Shaken Baby Syndrome: An Abusive Diagnosis.

By Archie Kalokerinos

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Foreword

Readers of this book will quickly realize that observations of illness patterns amongst Australian Aboriginal infants played a major role in enabling me to uncover mechanisms involved in the Shaken Baby Syndrome (SBS) and the Sudden Infant Death Syndrome (SIDS).

Before white settlement, Aborigines lived mostly isolated from the rest of the world. They ate fresh vegetables and a little meat. They were physically fit and free from the scourges of European diseases. When the white man arrived the Aborigines were forcibly removed from tribal land and their diet was promptly changed from fresh bush food to what I call *'white man's poison"*, namely refined flour, sugar and alcohol.

Within a short time the health of Aborigines descended into an abyss and infants and children developed diseases they never had. They were constantly ill with colds and a multitude of gastrointestinal disorders and the infant mortality rate (IMR) became one of the worst, worldwide.

Astonishingly, *no one* seemed to care.

As a medical student I was taught nothing about Aboriginal health and when I arrived in Collarenebri in 1957, authorities did nothing to alert me to what was going on. Worse still, when I tried to discuss what I observed, everyone became hostile.

I owe a huge debt to Aboriginal children. Their deaths enabled me to see through a quagmire, learn a great deal and enter a world where infants' deaths became a rarity. Had I established my practice in a *'rich and civilized'* part of Australia my life would have remained much less productive and certainly less rewarding.

Introduction

In the minds of many, nothing is worse than losing control and violently shaking an infant to death. This is regarded as the ultimate crime even by hardened criminals and in jails throughout the world child abusers, real or perceived, need to be protected and separately confined for their own safety. The usual rules of understanding and support disappear in a torrent of hate. Saturated with damning evidence, judges and juries tend to harshly lay down the law, assuming that brutal punishment is the only way to prevent similar "crimes" in the future.

Many highly qualified physicians have "specialised" in the subject and the bulk of the medical literature seems intent on *'proving'* the concepts and theories involved. Retinal haemorrhages, subdural haemorrhages, haemorrhages elsewhere, and fractures, either alone or in combination, are regarded by the vast majority of authorities as *'diagnostic'* of the

syndrome. Despite a slowly growing opposition and some remarkably wise decisions by a few judges, many individuals are convicted and thrown in jail, often without hope of appeal, and families are torn apart.

Strange as it may seem the described pathologies could have all been caused by illnesses that have nothing to do with inflicted trauma.

After intensely investigating more than 50 cases, I have yet to find a single one that clearly demonstrates that actual shaking caused all the findings. This is an important statistic that needs to be carefully considered. It may be possible to shake a baby to death but this has to be a very rare event and I certainly have never personally seen it.

Losing a baby is terrible. To be wrongly charged with killing a baby adds a form of trauma and suffering that defies imagination. Often, individuals are subjected to psychological torture and then offered a deal – plead guilty and the sentence will be relatively mild, or plead innocent and you will be locked up for a long time – or for life … or even for life plus ten years in some jurisdictions. Faced with this choice, many innocent individuals take the deal, particularly when they know they cannot afford a good defence.

There is more to come. The guilty plea means that the supporters of the Shaken Baby Syndrome can now use the various pathologies of the case as *'proof'* in the future. A retinal haemorrhage is declared diagnostic and a fractured rib pathognomonic of the syndrome and subsequent cases are reloaded with guilty verdicts.

To understand how I came to my convictions is not easy to explain because it involves a mass of complex medical sciences that require careful digestion. The mechanisms would never have become apparent to me had I not, for nearly 50 years, studied vitamin C, scurvy and a bacterial- derived toxin known as *endotoxin*.

Several years ago, I was asked to report on a Shaken Baby case just a few days before the trial ended. I remember how I sensed that something was strangely familiar. Then it hit me! The retinal and subdural (under the covering of the brain) haemorrhages, and fractures *exactly* matched pathologies described in a classical textbook *'Scurvy Past and Present'* written by Alfred F. Hess MD, an American paediatrician in 1920. That book was right in front of me. I even knew which pages to read. I found myself taking part in the creation of a piece of medical history.

However, there was still a lot to do. Since Hess' day, there had been an explosion of medical knowledge. I had the luxury of the Internet and the support of a faithful band of skilled colleagues. Together we learned about the complexities of vitamin C and glucose transporters, the effects of endotoxin, bone growth and disturbances, bleeding disorders, gastrointestinal disturbances, infections, and a host of other important issues. We learned how *'scurvy'* can develop when oral intakes of vitamin C are *'normal'*. We already knew that vitamin C, when administered in large doses intravenously or intramuscularly, can reverse many pathological conditions. We were able to learn why this was so. We were also able to understand how the pathologies found in what is now known as the Shaken Baby Syndrome, can occur without trauma. We knew how to prevent the development of the syndrome – and how to treat the infant, provided we initiated treatment early before irreversible damage rendered any chance of recovery impossible.

Unfortunately, this knowledge was not greeted with universal acceptance. Only a few exceptionally wise judges were able to overcome prejudices and view cases logically. Some defence lawyers do not even bother reading reports carefully compiled to help their case. They expect some short notes or a few pages to be sufficient to explain everything. This is like trying to explain to a classroom full of five-year-olds the finer points of quantum mechanics in one short lesson. Such a task is impossible. A great deal of education is necessary before such a complex subject can be understood.

In this book I have reviewed how the Shaken **B**aby Syndrome evolved with detailed references from the international medical literature. It should become obvious to readers that many of the vital issues were determined suddenly – as the significance of clinical observations and references became apparent.

I followed the *'scientific method'* during my studies and did not divert from the principles involved:

1. Observation and description of a phenomenon or group of phenomena
2. Formulation of a hypothesis to explain the phenomena
3. Devising experiments to test the accuracy of the hypothesis
4. Using the hypothesis to predict the existence of other phenomena.

Even when the experiments proved the hypothesis and became *law*, the study of mechanisms never came to a halt.

Sometimes a hypothesis is difficult to investigate and requires several clinical trials to prove or disprove. Sometimes a single case may be all what is needed to prove the point. When I observed the response to the first injection of vitamin C that I administered, I knew beyond a doubt, that I was on a winner. I had spent years thinking about it and making careful observations and this was a perfect fit; there could have never been another explanation.

It is important to make one thing clear. Although I originally thought that I had pioneered the use and proven the value of vitamin C injections, I was soon made aware that other physicians had preceded me. What I did was to put the pieces together in a way that vastly improved understanding.

Shaken Baby Syndrome is not an isolated condition. What initiates the pathological changes can be simple or complex and can lead to one or more final pathways. SBS is one of them. Another is Sudden Infant Death Syndrome (SIDS). Unless one understands all of this, one is unable to approach the problem in a logical way or to understand the very important fact that sometimes spontaneous recovery does occur without specific treatment. This will be explained in detail later.

While authorities have been busy prosecuting innocent people, a vast new understanding of the practice of paediatrics has been neglected. A dirtier page of the history of medicine is hard to imagine. In my mind, this even surpasses the awful days of witch trials.

There is everything needed to end this tragedy in the mountain of medical literature already available. Why the bulk of my colleagues have refused to act is difficult to understand. A few have been open and brave enough to voice serious concern but progress is slow – too slow.

The Early Days

Graduation in medicine and surgery from the University of Sydney in January 1951 was for me, the beginning of a career that, at first, was commonplace. Two years were spent as an intern in Australia before I sailed for England where I was led to believe that I would be gaining the wisdom and experience to convert me into a useful sort of doctor. This took nearly six years of hard but extremely valuable work in various hospitals. In 1957, when I thought I had learned enough, I returned to Australia.

Looking for a suitable place to hang my new brass plate was not easy. The medical agencies suggested several, but for various reasons, none were attractive. However, I did agree to act as a locum for three weeks, in semi-isolated Collarenebri, 500 miles from Sydney. The town had around 500 residents. On the edge of town sat an Aboriginal reserve with some 100 people, and depending on where one drew the line, the surrounding district provided 1,000 more individuals.

When I told my mother where I was heading she quickly told me, "You'll be happy in Collarenebri; that is where one of your father's countrymen is."

That gentleman was Emmanuel Petrohelos. Like my father, he was born in the Greek island of Kythera. In fact, he was born next door. A bigger coincidence, one could not imagine.

Emanuel's family adopted me the moment I arrived to Collarenebri and from then on, we had a wonderful and close relationship. I unpacked my brass plate and became Collarenebri's doctor. Fate often plays strange games: it had led me to where I would do something to change the practice of paediatrics … and change me at the same time.

Strangely, I was made aware of what was ahead by my mother's next-door neighbour who had been a nurse in Collarenebri… another coincidence. I recall the setting as if it was yesterday and I can still hear her saying "you will lose a lot of babies."

At the time, I certainly thought that nothing of the sort was possible! After all, in England I had been carefully trained in surgery, orthopaedics, paediatrics, obstetrics, medicine, and even how to do autopsies. I had learned how to extract teeth! I was, after all, a 'generalist'; I could do it all.

Reality set in very quickly as I saw that I had been thrown into a totally different world where rules did not apply; a world where everything was upside down, and nothing was like it was supposed to be.

Within a few months in Collarenebri, I had been hit by three sudden and unexpected infant deaths – all Caucasians. This was a statistic that did not fit into any textbook. That was just the beginning. Aboriginal infants also died in their own strange and unexpected ways. I had entered into a nightmare that was to take over my life and haunt me for a very long time.

Infant Deaths

The first infant died at home; I had never previously seen him. The autopsy I performed showed nothing.

The second infant died as the mother carried him into the hospital. He was also previously unknown to me and his autopsy was similarly negative.

The third infant, who had been under my care and had mild diarrhoea, suddenly collapsed and died. Her autopsy, also failed to provide any clues.

There was no need for me to study complex statistical data: Collarenebri evidently had a problem.

Aboriginal infant deaths literally exploded. One visit to the Court House to check the official records confirmed what I already suspected: the area had an alarming and unacceptable infant mortality rate. In the Aboriginal cemetery more than half the graves belonged to infants.
In addition, there was yet a bigger shock ahead: no one cared!

I toured the vast area of north-west Australia and talked to many doctors. They denied experiencing similar problems. These very educated professionals had evidently decided to simply close their eyes and I had to wonder what they were thinking when they signed all the death certificates.

I spoke to the health authorities. They looked at me as if I had just landed from Mars. A professor of paediatrics who had rescued the specialty from the doldrums was cordial and polite but did not want to pursue the issue. A leading paediatrician in Sydney was more than ready to offer an opinion. He thought I was stressed, overworked, and unsuitable to practice medicine in such a remote area. He suggested that I see a psychiatrist and have a holiday.

The absurdity of the whole situation was obvious. After all, babies did not start dying when I arrived to the area and I certainly did not imagine them. The dates on the Court House records and on all of those little graves were clear as day and they told of a situation which could not be denied or ignored. Action was needed!

As time passed, I made a simple yet important observation. Most infants who died had suffered from a series of apparently 'minor' infections.

Enter…. a real physician

Divine providence brought Dr. Douglas Harbison, the first specialist physician in a huge area, to the base hospital in Tamworth, a city 250 miles from Collarenebri. It soon became apparent that the man was blessed with great ability and I decided to send to him a little Aboriginal boy who was going through the multiple minor illness stage.

Douglas must have had extraordinary vision as he was somehow able to observe minute haemorrhages in some of the child's hair roots. To him, this was diagnostic of scurvy. Vitamin C injections were given and some days later, the boy was sent back to me.

When I saw him, I could not fail to notice that he looked so much better; he was less irritable, and more alert. He was healthy again, yet something bothered me. I had been orally supplementing the little fellow with more than the recommended amounts of vitamin C for months. I had not bothered informing Douglas because I thought that it was a routine matter. So, how could the little fellow have scurvy? For many nights, I tossed and turned in bed

trying to understand what happened. That issue continued to haunt me.

Then there were more deaths – and more observations.

Modes of death:

1. Most infants who died had suffered from a series of apparently 'minor' illnesses.
2. Ear infections were almost the rule – either serous (chronic) otitis media and/or acute otitis media
3. Gastrointestinal disturbances were almost universal. They included infections, parasites, and malabsorption. Bowel movements smelled vile and the nurses thought that this was an aboriginal characteristic. Of course it wasn't. The terrible odour resulted from the infections, broken-down blood and malabsorption
4. Some infants died suddenly, without warning. They just stopped breathing and their deaths, according to accepted criteria, were classified as typical 'sudden infant deaths' (SIDS). As time passed, I was to realize that such a diagnosis was a cover for a host of conditions. As investigations became more sophisticated, it became clear that a SIDS death did not necessarily mean that no abnormalities were found. Obviously many serious conditions were serious enough to lead to sudden death. More on that later.
5. A number of infants became excessively irritable; then died.
6. Some acted like they had meningitis; a few spontaneously recovered. Others died. Spinal taps were negative and in these cases, so were the autopsies.
7. Some infants and children developed various grades of liver tenderness. The worst had liver pain. Some recovered spontaneously. Others died. Some of these, at autopsy, had obvious pale areas in their livers similar to 'acute yellow atrophy'. I was told that this was due to changes that occurred *after* death. I knew that this could not be but needed to prove it. One day a little child died in my arms. I carried him to the mortuary and immediately exposed the liver. The changes were obvious but unfortunately, the authorities remained unimpressed.
8. Post-mortem examinations frequently revealed steatosis or fatty changes of the liver. I was told that this too was nothing to worry about but I never accepted this explanation.
9. Sudden shock; non-responsive to treatment, followed by death, was common.
10. Sudden unconsciousness, followed by death was also common. Autopsies explained nothing. Many years later I was able to compare this syndrome with infant deaths in Naples from what became known as *'The Dark Disease of Naples'*.

All these observations were the result of a lot of hard work. They were very important and they had never been considered as a group. They should have impressed my colleagues but unfortunately they did not. I remained isolated – and despised.

The Opal Miner

Eventually, I became severely disillusioned. I needed to get away from it all - to do something very different, and to experience the pleasure of being physically and mentally fit. Bill Petrohelos, my Greek mate in Collarenebri, had become an opal miner in Coober Pedy, which is south of Alice Springs. His letters home were filled with tales of instant riches and adventure. The temptation to join him was too strong and in early 1965 we entered into a partnership with two other Greeks. As far as I was concerned medicine was what in Australia is known as a *'mug's game.'*

I was happy digging holes some eighty feet into the ground. The rocks were my medicine [1]

For a while all went well. We even struck it rich in a minor sort of way. Then I became involved in a terrible brawl – wild-west style, with all the trimmings. The result was six fractured ribs and a ruptured kidney, which fortunately was not serious. It was my mental state which took the biggest dent.

One day I drove alone into what could only be called *'No Man's Land'*, the vastness of the Central Australian desert. There I met some semi-tribal Aborigines. They were a wild-looking lot, unwashed and un-kept. However, there was something about them that made me realize that they were remarkable people.

I also looked at their children and wondered why they got so sick?

This time, the answer came rather quickly and from the mouth of an Aboriginal woman: "*before white men came they never got sick and died as they do now.*" That was not exactly what she said because her command of English was not so good, but that is what she conveyed to me and that made me think, and think hard.

