be found in the writings of Symonds (1935), Turner (1923), Wagstaffe (1928), and Elvidge (1939). Finally, Foerster and Penfield (1930) stressed the part played by progressive intracerebral scar formation.

The very large amount of literature on late traumatic apoplexy has been ably surveyed by Symonds (1940).

The literature on mental disturbance following head injury is truly formidable. Most papers are modelled on that of Mickle (1892), who recognized as possible sequelae

to head injury: (a) psychoneurosis, such as automatism, stupor, melancholia; (b) paranoia; (c) organic disease, with dementia; (d) functional disturbance. At the B.M.A. Meeting at Cardiff in 1937 the mental effects of head injury formed a topic of important discussion. Mapother (1937) referred to the lack of unanimity among authorities and the different views held by civil and military experts. He quoted a series of 5,000 private patients, of whom 123, or possibly slightly fewer, owed mental disorder to head injury. Other speakers mentioned the following possibilities:

(a) Pre-existing mental instability disposes to gross hysterical manifestation after head injury.

(b) Persons of cyclothymic or manic-depressive mental constitution are prone to an attack of depressive psychosis after head injury.

(c) Subarachnoid haemorrhage must always be considered in cases of mental disorder following head injury. Similarly, cerebral oedema often plays a part.

(d) Much vague mental disorder after head injury could be prevented by clear, decisive, prompt, and positive clinical and legal handling of the patient.

(e) Howsoever they arise (and much is obscure) schizoid psychoses are common sequels to head injuries.

Of "chronic subdural haemorrhage" there is little to be said beyond what Trotter (1914) originally stated. He defined the illness as consisting of a relatively mild injury, a latent period, headache, drowsiness, and remarkable transitions between full consciousness and coma. A very good recent summary, well illustrated, is given by Fleming and Jones (1932) with details of 8 cases. Another review of 22 cases is that of Gardner (1935). Other literature of importance is: Pearson (1928), head injury in two boys (sequel in each case was a regression to the symptoms and behaviour of an illness each had had in infancy); Mock (1929), similar to Mapother; Le Fevre (1933), morbid anatomy; Hoch and Davidoff (1939), role of previous personality in the development of traumatic psychosis.

Injury to Bones and Joints

The best recent summaries of disease processes induced by injury in bones and joints were given by Buchman (1929) and Brailsford in 1936. The latter stated that he was familiar with localized rarefying osteitis or "osteochondritis" in 21 different sites, and said: "After carefully weighing the evidence obtained from over 100 cases personally observed, I am of the opinion that trauma is the exciting cause of these conditions, but in view of the fact that it is the minority only of the cases of trauma in which the sequence of characteristic changes develop, I feel that there must be some other contributory factor."

Two post-traumatic osseous maladies call for special mention. The first is osteochondritis dissecans, and it is quite noteworthy that König, who first described this in 1888, and Burr, who followed with a modern description in 1939, both thought that trauma was not solely responsible. However, Fairbank (1933), in a very careful survey, said he believed that osteochondritis dissecans of the knee (the usual site) was caused by trauma "pure and simple," and he explained the mechanism as violent rotation inwards of the tibia, driving the tibial spine against the inner condyle. Monteith (1934) published a remarkable case in close support of this. Funsten and Kinser (1936) reported a substantial series of cases showing the preponderating influence of trauma and the appearance of osteochondritis dissecans in sites other than the knee.

The second malady is post-traumatic osteoporosis, which, if accompanied by pain, swelling, and vasomotor disturbance, is sometimes called Sudeck's atrophy. Good accounts of this have been published by Gurd (1935)—24 cases beautifully illustrated; Leriche and Fontaine (1936a,

1936b)—16 cases, also beautifully illustrated; Middleton and Bruce (1934)—7 cases; Middleton (1937)—full clinical description; Beyer, 1938; and Simpson (1937)—a very obscure and unusual case of painless decalcification.

Diabetes Mellitus

Trauma and diabetes mellitus furnish a very rich and contradictory literature. I recently published a case (Walker, 1940) of diabetes mellitus which I thought was directly and solely due to injury. The whole of the literature, and all ideas hitherto expounded on this problem, were summed up in a very lengthy general survey written by Viggo Thomsen in 1938. The author minutely examined 81 cases hitherto published as "traumatic diabetes" and brought forward a large series of highly controlled observations on the changes in carbohydrate metabolism following accident in normal and glycosuric patients. He concluded a very just and erudite monograph with a denial that trauma could ever cause diabetes mellitus. This view had the honour of laudatory acceptance in an unusually long editorial leading article in the *Journal of the American Medical Association* of April 22, 1939, but there remain clinical problems and recorded cases which Thomsen leaves utterly unsolved. It is noteworthy that all Thomsen's work was done before the part played by the pituitary was fully realized. Pedrazzini (1939) expressed conviction that true diabetes mellitus may be precipitated by any kind of injury, and gave fair evidence.

Tuberculosis

The installation of tuberculosis by trauma may take one of four forms, according to May (1928). He recognized: (a) recrudescence of a pre-existing focal tuberculous lesion; (b) miliary tuberculosis following trauma at the site of a tuberculous focus; (c) tuberculosis arising at the site of an injury without history of previous tuberculous disease; and (d) phthisis after a non-thoracic injury. Very much more detailed and attractive propositions have been published by Oliver (1915), who gave four seemingly clear cases of post-traumatic phthisis; Tattersall (1922), who described two very convincing cases; Tattersall (1928), who surveyed 300 cases of phthisis, with an authentic history of provocative injury in 4; Stoichitza (1934), who gave an account of two cases of traumatic phthisis and himself described the evidence as "clear, precise, and irrefutable"; and Mayer (1935).

Other Conditions

Leukaemia.—Trauma as a cause of leukaemia has been described by Lewsen (1930), Weil and Bousser (1936), and more particularly by Olovson (1939), who reviewed all published cases and added two of his own. Olovson was disposed to think that trauma may well precipitate myeloid leukaemia in a person already disposed to it.

Appendicitis.—Trauma as a factor in acute appendicitis has been described by Ludington (1923), Behan (1927), and Bissell (1928). The cases described by the last-named are much more credible than the single case described by Ludington. Very lengthy reviews and commentaries were made by Fowler in 1938 and Grettoe in 1939. The conclusion from these five authors is that "it may occasionally happen." Recent cases of traumatic appendicitis include those of Burgess (1938), Rogers (1938), and Goodyear (1938). A great deal of correspondence followed these cases, and the *Journal of the American Medical Association* (June 4, 1938) gave the view, cautiously, that trauma may indeed provoke appendicitis, usually of a grave and fulminating type.

Gastro-duodenal Ulcer.—No paper of this type would be complete without reference to gastro-duodenal ulcer.

Although textbooks of medicine and surgery often mention trauma vaguely in discussing the cause of these maladies, no sets of authentic cases have recently been recorded. But in this connexion, as also in connexion with perforation, many authentic cases are on record in which the stomach has been ruptured by external violence without gross evidence thereof.

Pneumonia.—The possibility of trauma causing pneumonia is always mentioned in textbooks of medicine. It has been referred to over and over again in successive editions of Osler's *Principles and Practice of Medicine*. According to Brockbank (1926) the possibility was known to Morgagni. It was well known to Allbutt, according to his *System*. Several authors mention Litten's series and Stern's series, but I have not found these in the original. On the other hand, Rufus Cole of the Rockefeller Institute, according to his article in *Nelson's Loose Leaf System*, saw 700 successive cases of pneumonia without any trace of trauma at all.

Syphilis.—Trauma in a syphilitic may determine the site of syphilitic lesions in almost all organs of the body. Cases were given by Klauder (1922) as follows (all in proved syphilitics): gumma at the site of a laceration; gumma at site of repeated trauma; gumma of testicle after trauma; change of a negative Wassermann reaction to positive again as a result of trauma (2 cases); aneurysm developing suddenly after violent physical effort; delayed recovery from lacerations; paresis following head injury (3 cases).

At the beginning of this paper I mentioned that there is hardly any disease which has not at some time or other been attributed to trauma. A few case records deserve mention:

- Sundt (1921). Trauma as a predominant agent in many cases of pseudo-coxalgia.
- Platt (1922). Dissents from Sundt.
- Vance (1923). Traumatic lesions of the intestine caused by non-penetrating blunt force.
- Hartley (1923). Similar to Sundt.
- Moersch (1926). 2 cases of diffuse cerebral gliosis seemingly caused by concussion.
- Buchman (1928). Osteoporosis of the carpal bones. (Clinical descriptions not to be found elsewhere.)
- Sargent and Greenfield (1929). Close relationship between cranial trauma and haemangiomas of the cerebellum.
- Bolton (1929). Rupture of the stomach from external non-penetrating violence with no sign of external injury.
- Chandler (1931). 11 cases of spondylolisthesis (in a series of 18) in which trauma seemed to initiate the symptoms.
- Kendall (1931). Traumatic nephrolithiasis.
- Mouat, Wilkie, and Harding (1931). Importance of injury in Kienböck's disease.
- Capener (1932). 9 cases of spondylolisthesis (in a series of 34) giving a history of injury.
- Royal Society of Medicine (1933). Traumatic Argyll Robertson pupil.
- Chandler (1934). Bilateral suprarenal apoplexy due to trauma.
- Dodd (1934), Gardiner (1935), Hunter (1935). Ruptured spleen after trivial mishaps.
- Cooke (1934). Traumatic rupture of lungs without signs of trauma in the chest wall.
- Bramwell (1934). Auricular fibrillation caused by head injury.
- Fagge (1934). Fatal ulcerative colitis following head injury.
- Edström (1936). Five cases of rheumatic fever beginning at or near an injured joint.
- Hill (1936). Traumatic oedema.
- Muller (1937). Post-traumatic renal stone (in colliery and street accidents).
- Thomson (1938). Sudden post-traumatic senility.
- Moritz and Wartman (1938). Four cases of post-traumatic internal hydrocephalus.
- Meyerding and Pollock (1938). March fracture. (A very full and useful account of a malady now reappearing.)
- Monteith (1938). Myositis ossificans with favourable course.
- Bedell (1939). Traumatic retinal angiopathy (not necessarily head injury).
- Fallon (1940). Lung injury in an intact thorax.
- Findlay and MacCallum (1940). Recurrent traumatic herpes.