That night I lay awake under the glory of the inland stars and developed my *'hypothesis'*. I still do not know how I did it, in the days before computerised medical libraries. Nobody had ever raised the issues with me. It was indeed a gift from God.

I recalled how Douglas Harbison had diagnosed scurvy when I had been supplementing the patient with oral vitamin C for a long time.

Next, there was the issue of how Douglas administered the vitamin C: by repeated injections. Why did they work when the oral vitamin did not? Obviously, there had been something that inhibited the oral vitamin C, something that had rendered it ineffective.

Regardless, if this was so, then under certain circumstances one had to administer vitamin C by injection and only by injection to save a life.

This had to be!

Now I needed ONE case to test the hypothesis, just one case.

I had a clear vision, I had a hypothesis, I had a plan of action, but unfortunately, I also had ONE big problem. I did not have a practice. I decided to find a suitable practice, and make it all happen.

Easier said than done!

Apparently, my reputation had spread far and wide; the welcome mat had been rolled up and it had been packed safely away…but not entirely. The doctor who had replaced me in Collarenebri had moved on and the hospital board invited me to come back. I quickly

[1] Archie Kalokerinos. 1967. *In Search of Opal.* Published by Ure Smith. Library of Congress Catalog Card No. 67-28119.

accepted the offer while wondering how long I would have to wait for my ONE patient to come.

A few days later it happened.

Little Mary had all the signs of meningitis but the preliminary tests were negative. The clinical presentation was classical; I had seen it many times. This was going to be it!

I told the matron that I was going to administer some injections of vitamin C and wait 20 minutes. If there was no improvement, I would then do a lumbar puncture.

The matron thought that I was a mental case and told me that she would be sending Mary to a 'proper doctor' 100 miles away. We fought for possession and I won. In went the injections – quite a few, one after the other. Twenty minutes later Mary opened her eyes. She was back and very normal. I had performed a miracle! The photograph I took preserved the episode for the history books.

Mary's case marked the end of strange infant deaths in my practice. I used my clinical acumen and experience to determine which infants and children should be given the injections of vitamin C. Fortunately, my luck held up, and I was always able to commence treatment before irreversible damage had destroyed all hope of recovery.

Unknown to me at the time was a physician in America by the name of Frederick Klenner, who had beaten me to the winning post by many years. He had been using injections of vitamin C for a wide range of conditions. His results were outstanding and he had published most of what he had observed. His existence was brought to my attention quite a few years after I cured little Mary. Eventually I met this wonderful man. He had tears in his eyes when I produced facts that clearly showed that I did not intend to claim originality.

The Hard Work Commences

I immediately found myself tiptoeing in a minefield once I commenced using injectable vitamin C.

The mere mention of my discovery was enough to unleash intense hostility by many senior physicians and scientists. They had decided to reject what had been plainly documented in prestigious journals and were not about to allow me to change things or provide a pathway to better understanding of the practice of medicine.

But something lit a flame that kept everything alive.

A medical organization in Melbourne was looking for a new subject to study. The use and misuse of antibiotics was considered but seemed somehow difficult to launch. Glen Dettman, a medical technologist, had read about my work and had been outraged by the huge publicity it generated. The hierarchy also thought that what I was saying was a heap of rubbish that needed to be cleared away so Dettman and a handful of colleagues were dispatched to Collarenebri to straighten me out and put an end to a situation that was clearly getting out of hand.

This was not meant to happen. Instead, I gained my first "disciple" and a new friend. A better

supporter could not be imagined. Carefully, and in meticulous detail, Glen began to research my research, investigating and scrutinizing every detail.

Glen was married twice – first to his wife, then to his beloved Nikon microscope. By studying fresh specimens of blood, urine, and faeces he discovered findings that I was unaware of. Since my early days in Collarenebri I had carefully followed collection and transport instructions but unfortunately they were all wrong. Specimens deteriorated during transport so the results were wrong and the reports I received not only incorrect but often misleading.

As we slaved looking for answers, it became obvious that we needed to consult doctors and scientists outside of Australia and we travelled overseas to meet an American veterinary researcher.

Dr Robert Reisinger

Robert had a bee under his bonnet that would not let him rest. He was obsessed with a toxin produced mainly by gut bacteria. It was called *'endotoxin'*. Bob's life work as a veterinary researcher had convinced him that endotoxin was responsible for the majority of SIDS deaths in calves and other mammals. He was certain that the vitamin C injections detoxified endotoxin. He attached himself to me like a leech, and in a few short days Bob saturated my ears with most of what he knew, but it took a long time for the information to find its way to my brain.

The subject was, and remains, complex, and constantly in flux. I originally wanted to summarize the issues in this section of the book and elaborate later; but this is not so easy as every detail seems vital and essential. I will therefore attempt to carefully prioritise and simplify the issue without destroying what is necessary.

The bacterial envelope of gram-negative bacteria, when separated off as a fragment of lipopolysaccharide, is classified as an endotoxin, sometimes called "curlin". There are many varieties of gram negative bacteria, and nature has seen fit to situate some in the gut. Only small amounts of endotoxin are normally released into the gut. Each time one gram negative bacteria becomes two, a tiny fragment of endotoxin drop off into the environment. These small amounts of endotoxin are constantly being removed in the gut by lactulose, but if there are too many and they get through the gut wall, they are then denatured by the Kupffer cells (hepatic macrophages) in the liver. If the bacterial balance is disturbed, and e-coli numbers increase, that can put the liver and the immune system under stress. Gram negative bacteria multiply much faster during fevers, so heat results in greater quantities of endotoxin being released from multiplying bacteria. If gram negative bacteria are killed with antibiotics, then the whole bacteria envelopes quickly break into large amounts of endotoxin content forming a bolus dose, which is released into the gut. The lactulose and gut wall normally acts as a barrier that prevents small amounts of endotoxin from passing through and entering the circulation.

In certain conditions where the amounts of endotoxin are large, the gut-blood barrier breaks down and endotoxin enters the portal veins that drain into the liver. If the Kupffer cells (liver detoxification systems) are strong and the amount of endotoxin is manageable, endotoxin is detoxified. If not, terrible effects can result, often rather suddenly; as the liver detoxification

pathways are overloaded. Endotoxin, after **causing chaos in the liver**, passes into the general circulation where it creates a range of biochemical and immunological disorders that may culminate in death.

Excessive production of endotoxin can also result from a range of disorders that include gastrointestinal disturbances, bacterial and viral infections with fever (even mild ones), vaccinations, antibiotic therapy, disturbances in gut circulation, formula-feeding problems, immune disturbances, and some specific disorders. When the gut-blood barrier is disturbed, allowing endotoxin into the circulation, even small amounts can precipitate endotoxemia, serious damage in the body, and death. Under certain conditions, exaggerated sensitivity to endotoxin occurs with dramatic suddenness and disastrous results.

Endotoxemia can also occur without bacteremia or septicemia and without the presence of organisms in the blood. This important issue is only too often overlooked. Also overlooked are the many and diverse clinical presentations, some more common than others. Unless one is fully aware and constantly alert of all possible pathways associated with endotoxin damage, an accurate assessment of cases is impossible.

One important fact needs to be stressed: The early administration of large doses of vitamin C by injection will detoxify endotoxin. Even though the mechanism of action is not fully understood, clinical experience over many years has demonstrated that this is so.

Spontaneous cure can occur in cases involving endotoxemia without the use of vitamin C injections and patients do survive if their **innate** immune responses are strong and resilient. The infections are dealt with, and endotoxemia disappears.

Coagulation/Bleeding Disorders, Endotoxin, and Vitamin C Disturbances

In infants, retinal and subdural haemorrhages alone, or with other haemorrhages and bruises in various combinations, have been regarded by many as totally diagnostic of SBS. In particular, certain patterns of retinal haemorrhages and tears, even in the absence of other pathologies, are claimed to be pathognomonic. Many individuals have been jailed and many are still incarcerated because of those so-called typical retinal findings. Very sadly, families have been torn apart just because medical witnesses have repeatedly failed to become properly informed from the medical literature, in order to accurately diagnose the child's problems.

Fortunately, some judges have recently started to question the accuracy of some of the evidence alleged to represent shaken baby syndrome, but meanwhile many falsely accused individuals and their families continue to suffer.

As is common in most areas of medicine, many aspects of coagulation/bleeding disorders remain poorly understood, despite the availability of lifesaving knowledge.

There is also the problem of cost of technology and testing. Hospitals, even major ones, are not always equipped to do some tests, or they limit the range of tests they are willing to perform. When asked why certain tests were not done, I remember one expert who replied, "they are too expensive."

Of course, the subject of bleeding disorders is huge and complex, as a brief examination of

the relevant chapters in a standard text such as *The Merck Manual* [2], will reveal.
Most hospitals use one or more standard bleeding/coagulation profiles. If these do not reveal abnormalities it is quickly *assumed* that none exists. A report that simply states that no abnormality was found – can lead a doctor to assume that all is well.

Testing for coagulation/bleeding disorders is not always as thorough as one would expect. Almost always, a limited number of tests that do not always provide adequate information are performed, and not enough attention is paid to basic details such as the case history and the bleeding time. This is well illustrated in two references:

A single optimal screening laboratory test for hemostasis would evaluate vascular, platelet, coagulation and fibrinolytic functions. Unfortunately, such a test does not exist. The key factor in determining the presence of a bleeding diathesis is obtaining a detailed patient history [3]

Ac*quired bleeding disorders are common. They complicate well-defined clinical disorders that can be detected by history and examination. Inherited bleeding disorders are uncommon, but can be detected by careful clinical assessment, including family history. Clinical assessment has high sensitivity, although low specificity for the presence of a bleeding disorder. In contrast, both sensitivity and specificity of routine laboratory screening are low. Both false negative and false positive results are common with basic laboratory 'screening tests'. In a patient without suggestive history, they may well be inadequate.* [4]

After studying more than 50 SBS cases, I have yet to find one where a detailed analysis of the complete individual or family history, or a proper evaluation of all necessary coagulation/bleeding factors was undertaken. Often, a diagnosis of trauma due to shaking is made at an early stage and any further investigation is considered unnecessary.

It has been known for many years that retinal haemorrhages, subdural haemorrhages, and haemorrhages elsewhere, can occur in some cases of scurvy. Modern knowledge shows that haemorrhages can develop even when oral intake of vitamin C is high, because of problems associated with vitamin C transporters. Endotoxin can also precipitate haemorrhagic pathologies. Although the mechanisms involved are still not fully understood, enough knowledge exists to allow the recognition of an association.

Since pure dietary deficiencies of vitamin C are rare, one must, in most cases, look for factors that involve endotoxin. In all the 50 odd cases that I have investigated, the medical records present information clearly establishing an association. It is necessary to consider the variability of presentations of what could also be called *'endotoxin-initiated scurvy.'* It is also necessary to be able to explain all of the pathologies that are found. This includes the fascination of endotoxin-induced scurvy-type fractures that will be discussed in this book.

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[2] 'Merck Manual of Diagnostic Medicine'. Published by Merck Sharp and Dohme. *Approach to the Patient With a Possible Bleeding Disorder.* Online:
<http://www.merck.com/mmpe/sec11/ch134/ch134b.html?qt=bleeding%20disorders&alt=sh Accessed 10th August 2007>

[3] Sallah, S. et al. 1998. " Evaluation of bleeding disorders. A detailed history and laboratory provide clues**."** *Postgrad Med*. Apr;103(4):209-10, 215-8. Review. PMID: 9553596.

[4] McPherson, J. 1995. "Tests of haemostasis detection of the patient at risk of bleeding." *Aust Prescr* 1995:18:38-41. http://www.australianprescriber.com/magazine/18/2/38/41/

What I am writing is not just an academic exercise. Although, as already detailed, spontaneous cures to endotoxemia are possible, the need to reduce the risk of long term disability or death is always uppermost in the mind of any doctor who knows the medical information.

There are certain preventive steps that should be always used. For a long period before a pregnancy is considered, couples should care for their own health. Smoking should be banned. The consumption of drugs for pleasure should also be banned. As much as possible, pollution in the environment should be avoided. The consumption of good food at all times needs to be universally practiced before, during and after pregnancy. Breast-feeding the baby is a must. There should be proper training to ensure that all this is successfully implemented. Unless circumstances prevent it, breast-feeding should commence *immediately* after birth to ensure that the infant's gut is colonised by *good* bacteria.

There are other factors that can result in colonization with *bad* bacteria. Heading the list is the administration of antibiotics. I am not suggesting that antibiotics should never be used. However, I do suggest that their use should be carefully controlled, and consideration given to the use of supplementing the diet, when antibiotics are used, with *good* bacteria to minimize the widespread damage which antibiotics can cause to gut flora, and good bacteria throughout the body.

The use of vaccines is an issue that is not easy to deal with because of its complexity. The idea, of course, is to protect infants against a range of infections that can result in serious illness or death. However, there are complications that can follow vaccinations. I will deal with this important issue later.

Spontaneous Fractures

It has been known for a long time that spontaneous fractures can occur in some cases of scurvy. The sequence of events which start out as being "normal", progresses to bone cell disorders, and finally fractures, were first documented nearly one hundred years ago.

I was fortunate in finding how some subsets of SIDS had pathologies that were accepted as evidence of the existence of bone disorders that can lead to spontaneous fractures. This, to me, was like finding the Holy Grail. I had thought about it, dreamed about it, talked about it, and never thought that I would find it.

During the early 1970's I was visiting my wife's family in England. I had been reading some reports about SIDS cases compiled by Professor John Emery, a pediatric forensic pathologist in Sheffield. He had developed an interest in *'risk factors' i*n SIDS. This was one of my babies, so I rang him and arranged to spend a day with him.

I attempted to interest him with my work on vitamin C, but he was not receptive.

In 2006 I was surfing the internet and Emery's name came up. It led me to the title of an article he had written about bone changes in SIDS cases. This was not available on the Internet but the medical library provided me with a hard copy. It contained something of tremendous importance.

Emery did something that nobody else had bothered to do.

He examined the structure of bone cells in the growing portions of bones in SIDS cases *under the microscope*.

Perhaps this was generated by the knowledge that *'scars'* in the form of transverse lines are often found when the ends of bones are examined by X-rays. These are known as *'Harris Lines'* and for many years have been attributed to periods of growth disturbances generated by illnesses.

Emery found that a highly significant number of bones from SIDS cases (he used the ribs because in babies they grow very rapidly, so show biochemical alternations very quickly. showed marked cellular changes.[5] The microscope pictures that accompanied the text *exactly* matched what had been found many years ago in early cases of infantile scurvy! Vitamin C is crucial for the proper functioning of many pathways in babies. In bones which are growing very rapidly, vitamin C supply to bones is crucial to laying down the strong but flexible collagen part of the collagen/mineral composite[6] framework. Bones, particularly ribs in babies, develop very fast, and period of vitamin C lack reduces collagen, and the structure of the bones quickly turn to disarray, which is what Emery saw under the microscope. Furthermore, as I will show later, chronic infections disrupt bone growth plates. Put the two together, and a pathologist, knowing what to look for, will find the evidence.

This was the connection between SIDS and SBS that I had been searching for, for years. My prayers had been answered!

It was with a great deal of excitement that I attempted to ring Emery and show him the connections between the vitamin c/collagen formation, and the disturbance in bone structure. Sadly, he had died in the year 2000 while trying to rescue his dog from a house fire. I cried. Not to be able to talk to Emery and show him what he had done hurt deeply.

In scurvy cases, different bones may show changes during certain times. Bone cell turnover, occurs all the time but at different times, so, for example, a particular bone may show changes today, and another bone may show changes a week or more later. In some cases one or more bones will spontaneously fracture. Unfortunately, authorities interpret this as proof that violent acts of trauma took place at different times. The result is a heavy penalty. The suffering of accused individuals, and their partners, can be easily imagined.

The process – from normal bone cells to fracturing, is not instantaneous. Due to the huge dependence on energy, glucose and vitamin C, it can, however, be astonishingly rapid in babies.

Distinguishing Differences Between Inflicted Trauma and Scurvy-like Conditions

With inflicted trauma, fractured bones go from being normal to being broken in an instant. There is no intermediate stage, and technically speaking inflicted fractures should not show structural bone disturbances.

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[5] Emery, J.L.1967. "Evidence from bone growth that most of the infants dying in the neonatal period had been ill before birth." *Acta Paediatr Scand.* Suppl 172:55-9. PMID: 4961921.

[6] BME/me 456 Biomechanics "Bone Structure" http://www.engin.umich.edu/class/bme456/bonestructure/bonestructure.htm

Scurvy-like bone disturbances and fractures begin with bone cell disturbances caused by disruption in the collagen/mineral matrix. If the condition does not spontaneously resolve (as it may) these evolving bone cellular disturbances can quickly lead to more serious bone disruption of the collagen fibril deposition and orientation, resulting in a bone breaking.

Thus, it is important to know if the stage of cellular disorder, without fractures, exists. If bone cellular disturbance exists, inflicted trauma is not the cause. Unfortunately, this usually can only be determined if the infant dies. Since not all bones display the abnormality, it may be necessary for the pathologist to do what Emery did, and examine many bones before this condition is detected. Obviously, this can be a nasty procedure. It may result in many incisions and the removal of many bone samples. I have never come across a case where this has been done properly with the use of a microscope. Usually, a callus is seen on an x-ray and declared to be a break without microscopic proof. However, if there is a possibility that it may save an individual from death row, or many years in jail, it should be considered. I live with the hope that less traumatic investigations will be developed.

If every autopsy on disputed shaken baby syndrome deaths were to include systematic bone analysis, findings of bone disorders would greatly assist in expanding differential diagnoses of, and differentiating between intentional inflicted abuse and metabolic disorders.

Another somewhat related investigation may be useful. A study documented by Zilva and Wells in 1919 showed scurvy changes in the tooth structure of guinea pigs. Its occurrence was *'observed in quite early stages of the disease. The change appears to start first in the odontoblastic cells at the top of the pulp…The entire pathological picture is characteristic of scurvy'*. **If tooth analysis was also added to autopsy requirements, again, it could further a doctor's ability to differentiate between intentional abuse and metabolic disarray.**

Sudden infant death syndrome (SIDS) and shaken baby syndrome (SBS) have common roots.

All that is needed to substantiate this claim can be found in the *'peer reviewed medical literature'*. While literature may indeed be "peer reviewed" I do not like the term, because far the review turns out to be far from accurate, because of lack of understanding by the reviewers. However, publishing information should open the way to constructive discussion. If debate is managed logically and scientifically, the truth will eventually win the day.

For various reasons a consideration of SIDS deaths is more complex than doing something similar with the cases involving SBS. This is because the pathologies involved with SBS are mostly obvious – hemorrhages, and fractures. When first examined SIDS cases may appear to have no definable pathology. A vast amount of knowledge is needed to enable one to delve deeply and find subtle abnormalities which are potentially fatal. When this is done the association between SIDS and SBS becomes apparent.

There are two major errors committed by many forensic pathologists who are called upon to investigate SIDS and SBS cases. The first (and it is major) is the failure to consider, fully enough, or carefully enough, the case history. Too often a diagnosis is made by guess-work and from that point on, is prejudiced by incomplete data. Why this is allowed to continue is

beyond my understanding. It goes against the most basic of medical training.

There are two ways to *'win'* shaken baby cases. The first is to detail how the pathologies can develop without involving inflicted trauma. This is the clean and most satisfying way. The second is to show clearly to the court, that the autopsy reports, and, sometimes other reports, are criminally incorrect. It is surprising how often this happens. For example, in one notorious case, the pathologist who performed the autopsy details what he found when he examined the baby's heart. There was, however, a major problem. The heart had been taken out of the body for a transplant before it was sent to the pathologist – and that was just the start of many provable errors!

To understand the biochemical pathways requires a deep knowledge of medicine, so there is no simple easy way to present to a judge or jury, all the information needed to understand the case. The alternative is to accept what various witnesses present, which is not always ideal. Obviously, courts are not the best places to settle the issues, but until something better is designed, we are stuck with what exists.

The old concept of SIDS was based on two assumptions.

1. That the death was unexpected, and the infant had been *'perfectly'* well
2. That no abnormal pathologies were found during the autopsy, or when *'investigations'* were carried out.

There was however a serious problem with this as it became apparent that many infants had not been perfectly well and basic investigations often revealed a host of abnormalities. The assumption was made that various problems before death and abnormalities found after death were not sufficient to cause death. This was, indeed, another error of major dimensions.

Investigators began to find all sorts of abnormalities and as each one was unearthed, it was claimed that at long last, the *'cause'* of SIDS had been found. The medical literature is cluttered with many such claims. **When researchers such as a veterinary scientist Robert Reisinger honed in on endotoxin, the atmosphere began to clear for some of us.**

At the same time, the use of intravenously administered vitamin C by Dr Frederick Klenner, myself and others, unveiled some astonishing clinical findings. We all found that a major subset of SIDS could be prevented by using vitamin C injections for those infants who displayed features that were becoming known as *'risk'* factors. Heading this list were ***gastrointestinal disturbances and viral and bacterial infections***. I soon found another – the ***administration of vaccines to sick infants*** which lead to the publication of a book called *Every Second Child*[7].

How does intravenous vitamin C work? This had remained a mystery, until researchers discovered the world of vitamin C and glucose transporters. Eureka! I believe this was a revelation from God, passing on to humans one of His most important secrets.

By far the most efficient, and major way that enables vitamin C in the diet to pass through the gut wall into the bloodstream and then into various organs and tissues is via vitamin C transporters. There are a host of these throughout the body. The process requires a considerable amount of energy.

[7] Kalokeronis, A. 1974. *Every Second Child*. Thomas Nelson (Australia) Limited . SBN 17 001987 X

Vitamin C lies at the very core of our survival. Glucose transporters take vitamin C into cellular mitochondria. Without vitamin C carnitine cannot be metabolized in order to transport long chain fatty acids into the mitochondria, where they are burned for energy. Without vitamin C, carnitine levels in the body are severely depleted leaving mitochondria unable to perform crucial functions in the body to the maximum extent, which is why one of the symptoms of vitamin C deficiency is lack of energy, and fatigue. Vitamin C underpins crucial processes like collagen formation ensuring that all cell walls are strong. Vitamin C is crucial for neuro-transmitter biosynthesis, chemical chemotaxis and a vast number of other metabolic functions. Crucially, for babies, the innate immune system is dependent on vitamin C, for without that, the neutrophils, lymphocytes, and phagocytes which process toxins in the body come to a halt. Every major biochemical and immunological function in the body has at its core the effective transport of vitamin C through the body via either sodium or glucose transporters. When this is understood, it is easy to see why, and how, vitamin C deficiency was so destructive in previous decades.

While the vitamin C recommended daily allowance might be sufficient to avoid a pre-morbid state called "scurvy", it bears no relationship to the amounts required for the body to effectively manage essential biochemical processes brought into play after vaccines, toxin exposure, malnutrition, illness or stress.

In infants certain tissues/organs have enormous energy requirements. Vitamin C lies at the core of this provision of energy nature and it is utilized using vitamin C sodium transporters and also glucose transporters. From a chemical point of view vitamin C and glucose are very close relations, so this is not surprising.

However, under certain conditions, such as viral and bacterial infections (and these do not necessarily need to be clinically major), the transporters cannot function efficiently if they are disturbed by endotoxin. The result can be mild disorders or something much more serious – even death.

Endotoxin can have extremely rapid actions. Particularly under some conditions, the amount of endotoxin that is necessary to cause death can be extremely small. Furthermore, the tissues or organs that are mainly involved, vary enormously – but some tend to be targeted more often than others.

The end result can vary. The heart may stop beating. Cardiac and respiratory monitors fitted with alarms have been used to alert parents of the onset of such disturbances, in the hope that resuscitation measures may recommence breathing and cardiac function.

Thorough and complex investigations of these cases will often reveal biochemical abnormalities. These abnormalities are almost always secondary to the effects of endotoxin.

One would expect that with such a distressing and common condition as SIDS that everything that was to be found about the functions and utilization of vitamin C would have already been found and adequately aired for discussion by now, but this is not so.

Professor Hess and Scurvy

In 1920, Professor Alfred Hess- an American paediatrician - debuted his book, *Scurvy Past*

and Present [8]. It contains most of what was known about scurvy at the time. A careful reading of the text reveals how complex and variable the condition is. Although some presentations are regarded as *'classical'* Hess stresses the fact that such presentations must not be regarded as the only ones that permit the diagnosis of scurvy to be made.

Because I will be quoting extensively from the Hess's text I will in the pages that follow abbreviate the reference details and use the word *'Hess'* followed by the page number without quoting the complete details of the book.

By studying the various presentations of scurvy one can look for and understand the biochemical mechanisms involved to a significant degree. It is possible to fit together the pieces of a large jigsaw puzzle. This is highly significant because inconsistencies would cast doubt on the accuracy of the concepts.

A single presentation of scurvy, as a requirement for a diagnosis of scurvy is an error.

This may appear to be absurd but it is not. While defending cases I have, on several occasions, been hit with statements from medical *'experts'* who claim that a diagnosis of scurvy is impossible because some factors that are claimed to be necessary are absent. Hess deals with this matter in a way that illustrates the stupidity of such approaches. On page 183 he states:

'This is the syndrome which the medical student is taught to carry away to guide him in his every-day practice. It is the acute, florid type, and presents a striking picture, but must not be regarded as the common form of the disorder…the classical textbook descriptions must be augmented by portrayals of the disorder which are less crude and more difficult to recognise…'.

An indisputable fact

In the shaken baby syndrome cases I have reviewed, all have shown the basic pathologies reported in cases of scurvy. Of course Hess was not aware of shaken baby syndrome, but the various presentations of scurvy he details, *exactly match what can be found in shaken baby cases*. Included are retinal hemorrhages, (Hess: page 180), subperiosteal hemorrhages (Hess: page 191), edema, which was present in one of my cases (Hess: page 196), beading of the ribs - known as the *'scorbutic rosary'* (Hess: page 197), subdural hemorrhages (Hess: page 202), anemia (Hess: page 209), coagulation/bleeding disorders (Hess: page 211), increases capillary permeability (Hess: page 212).

Hess details a six month baby (page 229) which developed moderate scurvy, was put onto an antiscorbutic but even so, developed bronchitis, otitis, enteritis and later furuncolosis. Hess states that *'in spite of the fact that it* [an infant] *had been receiving an antiscorbutic for almost this entire period, it developed scurvy once more in February'*.

The importance of this gem must have been too much to absorb, because Hess's observations appear to have been viewed as a remnant of historical interest only. Had Avogadro or

[8] Alfred F. Hess. 1920. *Scurvy Past and Present.* J. B. Lippincott Company, Philadelphia, 1920, Library of Congress Catalog Card Number: 81:69886. (Reprinted in 1982, Academic Press, Inc. (London) Ltd. ISBN: 0-12-345280-5.

Einstein been medical graduates, perhaps the barrier to the information may have been broken earlier.

Even though today, there is ample material in the medical literature to explain and expand on Hess's observations, it's extraordinary that so few doctors today, appear to have barely a rudimentary grasp of crucial details. The information available explains clearly the reasons why vitamin C, under some conditions, cannot adequately enter some tissues, even when oral intake is within a range that is normally regarded as '*sufficient*'.

In most cases the trigger for this problem is endotoxin. Therefore, it is necessary to look carefully at this substance and become familiar with its actions. For reasons that will soon become apparent, its actions are intimately associated with vitamin C. It's a relationship that is, under healthy conditions, necessary for human life. But it can become a killer.

Endotoxin and Vitamin C

First, it is necessary to know that endotoxemia (endotoxin in the blood) is not always associated with the presence of live bacteria in the blood. For those who seriously want to, or need to know what this is about I suggest that they should study a paper written by myself and two colleagues – Dr Ian Dettman and Cliff Meakin [9]

Endotoxins are part of the outer membrane of Gram-negative bacteria. It is a *'lipopolysaccharide'* with a polysaccharide portion and a lipid portion. Toxicity is associated with the lipid portion.

Endotoxin is not toxic in its own right. Its toxicity is due to the presence of endotoxin receptors and transporters that, with endotoxin, create substances that are toxic.

Bacteremia does not always accompany endotoxemia. That is; endotoxin can exist in the blood without live bacteria [10]

Adverse responses to endotoxin can be extremely rapid – as seen in cases of meningococcal meningitis. In addition, there can be an increased sensitivity to endotoxin under certain conditions. There are at least two mechanisms involved in this.

Early viral infections can enhance sensitivity to bacterial products (endotoxin) [11]

Increased sensitivity to endotoxin can develop suddenly – as a severe allergic response. An injection of a somewhat less than fatal amount of endotoxin, followed by a second similar injection 12 to 24 hours later can result in death [12]

During the last decade, research on endotoxin has been vast and it continues to grow daily. With so many medical papers being published one needs to careful when arriving at

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[9] Kalokerinos, A. et al. 2005. "Endotoxin and Vitamin C: Part 1- Sepsis, Endotoxin and Vitamin C." *J Aust Coll Nutr Environ Med.* Vol. 24, No. 1 April. Pages 17 – 21.

[10] Danner, R.L. et al., 1991. "Endotoxemia in human septic shock." *Chest.* Jan;99(1):169-75. PMID: 1984950.

[11] Doughty, L. et al. 2001. "A role for IFN-alpha beta in virus infection-induced sensitization to endotoxin." *J Immunol* Feb 15;166(4);2658-64. PMID:11160329.

[12] Braude, A.I. 1964. "Bacterial Endotoxins." *Sci Am.* Mar. Mar;210:36-45. PMID 14133070.

conclusions. This is because, once endotoxin begins to cause problems, a cascade of *'abnormalities'* can be found if one bothers to look. In order to avoid getting bogged down in meaningless facts, a great deal of clinical experience is needed to answer this question;

"Are the abnormalities seen, the prime cause of the problem, or the result of a cascade of events that are initiated by, and can be traced back to endotoxin?"

This may seem to be a trivial issue, but it is certainly not so. If progress is to be made – particularly in the field of prevention, ***prime causes*** need to be separated from ***secondary factors***.