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REACTIONS AFTER TRANSFUSION OF STORED BLOOD

BY

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The transfusion of stored blood for many conditions has now become an established practice, and it may therefore be worth while to record some observations made on the incidence of reactions after its use.

Reliable statistics about reaction rates both from stored and from fresh blood transfusions are exceedingly difficult to obtain, mainly because there is little uniformity of opinion as to what constitutes a "reaction." Moreover, the reaction rate will vary with the person who carries out the transfusion, the method employed, the rate of administration, and the condition of the patient. Two disasters which cannot rightly be termed "reactions" but which may develop equally after the use of either fresh or stored blood result from an incomplete understanding of the technique of blood transfusion. They are: (1) pulmonary oedema with cardiac failure, due to overloading of the circulation of a patient whose heart is already embarrassed; and (2) renal failure due to transfusion of blood of an incompatible group. The more usual type of reaction that is apt to occur after a blood transfusion is a febrile reaction. It is unnecessary here to discuss the theories of the causes of such a reaction, although it is generally thought that the introduction of foreign protein into the blood stream plays an important part.

Reactions after Transfusion of Fresh Blood

The febrile reaction may be of variable severity. A simple rise of temperature without shivering or rigor is exceedingly common. Kordenat and Smithies (1925) maintain that nearly all transfusions of fresh blood are associated with some rise of temperature, even though this may be symptomless. Riddell (1939) is in agreement with this statement. Other observers believe that about 50% of fresh blood transfusions are associated with a rise of temperature or a rigor. A mere rise of temperature without constitutional effects is of little significance, but a rigor is more distressing and may even precipitate cardiac failure.

In considering the incidence of transfusion reactions, therefore, it is necessary that the reactions be divided into grades. The following classification is made by Riddell: *Grade I*, associated with a rise of temperature to 100° F., but no other objective features. *Grade II*, associated with a similar or greater rise of temperature and subjectively with feeling cold and shivery, but without having an actual rigor. *Grade III*, associated with a definite rigor. Riddell, giving his figures for his last 100 transfusions with fresh blood, noted rigors (*Grade III* reaction) in 11%. Fell (1938), analysing 500 cases, found reports of rigors in 4.8%. Edwards and Davie (1940) gave the following statistics of reactions after 100 consecutive transfusions of fresh citrated blood at the Liverpool Royal Infirmary: none, 37%; doubtful, 15%; *Grade I*, 15%; *Grade II*, 25%; *Grade III*, 8%. *Grade III* reactions are the most striking and easily recognized. Their average incidence in these three careful investigations on the use of fresh blood is 7.9%.

Reactions after Transfusion of Stored Blood

Edwards and Davie report that out of 1,364 bottles of stored blood administered by numerous surgeons in a variety of hospitals 69 (5%) gave rise to a *Grade III* reaction. These and other results with preserved blood, some of which are quoted by them, are tabulated below:

	No. of Transfusions	Grade III Reactions
Liverpool Royal Infirmary (Edwards and Davie, 1940)	1,364	5.0%
Milton Road Infirmary	—	4.0%
Walton Hospital	—	12.0%
Lundy, Tuohy, and Adams (1937)	149	4.2%
Cameron and Ferguson (1939)	1,000	2.8%
Elliott, Macfarlane, and Vaughan (1939)	50	8.0%
Hamilton-Paterson (1939)	46	6.0%
Biddle and Langley (1939)	150	5.0%
DeGowin and Hardin (1940)	1,458	3.9%
Brewer, Maizels, Oliver, and Vaughan (1940)	56	5.4%

The average incidence of *Grade III* reactions in all these transfusions with stored blood is 5.6%.

In order to determine the reaction rate and other results of the use of stored blood from the North-East London depot a label was attached to every bottle of blood sent out. This label consisted of a detachable reply-paid post-card which the medical officer who gave the transfusion was asked to fill in and return. Investigations suggest that in perhaps half of the transfusions carried out this request was complied with. The first 700 labels returned have been analysed, with the following results:

TABLE I.—Results of Transfusion of 700 Bottles of Stored Blood. Average Age of Blood, 10.8 Days

No. of transfusions	389	
Grade I reactions	44 (11.3%)	
" II "	17 (4.4%)	} 8.5% = 19.8 per 100 transfusions
" III "	16 (4.1%)	
Jaundice	6 cases	= 0.86%
Urticaria	4 cases	= 0.57%

Riddell's classification was slightly modified in that *Grade I* reactions were those in which any rise of temperature above 99° F. was reported but in which there was