How does endotoxin become involved in SIDS and SBS?

A study of cases, as will be documented later, clearly shows that gastrointestinal disturbances, infections (viral and bacterial), and the administration of vaccines, clearly form part of a crucial list. Sometimes, the pathologies can commence before birth. Infections do not need to be clinically severe.

If the baby has other health issues simmering below the surface and another insult (such as a vaccine) is added, the risks involved increase alarmingly.

I do not believe that infants die silently without reason. Pathologies must exist, even if they are not, or cannot, be found. *Endotoxin, unfortunately, can work with extreme rapidity* [13]. Endotoxin is closely associated with acute and chronic *(serous)* otitis media. *Dramatic and rapid cures (sometimes within minutes) after injecting vitamin C are part of this picture* [14]

One of my little patients had been suffering from serous otitis media, but was clinically well when he was taken to see a specialist for a routine check. Both ear drums were normal. Half an hour later he was screaming with pain and both eardrums were red and beginning to bulge. An injection of vitamin C *'cured'* him, and within ten minutes he was pain free and playing with his toys like a normal child.

This response can only be due to a rapid detoxification of endotoxin by Vitamin C. I must stress that oral doses do not result in such rapid cures.

One day I was asked to see an Aboriginal child. He walked into my consulting room, was smiling, and pain free. An examination revealed the presence of mild acute otitis media. Amongst Aboriginal and part-Aboriginal children, acute otitis media is not always associated with pain, even when an ear-drum later bursts.

I knew that there was a risk of sudden serious complications, so I admitted him to hospital where I had just received facilities that allowed me to determine the amount of vitamin C in urine samples. I issued instructions that stressed that an injection of vitamin C was not to be given until a urine specimen was collected.

The little fellow did not quickly oblige. After one hour he suddenly became unconscious. (see

[13] Hudgins, L.C. et al, 2003. "A single intravenous dose of endotoxin rapidly alters serum lipoproteins and lipid transfer proteins in normal volunteers." *J Lipid Res.* Aug;44(8):1489-98. PMID: 12754273.

[14] Kalokerinos, A. 1998. "Otitis Media -Towards a Final Solution." *Journal of the Australasian College of Nutritional & Environmental Medicine,* Vol. 17, No. 2, December pages 39-41.

photograph) A vitamin C injection slowly resulted in recovery.

This clinical picture is exactly similar to a syndrome known as *The Dark Disease of Naples,* that, from time to time, killed many Italian children living in the slums of Naples. Two thirds of the children suffered from upper respiratory tract infections. The other one third had recently been vaccinated against pertussis (whooping cough).

Persuading the Italian doctors to use injections of vitamin C was difficult. The television crew accompanying me, recorded the screams of a mother who had just been told that her child had died. Eventually reason prevailed, and the doctors even accepted that pertussis vaccine was a cause. For some time the vaccine was not used in Italy. The Dark Disease of Naples is now history. [15]

Before progressing further it is necessary to remember that endotoxin is not all bad. Human life cannot exist without it, but the amount and the method by which it is handled is normally carefully controlled.

The important subject of vitamin C transporters is documented by John Wilson [16] It demonstrates how knowledge has accelerated during recent years

The effect of endotoxin appears to be instantaneous since the inhibition seen in the cells without any preexposure was similar to the cells preexposed to endotoxin for up to 6 hours [17] This does not mean that the effects of endotoxin are always clinically apparent instantaneously.

Lipopolysaccharide (endotoxin) of E. Coli modifies the ascorbic acid uptake in a calcium-dependent manner. At low concentrations lipopolysaccharide exerts a stimulating effect on ascorbic acid transport and at high concentrations lipopolysaccharide produces a dose-dependent inhibitory effect. This inhibition of the ascorbic acid transport by the endotoxin can alter the ascorbic acid accumulation in the adrenal gland [18]

In this situation small amounts of endotoxin stimulate. Large amounts depress.

Endothelial cells (lining the blood vessels, the heart, and the lymph vessels) are in fact severely affected by endotoxin and may even be removed from the vascular wall, thus making accessible the subendothelial activating factor X11. Thrombin in turn affects the vascular endothelium therefore, once initiated, the process of intravascular activation will perpetuate, this the more as platelets in turn will be stimulated into activity [19]

This is another example of how circulatory disturbances can be initiated by endotoxin.

Because of its importance I will now quote from a paper by Urbaschek that I came across

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[15] Archie Kalokerinos, 2000. *Medical Pioneer of the 20th Century.* ISBN 0-646-40852-6, Pages 370-376.

[16] Wilson, J,X. 2005. "Regulation of vitamin C transport." *Annu Rev Nutr*. 25: 105-25. PMID: 16011461.

[17] Aleo, J.J. et al. 1985. "Inhibition of ascorbic acid uptake by endotoxin: evidence of mediation by serum factor(s)." *Proc Soc Exp Biol Med.* May;179(1):128-31 PMID: 3887415.

[18] Garcia, R. et al. 1990. "Effect of Escherichia coli endotoxin on ascorbic acid transport in isolated adrenocortical cells." *Proc Soc Exp Biol Med.* Apr;193(4):280-4. PMID: 2181454.

[19] Aleo, J.J. et al. 1985. "Inhibition of ascorbic acid uptake by endotoxin: evidence of mediation by serum factor(s)." *Proc Soc Exp Biol Med.* May;179(1):128-31 PMID: 3887415.

some years ago; [20]

The biological activities of endotoxin are manifold. Besides the drop in platelets and the biphasic change in the number of leukocytes, severe disturbances in the capillary bed are among the first changes observed following the administration of endotoxin. It is well known that endotoxins cause the release of various vasoactive mediators. According to our results endotoxins enhance the activity of histamine and serotonin; these findings may contribute to a better understanding of the action of histamine and serotonin in the early post-endotoxin phase. The histamine-sensitizing effect of endotoxins is not prevented by antihistamines. Endotoxins and biogenic amines cause similar disturbances in the capillary bed. The changes that are observed in the content of the vessels, the vessel wall, and the perivascular region are the following: slowing down of the blood stream, degranulation of perivascular mast cells, granulocytosis, wall adhering granulocytes, plasma skimming, rouleaux-formation of erythrocytes, reduction in plasticity of many erythrocytes, acanthocytes, acanthocytosis, appearance of spherocytes and microcytes, and formation of massive aggregates of platelets and of microthrombi. Also, occasionally cell aggregates dissolve and as microemboli form new thrombi. Swelling of pericytes, endothelial, and periendothelial cells is observed, and dissociation and deformation of the endothelial cells occur. By means of contact of the vessel contents with the collagen, there is an additional activation of the coagulation system by factor XII possible. The changes of the epithelial lining and the wall adhering cells enhance the narrowing of the vessel lumen. Prestasis and occasionally stasis occur. One observes increased swelling of the endothelial and periendothelial cells, increased permeability of the vessel wall, passage of plasma and occasionally blood cells, especially erythrocytes, through the endothelium and massive microbleedings. While stasis is observed in the nutritive capillaries, in regions where arteriolar-venular shunts exist the flow continues. The systemic blood pressure may therefore remain unchanged during this phase, although the severe disturbances described occur in the capillary bed. Metabolic alterations, especially in the carbohydrate metabolism are mentioned.

This paper raises a few important issues. The first involves the use of antihistamines for infants who are suffering from viral or bacterial infections.

Very early in my medical career I noticed that some sick infants reacted excessively to standard doses of antihistamines. Some became unconscious. Obviously, antihistamines should not be used in such circumstances. On one occasion when I was waiting to board a plane to return to Australia I was approached by the mother of a sick infant who had just been prescribed an antibiotic mixture and an antihistamine. I was asked if these medications were safe. I strongly recommended that the antihistamine should not be used.

A few hours later, halfway to Sydney, I was asked by an air-hostess to see an infant who had become unconscious. He had been ill and a doctor prescribed the same medicines prescribed to the previous baby. With nothing else but some vitamin C powder in my bag, I was obviously not well equipped. However I did dissolve some of the vitamin C and slowly administered it orally. By the time we arrived in Sydney the little fellow was beginning to recover.

According to the Center for Disease Control and prevention in America[21], death can follow

[20] Urbaschek, B. 1975. "[Pathophysiological significance of endotoxins]" *Fortschr Med*. Aug 14;93 (22-23):1067-71. PMID: 57913.

[21] MMWR, 2007. "Infant Deaths Associated with cough and Cold Medications." Jan 12, 56(01);1-4

the administration of antihistamines to infants/children so caregivers should be made aware of *'risks'* when antihistamines are prescribed.

Endotoxin induces hypersensitivity to histamine. This was documented by Pieroni[22] et al,

The capacity of typhoid and possibly of pertussis endotoxins to induce histamine-shock susceptibility in some of the mice that survive graded doses of these endotoxins was confirmed. It was demonstrated, however, that pertussis endotoxin cannot be the main source of the typical histamine sensitization of pertussis vaccine. The following points are made. (1) With typhoid and pertussis endotoxins as inducers of histamine shock, no systematic relation between deaths and induction dose could be found, and 100% mortality could not be achieved. In contrast, with pertussis protective fraction as inducer, there was clear dose-response regression, with 100% mortality possible. The major part of the histamine-sensitizing activity of pertussis vaccine or its extracts was destroyed by trypsinization or by heating for 30 min at 100 C. These processes do not affect the histamine-sensitizing activity of the endotoxins. The implication for purified pertussis vaccine with high histamine-sensitization capacity is that endotoxin need not necessarily be present. The significance and possible mechanisms of action of endotoxin-induced histamine sensitivity are briefly discussed.

The second important problem that the paper by Urbaschek raises concerns about, is that during the early stages of endotoxemia the systemic blood pressure may remain unchanged, despite the severe disturbances occurring in the capillary bed.

In a sizable number of cases studied by myself the caregivers were concerned about their infants – even to an extent that led to urgent hospitalization and specialist consultations.

The result was 'reassurance' by medical professionals that everything was normal. Soon afterwards a collapsed or dead infant was obvious to everyone, and someone was charged, because, according to the doctors, the conclusions they came to, from the symptoms they saw, had to be a shaken baby.

The logic behind all of this defies understanding when records show perfectly valid alternative medical explanations. Munchausen's syndrome, despite being largely discredited a few years ago, remains firmly entrenched. Once its existence is suggested, a cascade of assumptions and untruths follow. Often, the diagnosis takes charge. The once sacred principles of a differential diagnosis are thrown out of the window.

A very thick file on a case is on my desk at the moment of writing this. Pages and pages of details stress how the accused must be guilty. However, I am still waiting, after many weeks, to have the full pathology results concerning blood and urine tests placed before my eyes. What sort of medicine is it, which fails to provide rudimentary baselines and test results?

I often think back to my student days. The war had ended and the first post-war conference on medicine in Australia was held in a Sydney hospital. Only one Englishman was there. He looked insignificant. His clothes were patched. He was seated near the back, amongst the

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http://www.cdc.gov/MMWR/preview/mmwrhtml/mm5601a1.htm

[22] Pieroni, R.E. et al. 1966. "Endotoxin-induced hypersensitivity to histamine in mice. I. Contrasting effects of bacterial lipopolysaccharides and the classical histamine-sensitizing factor of Bordetella pertussis." *J Bacteriol.* Jun;91(6):2169-74. PMID: 5943934.

students. The *'important'* doctors occupied the front seats. One case under discussion concerned a man who had constant abdominal pain. His file was very thick. He had been subjected to many exploratory procedures. One by one the big boys expressed their opinions, many of which were quite bizarre. Then someone remembered the Englishman. Politeness decreed that he should be asked for an opinion. I will never forget how he stood up and quietly said, "It's a forgotten swab." Then he sat down.

Next day that swab was removed.

Today the world needs more doctors like that Englishman. Plain thinking and logic have almost disappeared in a quagmire of rubbish.

Here are more references – showing how endotoxin can be involved in shaken baby pathologies;

Endotoxin affects the permeability of the blood-brain barrier and causes activation of brain microglia [23]

Low doses of endotoxin administered to human volunteers stimulate activation of fibrinolytic, contact and coagulation systems [24]

Activation of clotting factor X1 in experimental human endotoxemia. This provides the first evidence for Factor X1 activation in low grade endotoxemia and suggest that F1 is activated independently of FX11.[25]

Low grade endotoxemia induces a rapid fall of platelet counts, which is followed by an early increase in reticulated platelets and plasma thrombpoietin levels but not of glycocalicin levels. Finally, peripheral platelet counts increase several days after endotoxin infusion [26]

Endotoxin-mediated alteration of platelet function may contribute to bleeding diathesis in endotoxemic patients [27]

There is ample clinical evidence for antibiotic-induced endotoxin release. This is potentially a problem, because antibiotics are often considered necessary. A degree of protection can be provided by proper breast-feeding and/or supplementing the diet with mixtures of *'good'* bacteria. Supplements of zinc and vitamin C should be standard.

There is evidence of a direct role of endotoxin on specific cell populations of the central nervous system which is likely to be responsible for the transcription of proinflammatory cytokine , first within accessible structures from the blood vessels and thereafter through

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[23] Mayer, A.M. 1998. "Therapeutic implications of microglia activation by lipopolysaccharide and reactive oxygen species generation in septic shock and central nervous system pathologies: a review." *Medicina.* (B Aires) 58(4):377-85. PMID: 9816700.

[24] Wyshock, E.G. et al. 1995. "Cofactors V and VIII after endotoxin administration to human volunteers." *Thromb Res*; Dec 1;80(5):377-89. PMID: 8588199.

[25] Minnema, M.C. et al. 1998. "Activation of clotting factor XI without detectable contact activation in experimental human endotoxemia." *Blood* , Nov 1;92(9):3294-301. PMID: 9787166.

[26] Stohlawetz, P. et al. 1999. "Effects of endotoxemia on thrombopoiesis in men**."** *Thromb Haemost*. Apr;81(4):613-7. PMID: 10235449.

[27] Sheu, J. R. et al. 1999. "The antiplatelet activity of Escherichia coli lipopolysaccharide is mediated through a nitric oxide/cyclic GMP pathway." *Eur J Hematol*. May; 62(5):317-26. PMID: 10359060.

scattered cells [28]

That is; systemic injections of endotoxin (into the body) increases the release of inflammatory mediators in the brain and sets into motion damage to brain tissues.

The wording of the above reference is slightly misleading because endotoxin does not cause pathologies in a direct manner. Receptors are required.

Telencephalic white matter of the neonatal kitten frequently contained astrogliosis or focal necrosis (sometimes including the thalamus and the caudate) following a single injection of endotoxin. No evidence for a disseminated intravascular coagulopathy was found. Large hemispheric cavity lesions are not accompanied by neurological deficits in the kitten.[29]

Somewhat similar, but not so extensive pathologies have been seen in some human infants.

Immunological imbalance produces susceptibility to endotoxin [30]

Susceptibility to endotoxin has been largely neglected. As already stated, controlled amounts of endotoxin are essential for health and life. However, infants who have immune problems, as illustrated by frequent infections, such as gastrointestinal disturbances, are prime targets for endotoxin-induced problems.

Vaccine Problems

There are complex issues that surround the subject of vaccines. To discuss them all is impossible so I will highlight only some.

When two toxins are administered at the same time there can be a synergistic effect resulting in a much greater risk of enhanced side effects – some of which can be fatal.

For example; *staphylococcus aureus toxins preparations showed high lethality when tested alone. E. coli toxin preparations showed high lethality except in high dilutions. When the same toxin preparations were tested simultaneously in combination, lethality rose to 14 out of 115. Similar findings were observed over a range of dilutions* [31].

During my early work with Aboriginal infants I noticed that when infants were suffering from otitis media or gastrointestinal disturbances where the possible origins was gram negative bacteria with a probable endotoxin component, the administration of vaccines precipitated severe states of collapse. So I delayed administrating vaccines until infants were clinically well. Obviously, as just documented, the vaccines had effects that were similar to what could happen when two endotoxins were present together.

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[28] Lacroix, S. et al. 1998. "The bacterial endotoxin lipopolysaccharide has the ability to target the brain in upregulating its membrane CD14 receptor within specific cellular populations." *Brain Pathol*. Oct;8(4):625-40. PMID: 9804372.

[29] Gilles, F.H. et al. 1977. "Neonatal endotoxin encephalopathy." *Ann Neurol*. Jul;2(1):49-56. PMID: 409336.

[30] Chedid, L. 1973. "Possible role of endotoxemia during immunologic imbalance." *J Infect Dis*. Jul;128; Suppl:112-7 PMID: 4146349.

[31] Drucker, D.B. et al. 1992. "Lethal synergistic action of toxins of bacteria isolated from sudden infant death syndrome." *J Clin Pathol*. 1992 Sep;45(9):799-801. PMID: 1401211.

Unfortunately, my colleagues did not agree with this.

When I was asked to present my work to a medical organisation in Melbourne, I employed a doctor to look after my practice for a few days. Carefully, and as diplomatically as possible, I advised him not to vaccinate sick Aboriginal infants – and I explained why.

As soon as I left town the doctor spoke to some men and declared (I will use the words he used), "Archie Kalokerinos is all bullshit and his theories are all bullshit and I have no intention to carry out his methods of treatment."

He saw one Aboriginal infant who was almost certainly the best-loved and cared-for infant in the district. He had an infection. So in went some antibiotics. So far, so good. But what followed was not. The doctor observed that the routine vaccines were due. Against my specific advice they were administered. The boy died.

A few days later the doctor saw another sick Aboriginal infant. Antibiotics were administered, plus the vaccines.

I returned from Melbourne expecting to take over and be made aware of whatever was necessary. I parked my car, noticed that there was a strange quietness in the air, and decided to go straight to the hospital. That was when I found the girl dying.

The doctor had vanished.

It is not my intention to become involved in arguments about the benefits of vaccines compared with the risks of administrations. I am simply pointing to risks that were not being properly considered then, and still are not studied or recognized today.

At that time the pertussis vaccine that was in use was 'the whole cell vaccine'. This contained a relatively large amount of endotoxin. Despite claims that severe reactions were rare, serious reactions occurred at unacceptable rates. Later, an 'acellular' vaccine was introduced and this was much safer, but not entirely so. The following article details some of the factors involved with the older form of vaccine, which was the vaccine that was used by my relieving doctor.

'Effect of hyperreactivity to endotoxin on the toxicity of pertussis vaccine and pertussis toxin in mice' In mice, greatly enhanced susceptibility to the lethal toxicity of whole-cell pertussis vaccine (PV) was produced by agents known to induce hypersusceptibility to endotoxin (LPS). The decreases in LD50 were 100-fold, 125-fold and 16-fold with galactosamine (GalN), actinomycin D (AcD) and lead acetate (PbAc) respectively and the animals died within 1-2 days. However, these decreases were less than those observed with extracted E. coli LPS, the LD50 of which was reduced approximately 500-fold, 800-fold and 50-fold respectively by these agents. In control mice, without drugs, the main lethal factor in the PV used here seemed to be pertussis toxin (PT), since deaths occurred at 3-5 days after injection, and heating the vaccine at 80 degrees C for 30 min raised the LD50 from 4 to greater than 6 single human doses (SHD) per mouse. In GalN and PbAc-treated mice, the toxicity of PV can be explained by its LPS content in view of the failure of heating at 80 degrees C to reduce toxicity. However, in AcD-treated mice, the 80 degrees C heated vaccine was threefold less toxic than the unheated material, suggesting a contribution of PT to vaccine toxicity in these animals. Indeed the toxicity of PT was increased by AcD. The possible bearing of these

observations on children who appear to show serious adverse reactions to PV is discussed. Two acellular vaccines were devoid of lethal toxicity in either normal mice or in mice treated with any of the three drugs.[32]

Hypersusceptibility to endotoxin has already been detailed. This includes a sudden susceptibility. If endotoxin is a factor and another toxic substance is added, there may be a synergistic response with a much more serious reaction.

This is why it is not advisable to vaccinate sick infants. During discussions with health officials and doctors, raising this issue often results with statements like, "But the Aboriginal infants are *always* sick, and we must immunize."

This is like giving infants a double dose of toxin, but to continue to object, rarely results in a logical discussion.

Bleeding Coagulation Disturbances

There is an enormous amount of knowledge concerning bleeding/coagulation disturbances, but this does not mean that knowledge is complete. Nor does it mean that available knowledge is properly utilised. The vast majority of over 50 shaken baby syndrome cases that I have investigated, fit into this category. It is apparent to me, that once a diagnosis of assumed intential abuse is made at the start, it is then not considered necessary to fully investigate any other possibility. Common errors include the failure to take a proper case history and not do a bleeding time.

Inflicted trauma is not the only cause of hemorrhages, including retinal hemorrhages, and subdural hemorrhages. There are no specific types of retinal hemorrhages that are specifically restricted to shaking, despite claims to the contrary.

Because hemorrhages that are found in shaken baby cases exactly match what has been described in infantile scurvy it is reasonable to look at what Hess wrote in *Scurvy Past and Present.*

Hemorrhage is such a striking manifestation that it is not surprising to find it is regarded by the older writers as the pathognomonic sign of scurvy. The bleeding may take place in to almost any organ, and varies from small petechiae to very extensive extravasations. (Hess: page 84)

Brownish pigment, undoubtedly derived from the blood, is frequently found in the neighbourhood of the hemorrhagic areas. (Hess: page 85).

This is old blood, and an important issue, because authorities claim that it represents multiple acts of violence with bleeding at different times.

Hemorrhage may occur into the brain substance, into the cord or the membranes surrounding them. (Hess: page 93).

[32] Sidney, F.M. et al.1989. "Effect of hyperreactivity to endotoxin on the toxicity of pertussis vaccine and pertussis toxin in mice." *Vaccine.* Jun. 7(3)237-41. PMID: 2781857.

The subperiosteal hemorrhage has long been recognized as a lesion characteristic of scurvy. …it may, however involve any bone…The underlying blood coagulates rapidly, and the periostium begins to calcify in a few weeks. (Hess: page 95).

Retinal hemorrhages were found by Jacobsthal and by Kitamura. (Hess: page 105)

Hess and other authors at the time did not have modern knowledge about endotoxin. Furthermore, when Hess wrote his book, deficiencies of vitamin C intakes were reasonably common. There were at least two factors causing pathologies – a deficient oral intake of Vitamin C, and in some cases, the added effects of endotoxin. Nowadays, it is endotoxin that takes over as a prime factor, which disturbs the vitamin C transporters. Thus, the presentations may differ sometimes, to a degree, when compared with what happened nearly 100 years ago.

Fractures

These are not always found in shaken babies, but when they are the utter stupidity of otherwise intelligent doctors becomes apparent. Fractured bones do not always mean that the causes are inflicted or accidental trauma. Osteogenesis imperfecta is, of course, a recognised cause of spontaneous fractures. However, scurvy can also cause spontaneous fractures in infants, children, and adults through the breakdown of the collagen fibril orientation, and the destruction of collagen fibre mineral composite.

I use the word scurvy, with a great deal of hesitation because scurvy is not a specific single disease. It is a complex mixture of several disorders. How I arrived at this conclusion demands consideration.

Originally, scurvy was regarded as a disease due to a deficiency of vitamin C. Then Hess documented cases that occurred when the diet contained what could be regarded as sufficient vitamin C. [33]

Infections were observed to precipitate scurvy [34]. This could not be adequately explained, and for many years remained in the too-hard basket, until the existence of vitamin C transporters and endotoxin became known.

Unfortunately, many authorities overlooked this explosion of knowledge and continue to live mentally in the age of darkness.

When Professor Emery published his paper *'Evidence from Bone Growth that most of the Infants in the neonatal Period had been Ill Before Birth'*[35] the enormous significance of its contents was not adequately appreciated. A detailed analysis will demonstrate that this is so.

Emery states:

The period after the 1914-18 European war was the time when the pathology of rickets, scurvy, and the great deficiency diseases of childhood were largely worked out by Follis and

[33] Alfred F. Hess. 1920 *Scurvy Past and Present*. page 229.
[34] Alfred F. Hess. 1920 *Scurvy Past and Present*. page 219.
[35] Emery, J.L.1967. "Evidence from bone growth that most of the infants dying in the neonatal period had been ill before birth." *Acta Paediatr Scand.* Suppl 172:55-9. PMID: 4961921.

Park in the United States. There was also the fascinating correlation of the radiological findings in bone of lines of growth arrest described by Harris. This work is summarised in a magnificent way by Park in 1964 in his Goldberg lecture. He shows how postnatal general and nutritional diseases leave lasting effects on the structure of the bones of the child. That work concerned childhood and those who worked on the osteochondral junctions of children dying in the newborn period, simply remarked that those too, showed changes of 'rickets'.

This sets the stage for what is to follow.

Approximately fifteen years ago, we first started using the results of Park's study as a means of assessing the previous health of children who had been found unexpectedly dead (the so called 'cot deaths'). Having found this to be extremely useful, we went on to attempt to apply the same principals to perinatal deaths.

This was a brilliant move that retained the importance of clinical observations. That is; it sidestepped many of the errors that can be generated by overdependence on theoretical details.

Emery states:

Most clinical work on bone has been done on the lower end of the femur and the head of the radius, largely because these bones are most easily available for x-ray studies, but, ***for doing microscope studies, the rib is much better, as it grows in a linear fashion throughout almost the whole of uterine life. The more rapid the basic growth rate of a tissue, the more obvious and early are the effects of growth arrest.***

A rapid growth rate needs a lot of energy. This is supplied indirectly by vitamin C, and directly by glucose. Mitochondria (the *'energy factories')* are involved. So are vitamin C and glucose transporters. These are particularly sensitive to endotoxin damage. The word that is often used to describe this is *'targeting'*. More attention will be paid to this shortly.

The energy requirements for this *'hive'* of activity is huge. The massive blood supply plays an important role in providing this. The following slide shows how concentrated the blood supply is in the growing bones of infants. .

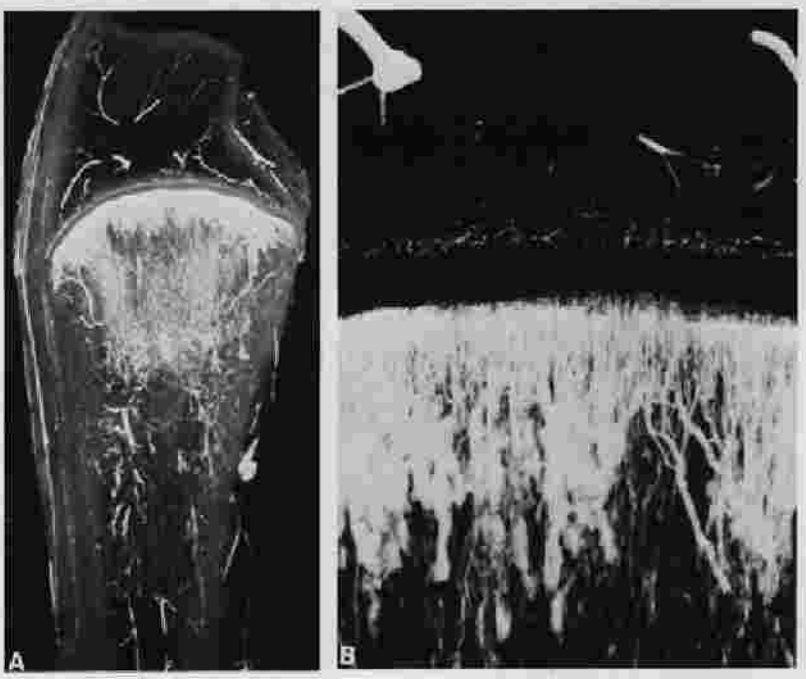

FIG. 1-7 Normal immature canine radius. (*A*) Microangiogram of distal epiphysis, metaphysis, and adjacent diaphysis shows the overall afferent vascularization. Note that the only vascular connections between metaphysis and epiphysis are along the periosteum. (original magnification × 5). (*B*) Center of the growth plate (enlargement from *A*). Observe the massed end-arterioles beneath the plate, at the site of longitudinal growth. The arterioles on the epiphyseal side of the plate are inactive in comparison. (original magnification × 20) (Rhinelander FW, Wilson JW: Blood supply to developing, mature and healing bone. In Sumner-Smith G (ed): Bone in Clinical Orthopaedics: A Study of Clinical Osteology, chap 2. Philadelphia, WB Saunders 1982)

However, there is a price to pay for all this energy. The transporters of various sorts are easily damaged, particularly by endotoxin.

Anoxia, and some toxic substances, such as retinoids, can also disturb bone growth areas. The disruption caused is similar to changes seen in endotoxemia.

The changes are also somewhat similar to those seen in early cases of infantile scurvy.

The article accompanying the slide states, '*The observed disruption of growth processes can be severe enough to produce interruption of the bone plate.*'

In other words, the bone breaks.

When the enormous dependence on a continuous supply of glucose and vitamin C in the growing portions of bones is disturbed, the cells undergoes structural changes. This is what Emery found. The rapidity of the changes varies. Furthermore, all the bones in the body are not affected at the same time or to the same degree. Healing calluses, where calcium and collagen are rushed to the area to repair the area where collagen calcium deposit was disrupted are then misinterpreted as fractures, in the process of healing, can be clearly seen when shaken baby cases are examined. They are also characteristic of some cases of scurvy.

In many SBS cases authorities misinterpret this. They claim that the cause is repeated episodes of violence over a period of time. If anything could match the witchcraft trials of old, this is it.

To make matters worse, endotoxin is a primary initiator for these pathologies. Therefore, hemorrhages in 'selected' areas can sometimes also be found. This, also, is another feature of scurvy, which is an important issue, because it leads to a vital observation: bone changes and

hemorrhage can occur together. In fact where vitamin C and endotoxin work hand in hand, no doctor should be surprised to find the two pathologies in the same child, since the biochemical pathways are linked.

Therefore it is not surprising to find that SBS pathologies and scurvy are sometimes similar. Endotoxin disturbs vitamin C and glucose transporters. The end result is the same as what one would expect to find when intakes of vitamin C are seriously low.

Vitamin C Transport Across the Placenta

During pregnancy the vitamin [vitamin C] *is actively transported across the placenta in the fetus. At term fetal blood levels are about double those in maternal blood* [36]

Obviously, vitamin C, in large amounts, is necessary for fetal and newborn survival.

After birth infants are left without the placental vitamin C pump and must depend on intake from milk and the efficiency of other various tissue pumps that, if functioning correctly, provide vitamin C to tissues as necessary. In premature infants, born before the pumping facilities are properly established, serious problems can develop [37]

We have created mice deficient in a rat ascorbic acid transporter Svct2. Mice died within a few minutes of birth with respiratory failure and intraparenchymal brain hemorrhage [38]

This is an extreme example of what can happen when vitamin C transport is disturbed.

Using a mouse mutant that fractures spontaneously and dies at a very young age, we identified that a deletion of the GULO gene, which is involved in the synthesis of vitamin C, is the cause of impaired osteoblast (bone forming cells) *differentiation, reduced bone formation and the development of spontaneous fracture. Based on these and other findings, we propose that ascorbic acid is essential for the maintenance of differentiated functions of osteoblasts and other cell types.* [39]

If vitamin C transporters cannot function properly in some tissues, it is now possible to understand the selective manner of the distribution of scurvy-like pathologies when transporters are disturbed. Fortunately, in most cases, clinical experience has demonstrated that injections of large amounts of vitamin C overcome the problems involved.

Endotoxin is not the only substance that can cause disturbances in parts of growing bones. The slide[40] shown below demonstrates damage done by retinoids (a form of vitamin A).

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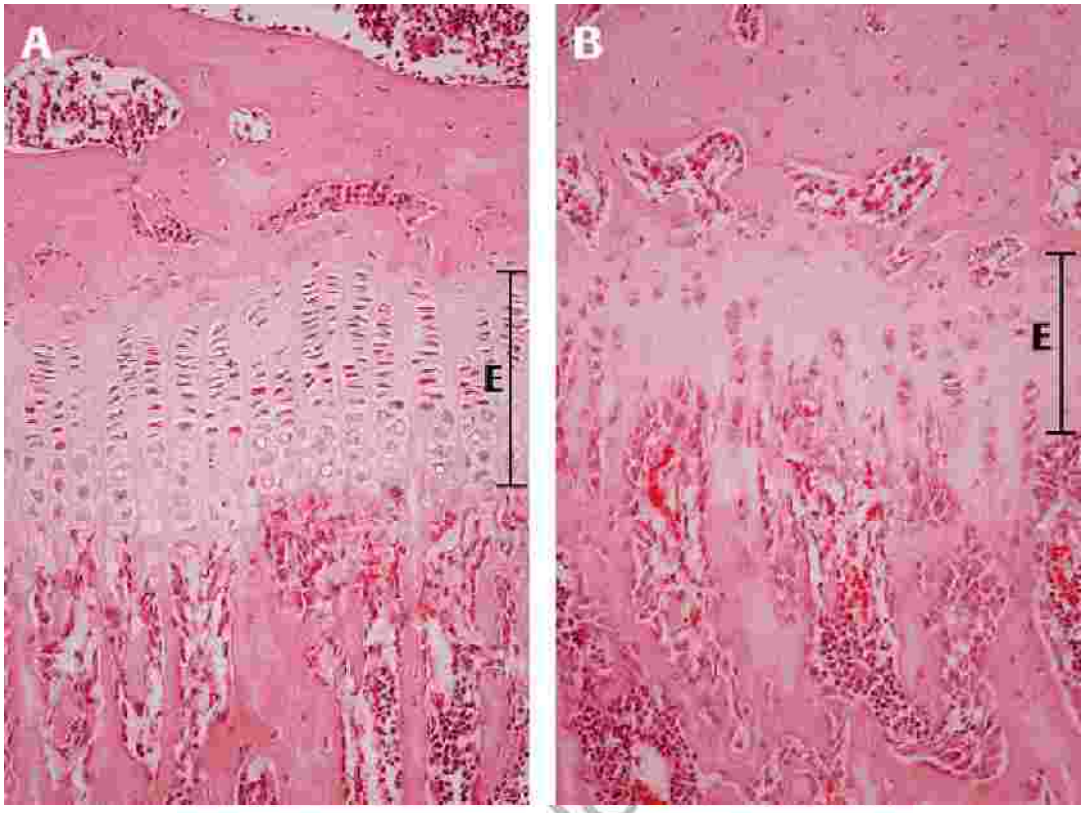
[36] Recommended Dietary Intake. Ear in collaboration with Australian Government Department of Health and Ageing, http://www.nhmrc.gov.au/publications/synopses/_files/nrvqa.pdf

[37] Sotiriou, S. et al. 2002. "Ascorbic-acid transporter Slc23a1 is essential for vitamin C transport into the brain and for perinatal survival." *Nat Med.* May;8(5);514-517. PMID: 11984597.

[38] Sotiriou, S. et al., 2002. "Ascorbic-acid transporter Slc23a1 is essential for vitamin C transport into the brain and for perinatal survival." *Nat Med.* May;8(5);514-517. PMID: 11984597.

[39] Mohan, S. et al. 2005. "Spontaneous fractures in the mouse mutant sfx are caused by deletion of the gulonolactone oxidase gene, causing vitamin C deficiency." *J Bone Miner Res.* Sept;20(9):1597-610 Epub 2005 Apr 18. PMID: 16059632.

[40] Source: Dr. Barbara Lenz, PRNS, Roche



Detail of the epiphyseal plate of a rat femur (E)
A Control
B Retinoid treatment, showing loss of orderly cartilage structure and narrowing of the epiphyseal plate.
Sections stained with hematoxylin-eosin

In his paper, Emery states:

If, for any reason, there is a diminution in the rate of growth, the 'firing' rate of the cells diminishes and two things become rapidly obvious. ***First, there is a thickening and irregularity of the strands between the cartilage columns*** *and second, if at any time the actual discharge of the cells ceases, then* ***a thin cap of matrix occurs between the terminal cartilage and the marrow cavity****. If this process continues for any length of time, a cross-banding of matrix occurs, often over-capping several cartilage cell columns. At the same time, the marrow cavity continues to absorb the trabeculae* (to be discussed later) *so that there is* ***bridging of trabeculae*** *over groups of cartilage columns.*

When the rate of growth is intermittent the ***cartilage cells proliferate behind these bands*** *and bridges and* ***the latter are left behind within the bone as a series of tide-marks which correspond at the microscope level to the calcified cross-striation in bone known as Harris's lines. These cross bands cannot be shown on an x-ray plate both because of their size*** **(very small)** ***and because they are not usually calcified. In practice, this type of lesion can be very frequently found.***

When there has been disturbances of growth over a continuous period *with incomplete cessation of growth, the whole costochondral junction loses its general regular form,* ***the bands of matrix that are left behind in the bone are similarly irregular and the cartilage columns loose their direct longitudinal orientation****. This is a picture which we describe as bizarre. It has some superficial resemblance to the changes seen in rickets during infancy and it is this picture which undoubtedly led the early workers to consider that the normal costochondral junction of the newborn showed the changes of rickets. The criteria for assessment of the ribs are shown in Table 1. These changes in the growing ribs seen in neonates correspond very closely to those described in older children by other workers.*

Why it was left to Emery to make these observations is difficult to understand when the size of problems involving SIDS and SBS is considered together with the enormous amount of research that has been published over many years.

What Emery did reveal was enough to have thrown open a new page in the history of medicine. I wonder why neither he nor his findings, received adequate recognition during his lifetime. It seems that doctors sometimes wander around in a maze of their own creation and cannot read the signs that point to the way towards what is so clearly evident.

Emery continues with:

We have done histological examinations on the ribs of every child coming to necropsy for the past fifteen years and our observations are thus based on examinations of the costochondral junction of the ribs of over 4,000 children, over 2,000 of which died in the perinatal period. The details of handling the ribs and assessment and measurement are described elsewhere.

The assessment of normal structure is one of the most difficult in pathology of the newborn period. Since we have very frequently seen obvious signs of intrauterine disease, such as fatty liver, in children who have apparently died from trauma to the brain during delivery, we have been extremely strict in our criteria for assessing normals. The only ribs that we have accepted have come either from children why have died immediately in utero as a result of a pregnant woman being involved in a road accident, or from children dying during labour as a result of vasa previa. We have not accepted placenta previa.

This is a strict method of selection. Fatty liver (steatosis) for example, can be caused by factors that predispose to sudden death or death from a variety of pathologies. In my pre-vitamin C injection days a significant number of infants under my care, who died suddenly, or mysteriously, were found to have steatosis. I did not do microscope examinations of ribs or other bones because they looked normal. I now know that this was an error.

Emery continues with:

Kalpaktsoglou and I recently made a definitive study of ribs from a series of 1,064 perinatal deaths. The cases came from two groups of children: 684 consecutive cases from the files of the Children's Hospital in Sheffield and 380 coming from children who had come to necropsy during the recent Mortality Survey carried out in England in 1961 and in which the pathologists had kindly sent me the ribs of all their cases dying during the selected month. We had thus, our own fairly large series and smaller, almost random *group from the whole of the rest of the United Kingdom.*

Of the total of 1,064 ribs, 332 only could be considered as within the range of normal and 737 showed what we considered to be definite changes indicating that the child had been ill and not growing for at least a week prior to the onset of labour. The full details of the cases and results are presented elsewhere. The results were analysed in a variety of ways including gestation age, body length and history.

When we studied our findings from the point of view of the proportion of deaths at different gestational age showing significant rib growth disturbances, we found that the instances of lesions in the Sheffield series coincided almost exactly with those obtained from ribs of children dying elsewhere. The trend of both these series is quite distinct and statistically valid. The gestational age at which the highest proportion showed no evidence of intrauterine disease was less than 32 weeks when the proportion was around 40%. As the deaths occurred at later gestational ages, the proportion of children with normal ribs diminished progressively so that around full term, the proportion was only about 25% and this figure reached 6% only in one group of children dying after prolonged gestation (42+ weeks).

If these assessments are correct, the implications appear to be that in the perinatal period, the great majority of deaths occur in infants who have been ill long before the onset of labour and that this applies mostly to the children born around term. This does not mean necessarily that birth trauma or other stresses of labour had no part in these children's deaths, for in children already ill the 'normal' trauma of birth would be of greatly increased importance. It would seem to imply, however, that if we are to further diminish perinatal mortality, we must look with greater concentration at the foetus during later pregnancy for evidence of diminution in growth rate or of some chemical indication of intrauterine athrepsia in order to shield these infants during labour or induce labour while the child is fit enough to stand its stresses.

The three images that accompany Emery's are reproduced below.

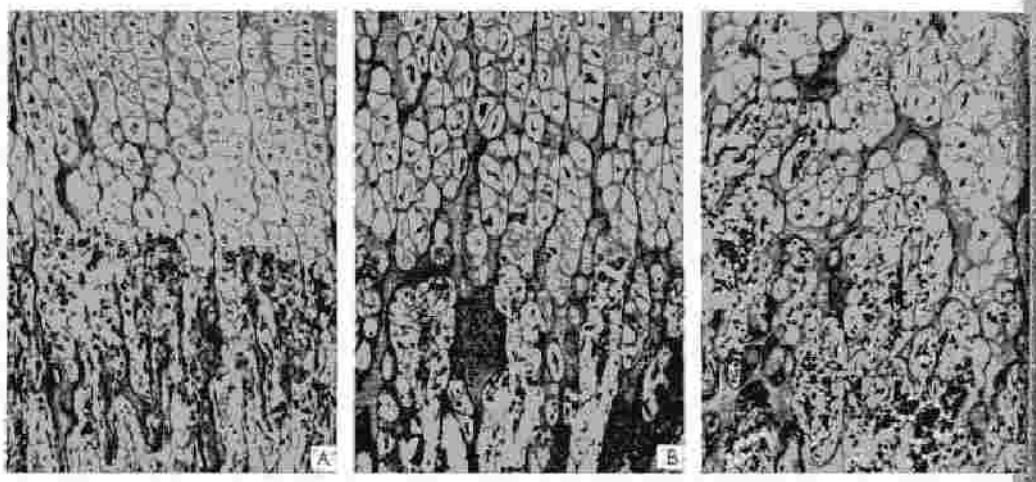


Fig. 1. Photographs of costochondral junctions from three children, all perinatal deaths. (*a*) normal junction. Note the long rows of cartilage cells leading off directly into the bone with long thin strands of trabeculae matrix. (*b*) A junction showing a period of growth retardation. Note the great increase in the amount of cartilage matrix and the building up of this matrix between the cartilage cells and the bone marrow. (*c*) A junction showing a bizarre picture. The general junction line is not obvious and these are irregular masses of matrix. The marrow blood vessels are also penetrating in an irregular manner and the cartilage cells occur in large, irregular nests

the head of the radius, largely because these bones are most easily available for x-ray studies, but, for doing microscopic studies, the rib is much better, as it is probably the most rapidly growing long bone and it grows in a linear fashion throughout almost the whole of intrauterine life. The more rapid the basic growth rate of a tissue, the more obvious and early are the effects of growth arrest.

The costochondral junction normally appears as a series of columns of cartilage cells between strands of cartilaginous matrix and these strands continue on into the bony trabeculae. This has a rather rigid and static appearance.

The costochondral junction, however, is an extremely active structure. A fully distended cartilage cell is about 14 μ. thick. When the size of the cartilage cells is taken into consideration together with the increasing length of the bone (0.43 mm. or 430 μ a day), we find that at least the length of a whole column of the ballooned cartilage cells must be replaced every day. If we were able to look at the living costochondral junction, the actual blowing-up of the small cartilage cells into the large ballooned cells is so rapid that it could almost be seen occurring. The costochondral junction is thus not a static structure at all, but much more like a series of small rockets, or a sort of slow-firing multi-barrelled jet; the cartilage cells distend and burst into the cartilage cavity so that the cartilage recedes from the shaft, leaving a slip-stream of matrix behind.

In the fixed section of the normal costochondral junction, the marrow ends of these rockets (columns of cartilage cells) are open. There is a progressive increase in size of the cells as the marrow cavity

If the bone changes found by Emery had progressed, in some cases, to fractures, a diagnosis of SIDS would not have been considered. The same, almost certainly, applies to substantial hemorrhages. Because of the lack of knowledge or understanding of biochemical disturbances affecting bones, a diagnosis of intentional shaken baby syndrome could have been seriously considered.

Emery mentions another important finding;

Since we have frequently seen obvious signs of intrauterine disease, such as fatty liver on children who have apparently died from trauma to the brain during delivery.

There is no doubt that, in these infants, there must have been intrauterine problems involving the liver and endotoxin. The brain hemorrhages, almost certainly, were a complication of this. That is, coagulation/bleeding disorders existed.

Babies do not die, either intrauterine or post-natal, for no reason. It is not always possible to discover why. Gastrointestinal disturbances and infections (even 'mild 'ones) are common causes. Detailed case histories are therefore essential. So are post-natal examinations of the gut bacteria and gastrointestinal tract. A search for anything that can lead to endotoxemia should be intensive.

The pathologies can be slow to progress, or they may appear suddenly. From appearing to be normal, to death can sometimes take minutes. Or it may take a few hours. I have been faced with it all, and often enough to force me never to forget. And to think that a few injections of vitamin C could have prevented most of them!

The effect of endotoxin appears to be instantaneous since the inhibition seen in the cells without any preexposure was similar to the cells preexposed to endotoxin for up to 6 hours [41]

At least, that is how endotoxin has been described. It depends on how one defines *'rapid'*, because endotoxin does not act alone. Transporters are necessary.

This is where I went wrong during my first years in practice.

The effects of vitamin C injected intravenously were dramatic. Extensive assays, performed by the Australian government and Roche Laboratories, clearly showed that Aborigines were certainly vitamin C deficient – and seriously so. As time passed, my biochemist colleague, Dr. Ian Dettman, introduced me to the world of vitamin C and other transporters. That is how I came to know that if something disturbs the transporters in certain tissues and organs with varied susceptibility, they can be denied essential supplies of vitamin C and glucose. Yet how many doctors understand that these disturbances can have deadly effects in minutes, hours, or a few days?

Scurvy is Not a Specific Disease

Humans and a few animals that do not synthetise their own vitamin C will, if denied sufficient vitamin C intakes, develop a variety of symptoms known as *'scurvy'*. Some

[41] Aleo, J.J. et al. 1985. "Inhibition of ascorbic acid uptake by endotoxin: evidence of mediation by serum factor(s)." *Proc Soc Exp Biol Med.* May;179(1):128-31 PMID: 3887415.

presentations are more common than others, and the variety is rather large. Much of this is due to factors that are not directly related to vitamin C deficiency. For example, endotoxin can take over and introduce a variety of complications that are not directly due to scurvy, or endotoxin can accelerate an already existing pre-scorbutic process.

The old standard method of diagnosis was to administer the vitamin C by mouth, and if there was an obvious beneficial response this was accepted as a diagnostic factor of scurvy. However, when intravenous vitamin C in large doses became available this had to be scrapped. For example I found that I could make acute alcoholics almost instantly sober by administering large doses of vitamin C intravenously. (I do not recommend that physicians attempt to do this without special training).

There were problems because almost always alcoholics insisted that the infusion be stopped early before the body could clear sufficient amounts of alcohol. Obviously, what I was doing affected the receptor sites for alcohol.

I was able to apply this method of treatment to patients who used more powerful drugs. Results were good in many ways but I soon discovered that the drug world was a nasty and dangerous part of society. So I pulled the plug and moved away into safer pastures – to the quietness of a country town not far from where I was born.

Eventually, I was able to sit back and see where my profession had gone off the rails and made a series of tragically fundamental errors when it failed to consider the literature that was available on the causes and pathologies found in cases of SIDS and SBS.

Dr. John Caffey

Many doctors contributed to the development of myths surrounding SBS. Caffey was regarded as a prime mover of the belief that the symptoms of Shaken Baby Syndrome are always violent intentional abuse inflicted by a caregiver. In February 1972 he was honoured by being asked to present the first annual Neuhauser Presidential Address of the Society for Pediatric Radiology [42] The subject was *'THE PARENT-INFANT TRAUMATIC STRESS SYNDROME; (CAFFEY-KEMPE SYNDROME), (BATTERED BABE SYNDROME)'.*

Dr. Caffey's lecture presented a picture that would be impossible to justify in every case today, because modern knowledge of the subject cannot be aired without considering vitamin C and glucose transporters, with endotoxin.

Caffey stated;

The subject of this report is the history of the radiographic discovery and early development of the parent-infant traumatic stress syndrome (PITS) and current status of radiographic findings in it. This story is particularly appropriate for presentation to this society because, and I need not tell you, the very concept of PITS was begotten by these pioneer radiographic studies of the skeleton which prepared the way for the full syndrome later. These bone lesions were discovered and originally evaluated by America pediatric radiologists exclusively – radiographic all members of this Society. Several new radiographic signs of trauma to

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[42] Caffey, J. 1972. "The parent-infant traumatic stress syndrome; (Caffey-Kempe syndrome), (battered babe syndrome)." *Am J. Roentgenol Radium Ther Nucl Med.* Feb;114(2):218-29. PMID: 5058509.

growing bones were detected in these studies which have proved to be the pristine probe – the key and the cornerstone to the discovery and growth of the PITS syndrome.

Wilful assault is the legal charge which accused parents must face when on trial for intentional injury to infants…

Caffey does not consider a full differential diagnosis. This is a fundamental error.

It is extremely serious because Caffey could not deny knowledge of scurvy, because he had published an article about infantile scurvy. It was the first paper that was brought to my attention in 1967 when I recognised the existence of infantile scurvy. Apparently, Caffey did not adequately consider a differential diagnosis, even within the scientific facts he had previously written. As I have stated earlier, the pathologies that are claimed to be due to be always due to deliberate inflicted trauma, were carefully described by Hess in 1920 as varieties of scurvy. References have been documented in early pages of this book.

Caffey refers to a paper by Astley, and notes that it contains *'some important new clinical observation. He found that the metaphyseal lesions caused surprisingly little pain or tenderness'*. Hess documents this fact in his book written in 1920. It is a feature found in many so-called *'shaken baby'* cases. Its significance has been mostly ignored. How can bones be broken and no pain exist? Obviously, the cause is not inflicted trauma. Sometimes there are multiple fractures of different ages. Are the babies involved given powerful sedatives? Of course not! This feature should be accepted as proof of innocence – not guilt.

What about external signs of inflicted trauma? Sometimes in scurvy cases there can be bruising. Often there is none. When there is no bruising, or soft tissue damage of any kind, how does one explain how fractures are caused? Do the infants concerned have special pain-killing tissues? Of course not.

In reviewing the history of the SBS infants that I have investigated, some had not been well, were taken to hospital or doctors, examined, and because no specific abnormalities were detected, sent home. Some of these babies had been thoroughly examined by doctors visually, and manually, from head to toe, several times. How were multiple fractures missed? Has God created a special breed of pain free babies? Doctors have been deeply indoctrinated. They can no longer see what is obvious – even when the evidence is crystal clear.

On page 224 Caffey states;

The traumatic lesions in the growing skeleton are rarely explored surgically and have never been studied adequately at necropsies [at the time of writing]. *Current knowledge rests entirely on the nature of the radiographic images. The most comprehensive description of them is in the British Journal of Radiology and in the text, Pediatric X-ray Diagnosis, Sixth Edition. In the PITS syndrome, all of the traditional signs of trauma may be seen radiographically such as fractures, dislocations and injuries to the cartilage plate with displacement of the contiguous epiphysis. However, the most common radiographic changes usually are found in the absence of these traditional traumatic changes, namely metaphyseal infractions, and in the absence of these traditional traumatic changes, namely metaphyseal infractions, and in traumatic involucrums. Such lesions are rarely seen in mature bones and they diminish in both frequency and size with advancing age. In infants they are practically always diagnostic of trauma when found in otherwise normal bones.*

This statement exposes major errors in the manner by which Caffey arrives at these conclusions. The first is the failure to consider a full case history. Without this, any decision arrived at is suspect. The absence of pain has already been mentioned. It is a major issue. Next, when parents/caregivers deny harming babies, instead of considering this issue carefully, it is presented as a classical form of 'denial'. It is presumed that the parents are showing a psychological response that proves guilt. This is a modern version of the old witchcraft trials, only much worse because we are now considered to be beyond such stupidity.

While Caffey and others have been busy unjustly destroying many families, the books on infantile scurvy by Hess and others have become covered with thick layers of dust, and subsequent medical literature likewise ignored.

In 1950, when I sat for my final medical exams, if I had written about a medical case in such a manner, I would have been told to try again, or go and sell trousers in a nearby drapery shop. To break the primary rules of diagnosis when the issues are so important is unforgivable.

Caffey details another issue:

The high diagnostic value of these radiographic lesions has now been proved for many years; the metaphyseal infractions are diagnostic immediately after, and the traumatic involucrums within several days after the injury. Multiple lesions of different ages in different bones of the same infant are indicative of multiple traumatic injuries inflicted at different times. However, they neither identify the perpetrator nor his motive.

I have already discussed this issue. Multiple lesions of different ages in different bones is a classic feature of infantile scurvy. And if the bones of any dead babies considered to be traumatically injured, had been subjected to Emery's microscope examination, what might have been found then? We don't know, because pathologists don't examine the bones microscopically, to look at the bone changes which would indicate biochemical disturbances.

Prosecution witnesses have approached some SBS cases in a manner that cannot be scientifically sustained. Included are statements such as:

1. Some retinal hemorrhages have characteristics that are diagnostic of SBS. (This absurdity is impressive to some but certainly not universally accepted as fact.)
2. Retinal hemorrhages alone are diagnostic.
3. Subdural hemorrhages alone are diagnostic.
4. Fractures alone are diagnostic.

In all such cases which I reviewed, correct attempts to consider a full case history and a differential diagnosis were not carried out.

Attempts by the accused to deny guilt, are considered proof of guilt, which is now a commonly accepted piece of psychology dogma that is in most cases, quite incorrect.

If a baby suddenly collapses at home there is a natural tendency to shake the baby, either gently or more severely. The pathologies that are found later can be wrongly assumed to be

due to shaking. The accused person may even become convinced that this is so. The statistics become meaningless. So does the factual reasoning upon which individuals in later cases may also be found guilty.

Glucose Disturbances and Glucose Transporters

It has been known for a long time that infections disturb metabolism - including glucose metabolism. [43]

Infection leads to profound alterations in whole-body metabolism, which is characterized by marked acceleration of glucose, fat and protein, and amino acid flux. One of the complications of infection, especially in the nutritionally supported setting, is hyperglycemia. The hyperglycemia is caused by peripheral insulin resistance and alterations in hepatic glucose metabolism. The defects in hepatic glucose metabolism include overproduction of glucose and a failure of the liver to appropriately adapt when nutritional support is administered. Investigators have suggested that multiple factors contribute to the observed defects. In this review, I focus primarily on alterations in carbohydrate metabolism, examining both the metabolic response to infection and inflammatory stress, the role of the accompanying neuroendocrine and inflammatory responses in the metabolic response, and the interaction between the endocrine response to infection and nutritional support.

However response to infections and endotoxemia does not always present with hyperglycemia. Hypoglycemia can also occur. [44]

The roles of renal gluconeogenesis and glucose utilization in control, hemorrhaged, and endotoxin-injected animals were investigated using anesthetized, eviscerated, nonnephrectomized and nephrectomized dogs. Results demonstrate an increased glucose utilization in both hemorrhagic and endotoxic shock which was marked after endotoxin. Since blood glucose values dropped more in nephrectomized, hemorrhaged animals, in contrast to the nonnephrectomized, hemorrhaged dogs, the kidneys were assumed to perform a significant gluconeogenic role. The kidneys did not appear to perform gluconeogenesis in endotoxin shock since blood glucose levels were comparable in eviscerated, endotoxin-treated animals whether nephrectomized or not. To ascertain the tissue responsible for the increased glucose utilization in endotoxin shock, a study was performed with endotoxin added to blood in vitro (estimated LD100 concentration). The endotoxin-treated blood (n = 7) demonstrated an increased glucose utilization compared with saline controls (n = 7) (P less than or equal 0.02). Accelerated glucose utilization rates were comparable between the eviscerated, nephrectomized animals and in vitro experiments. These data suggest that excessive glucose demand by certain blood components may partially explain the lethal hypoglycemia of endotoxin shock.

Liver involvement during endotoxemia can be dramatic and rapid. Autopsies that I performed showed large areas of acute yellow atrophy in the liver in some sudden infant deaths and

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[43] McGuinness, O. P. 2005. "Defective glucose homeostasis during infection." *Annu Rev Nutr.* 25:9-35 PMID: 16011457.

[44] Archer, L. T. et al. 1975. "Roles of Renal Gluconeogenesis and Increased Glucose Utilization in Hemorrhagic and Endotoxic Shock." 19 Dec. Accession Number ADA021839. http://stinet.dtic.mil/oai/oai?verb=getRecord&metadataPrefix=html&identifier=ADA021839
<See also: Archer. L.T. et al. 1976. "Renal gluconeogenesis and increased glucose utilization in shock." *Am J Physiol.* Sep;231(3):872-9. PMID: 970470.>

following infections. Sometimes this was preceded by liver pain and/or liver tenderness. The rapid resolution of liver pain and tenderness following intravenous injections of vitamin C remains as a highlight of my early career.

One would expect to find glucose disturbances when endotoxemia is present. The severity of this would depend on the cause and how quickly the body can recover effective immune responses, or utilize detoxification processes.

McCallum et al published a relevant paper;[45]

This study was undertaken to characterize the nature of carbohydrate loss due to endotoxin poisoning in mice and to elucidate mechanisms responsible for the changes. Female ICR mice, fasted overnight, were injected intraperitoneally with a mean lethal dose of endotoxin extracted from Salmonella typhimurium strain SR-11. Liver glycogen levels, alanine-U-(14)C and pyruvate-2-(14)C incorporation into blood glucose and liver glycogen, glucose-U-(14)C incorporation into liver glycogen, and liver glycogen synthase activities were measured at intervals after treatment. Liver glycogen in fasted mice given endotoxin was diminished significantly as early as 1 h after treatment. Liver glycogen synthase was significantly decreased in poisoned mice at 17 h. The use of actinomycin D showed that the induction of this enzyme due to fasting or hydrocortisone, or both, was inhibited by endotoxin. The incorporation of the (14)C-label from alanine-U-(14)C, pyruvate-2-(14)C, or glucose-U-(14)C into blood glucose and liver glycogen was substantially impaired in endotoxemic animals at 12 h. Decreases in incorporation occurred as early as 4 h after treatment. The progressive increase in glycogen synthase activity observed in fasted controls was not seen in endotoxin-poisoned mice. The administration of a glucose or pyruvate load to endotoxin-treated mice did not restore gluconeogenesis, glycogen synthesis, or liver glycogen synthase activity to normal levels. The in vivo activation of glycogen synthase by glucose was significantly reduced in endotoxemic animals. These changes indicate reduced carbohydrate synthesis as a probable cause for rapid sugar loss during endotoxemia in mice.

Hyperglycemia upsets the cellular intake of vitamin C. [46]

The cellular uptake of vitamin C (ascorbic acid, ASC) is promoted by insulin and inhibited by hyperglycemia. If a rise in plasma ASC is uncoupled from insulin replacement in insulin-dependent diabetes mellitus (IDDM) then the degree of hyperglycemia could account for "tissue scurvy" in IDDM. Leukocyte ASC is lower in IDDMs compared with nondiabetics when vitamin C consumption is adequate and our data suggest that this is a variable component of the pathophysiology of IDDM.

The complications of diabetes mellitus are believed to result from either the intracellular accumulation of sorbitol or the nonenzymatic glycoxidation of proteins or both. With respect to the abnormal cellular accumulation of sorbitol, vitamin C supplementation has been shown to be effective in several studies of adults with diabetes; the situation regarding the prevention of protein glycoxidations by supplementation is presently unclear. The roles of ASC as an aldose reductase inhibitor and a water soluble antioxidant in body fluids are potentially very important as adjuncts to tight glycemic control in the management of

[45] McCallum, R.E. et al. 1973. "Effects of endotoxin on gluconeogenesis, glycogen synthesis, and liver glycogen synthase in mice." *'Infect Immun'*. 1973 Apr; 7(4) :642-54. PMID: 4202664

[46] Cunningham, J. J.\, 1998. "The glucose/insulin system and vitamin C: implications in insulin-dependent diabetes mellitus." *J Am Coll Nutr*. Apr;17(2):105-8. PMID: 9550452.

diabetes. Tissue saturation and maximal physiologic function in IDDM may require supplemental vitamin C intake

The use of the words *'tissue scurvy'* needs to be explained. Tissue Scurvy doesn't mean there is a vitamin C deficiency. In specific tissues, 'tissue scurvy' can mean that there is a failure of vitamin C transporters, to transport vitamin C into those tissues.

SOME SHAKEN BABY CASES

As a small child I was made aware of what seemed to be an axiom that doctors were a special and revered group of individuals who were next to God in the list of human beings. In medical school and as a young doctor this glorification expanded, because doctors I came in contact with did their best to help the lame and the sick. In recent years this has changed. A worrying number of doctors appear to now be possessed with minds that have become twisted and corrupted. The same could be said for some lawyers and judges. It only takes a few to cause havoc and destroy innocent individuals forever and ever.

This is not always a deliberate tactic. Many doctors, lawyers and judges sincerely believe that they are right when they are not. In such situations the individuals charged have little hope of ever being treated as anything else but dangerous and violent criminals.

In the earlier portions of this book I have explained how the *'classical'* pathologies found in so-called *'shaken baby cases'* are initiated without inflicted trauma. It is now necessary for me to illustrate how doctors, lawyers and judges have ignored what is available in the best medical literature, and wrongly destroyed not just individuals, but entire families.

There are two ways by which authorities end up convicting innocent individuals.

1. By accepting evidence from doctors who deliberately misrepresent the evidence.

2. By accepting evidence from doctors who have neither read historical literature, nor kept up to date with current literature.

I have witnessed both – many times – while investigating more than 50 cases.

Unfortunately, more often than not, my evidence was ignored.

The first case involved a young Aboriginal man. At the time I knew virtually nothing about shaken babies. My involvement commenced just a few days before the trial was due to end. The file that was sent to me was, initially, not helpful. For two nights I slept with difficulty as I tried to find an explanation for the pathologies. Then it suddenly hit me. The fractures and hemorrhages exactly matched those reported many years ago, by Professor Hess in America. The cause? It was scurvy. In Aborigines, that was highly likely, based on the work I had previously done, testing them for vitamin C.

It was, of course, also necessary for me to allow for problems involving vitamin C transporters rather than just a dietary deficiency of vitamin C.

I had struck it rich – something that few doctors have experienced.

But the doctors and lawyers would not accept what I had discovered. The accused man was sent to jail.

All was not lost. The next case was heard by a judge who was full of wisdom. He was faced with two opinions – one from the *'big shots'* and another from myself and a colleague. The prosecution was recalled and asked to comment on our evidence. They were unable to do so and the judge decided that it was impossible to clearly hand down a guilty verdict. The accused was freed. I read about it in the papers and looked at the photograph included with more than a little satisfaction.

A Case with New and Important Features

During 2002 I was asked by a coroner to report on an unusual case. A detective was sent to interview me and deliver a copy of the case notes.

In 1997 the infant's mother had telephoned for an ambulance. The infant, AB (name changed) was breathing in a slow, laboured manner and was making groaning noises. A doctor made a provisional diagnosis of raised intracranial pressure and coma caused by either overwhelming infection or head trauma.

On admission to a large hospital the child was gravely ill, pale, and mottled. This last detail, as I had seen in my years in practice and working in hospitals in the past, is one feature of endotoxic shock – amongst other pathologies. A CT brain scan showed bilateral subdural hemorrhages, an acute left temporal hemorrhage and bilateral retinal hemorrhages. These pathologies were considered to be consistent with the baby having been intentionally, violently shaken.

Later on the same day an ophthalmologist diagnosed bilateral multiple retinal hemorrhages, and both pre- and intra-retinal hemorrhages. There was bilateral pallor of the optic nerve head. The doctor stated that these pathologies were consistent with violent shaking. She also stated that the optic nerve pallor made her suspicious that there had been previous episodes of insult to the optic nerves.

The infant died shortly afterwards.

The doctor who performed the autopsy reported that the injuries were indicative of a rotational injury to the head, commonly called SBS.

An examination of records revealed that when the mother was approximately 36 weeks pregnant an antenatal ultrasound was done. The fetus appeared to have a small defect in the left anterior cranial fossa with a small meningocele (a cyst filled with cerebrospinal fluid). This, in itself, is a complex issue that is difficult to assess clearly, but one detail was apparent – there was an intracranial problem of some sort.

Yet when the infant was only a number of hours old, the doctor saw no indication of any abnormalities in the brain or eyes.

Furthermore, the doctor stated that, "I cannot explain the unusual ultrasound appearance." The correct approach would have been to hold a conference with various experts and consider a *'differential diagnosis'*. This was not done. An opportunity to properly investigate this baby, was lost.

On August 19, 1997, the baby was admitted to hospital because of vomiting and lethargy. Nothing that was significant was detailed.

The mother reported that her baby had been vaccinated on two occasions. There was a 'bit' of a reaction to the two-month needle. Of more importance was a statement made by a paediatrician that the infant had Marfan's syndrome. The disease is a heritable disorder of the connective tissue that is manifested by skeletal changes. There appeared to be no follow-up of this.

The child's grandmother stated that two weeks prior to death the child was sick and was admitted to hospital for a period.

Unfortunately, I was not asked to appear in court. One witness, when asked about my report stated that my "opinion didn't seem to hold much weight….it just didn't seem to make much sense."

Further questioning of this witness highlighted an attempt to delve further.

Question: *You say "other medical experts have been spoken to and all are of the opinion - I stress that you say that 'all are of the opinion that the child died as a result of being shaken.'" In point of fact Dr Kalokerinos he doesn't form that opinion at all, does he?*

Answer: *No, he didn't*

Question: *So it is not true to say that all they all had that opinion.*

The coroner earned from me a considerable degree of respect.

There were 229 pages of legal information sent to me. Some pages were more important than others. It was apparent that the prosecution witnesses had decided at an early stage that intentional shaking was the fundamental cause of the pathologies, and there was no need to delve more deeply, carry out a proper differential diagnosis, or to investigate what was available in the literature. The following information highlights one pathology that demonstrates a predetermined diagnosis;

On the second page of evidence provided by the pediatric radiologist, is the following:

'There is some thickening and splitting of the anterior cortex of both femora which I think is developmental and is not significant in the present circumstances'.

This description is not absolutely clear. However, it could be consistent with scurvy-like changes. Furthermore, no histology was carried out on the tissues involved. As discussed in the paper by Professor Emery earlier in this book, apparently normal bones may reveal significant changes when examined under a microscope. Another opportunity to investigate properly was lost.

Of more than passing interest was the report by the pathologist. He states: '***In addition there was focal dilatation of the large bowel'.***

I was shown a photograph of this pathology. The lesions were dramatic. There were portions where the bowel appears to be normal, then suddenly there were lengths where the bowel was dilated. The boundary was sharp. Unfortunately, I could not obtain a copy.

Certainly, to consider that shaking was the cause of the bowel pathology, is difficult to accept without clear evidence. According to the literature, there are many possible causes, some of which involve endotoxin.

Pieter Vanden Berghe et. al. [47] published an article that is extremely important because it explains some of the mechanisms involved in causing these pathologies.

Enteric [gut] *neurons controlling various gut functions are prone to oxidative insults that might damage mitochondria (e.g., intestinal inflammation). To resume local energy supply, mitochondria need to be transported. We used MitoTracker dyes and confocal microscopy to investigate basic characteristics of mitochondrial transport in guinea pig myenteric neurites. During a 10-s observation of 1 mm nerve fiber, on average, three mitochondria were transported an at average speed of 0.41 ± 0.02 µm/s. Movement patterns were clearly erratic, and velocities were independent of mitochondrial size… Transport was blocked by microtubule disruption… ($[Ca^{2+}]_i$) particularly in localized Ca^{2+} uptake and release... To optimally perform these tasks, mitochondria need to be positioned precisely at those sites that require high amounts of energy or extensive Ca^{2+} bufferin.. In highly polarized cells such as neurons, regions of high energy consumption (e.g., growth cones, synapses, etc.) can be located far away from the soma; therefore, the translocation of mitochondria along nerve fibers is crucial to maintain proper functioning… Due to their position in the gut wall, the mitochondria in these neurons are more prone to damaging insults, such as ischemia, anoxia, allergic reactions, or endotoxin exposure after intestinal infections…*

What exactly triggers mitochondrial traffic is as yet unknown. Growth, elongation, and maturation of nerve fibers) are likely candidates. Some kinesins have been shown to be upregulated in growing axons. Mitochondria are likely transported to regions of high energy consumption or high Ca^{2+} loads or to replace impaired mitochondria…

There is no doubt that the mechanisms involved are in many respects *'delicate'* . The opening sentence '*Enteric neurones controlling various gut functions are prone to oxidative insults that might damage mitochondria (e.g., intestinal inflammation),* speaks volumes.

In many ways it is surprising that problems involved are not more common, or better recognised.

Another issue is the fact that the entire gut is not involved at the same time. This is a feature of many pathologies, including scurvy pathologies, where only some tissues are involved during one stage, then later other tissue areas suffer. It is, of course, why many prosecutors wrongly assume that multiple acts of violence take place at different times.

Obviously, the mitochondria are mobile for a reason. If they were not, supplies of energy could not reach tissues under certain conditions. The alternative open to nature would be to ensure that mitochondria were *'everywhere'* – an impossible situation because of limited space availability.

Like all delicate mechanisms, problems can arise when *ischemia, anoxia, allergic reactions, or endotoxin* enter into the equation (page 3 of the paper). I should add that each of these

[47] Vanden Berghe, P. et al. 2004. "Characteristics of intermittent mitochondrial transport in guinea pig enteric nerve fibers." *Am J Physiol Gastrointest Liver Physiol*. Apr;286(4):G671-82. Epub 2003 Oct 30. PMID: 14592946. http://ajpgi.physiology.org/cgi/content/full/286/4/G671

factors can quickly pave the way to endotoxemia, even when this is not a primary factor. For example, anoxia can open the gut barrier and enable gut endotoxin to pass through into the circulation.

The following paper explains, further, how segmental dilation of the gut occurs in some cases.

Gaffin et al. state [48]

Acute hypoxia is known to cause a marked reduction in intestinal and peripheral blood flow, in favor of blood flow to the brain and heart. Complete occlusion of the intestinal circulation is known to damage the gut wall, allowing potentially lethal endotoxins present within the intestines to escape into the circulation. We examined here whether the breathing of a hypoxic gas mixture could lead to sufficient damage of the intestinal wall to cause endotoxemia. Six anesthetized monkeys breathed air for 1 hr, then an hypoxic mixture (FIO2 = 0.13) containing N2O for 1 h and, finally, 100% O2. Plasma endotoxin concentrations were determined by two methods. After approximately 40 min of hypoxia, the plasma endotoxin level rose significantly from 0.39 to 1.60 ng X ml-1 (p less than 0.001) and then subsided to near control levels. Control monkeys breathing air only or 70% N2O in oxygen (FIO2 = 0.3) for 3 h showed no such elevation in plasma endotoxin concentration. We conclude that hypoxia leads to a temporary endotoxemia in primates. Reticuloendothelial system depression by whole body X-irradiation (200 rads) increased both the magnitude and duration of the hypoxia-induced endotoxemia. Prior administration of equine anti-lipopolysaccharide (anti-LPS) hyperimmune plasma greatly reduced the magnitude of the induced endotoxemia. Since endotoxemia may be lethal, the use of anti-LPS as possible prophylaxis should be considered in persons breathing artificial atmospheres or where acute hypoxia may be a danger. (Author's underlining)

Complete occlusion of the gut circulation is not necessary, as demonstrated during marathon races, or attempts to climb Mount Everest. Collapse or death, to an important degree, involves endotoxin.

Under consideration is the autopsy finding of segmental dilation of the colon in an SBS case. Death occurred before the condition was able to advance beyond a moderately complex state. The following article provide further evidence for this [49]

Toxic megacolon is an infrequent, but potentially fatal complication of a fulminant colitis. Toxic colonic dilatation, also caused by ischaemic or infectious inflammation like pseudomembranous colitis, mostly occur in patients with inflammatory bowel disease. Toxic mega-colon is defined as segmental or total colonic distension of >6 cm with the presence of clinical signs of acute colitis and systemic toxicity. Because of the associated high morbidity and mortality the early diagnosis and the management play an important role. The free perforation means a fourfold increase in the mortality of the acute colitis. Recognition of toxic megacolon is underlaying by x-ray of the abdomen with colonic distension and a lack of haustral pattern. Accompanying distension of the small bowel can predict the development of the disease. CT scanning shows a diffuse wall thickening, pericolic inflammation and abnormal haustral pattern and can also detect subclinical perforation or abscesses. The management of toxic megacolon should be with intravenous parenteral nutrition, adaequate supplementation of intravenous fluids and

[48] Gaffin, S.L. et al., 1986. "Hypoxia-induced endotoxemia in primates: role of reticuloendothelial system function and anti-lipopolysaccharide plasma." *Avait Space Environ Med.* Nov;57(11):1044-9. PMID: 3790022.

[49] Ruf, G. 2006. "Toxic megacolon--surgical point of view" *Schweiz Rundsch Med Prax*.Nov 1;95(44):1727-30. PMID:17111883.

correction of electrolytes abnormalities and the therapy of colitis with corticosteroids. Antibiotics are indicated in infectious disease or bacteriemia and also in colonic perforation. Surgical intervention is indicated by the onset of signs of progression of the disease and complications as perforation, uncontrollable bleeding or distension. The surgical procedure of choice is colectomy and ileostomy. The mortality and morbidity was decreased by avoiding rectal excision. The rectum is closed as a Hartmann's procedure or a mucous fistula is created. A secondary ileoanal pouch can be created at a later date. The interdisciplinary approach with optimal timing of surgical intervention can decrease the morbidity and mortality of toxic megacolon.

When I was a medical student I was taught to avoid making a double diagnosis when dealing with a case wherever possible. That is, extreme care must be taken because the chances are that doing otherwise will not end with a logical diagnosis. What I have presented explains everything with one primary diagnosis – and that is endotoxemia.

Role Played by Disturbances of the Gut

Normally, the gut acts a barrier that permits only desirable substances to be transported through to the blood stream. However, factors such as infections, endotoxemia, anoxia (including partial anoxia), can result in barrier breakdown of various degrees. Mechanisms involved need to be discussed.

The following article is a superb summary of the issues [50]

The cytoskeleton (structural framework of cells) *includes different types of protein filaments. Actinfilaments and microtubules are two fractions of the cytoskeletal assembly that are involved in maintaining intestinal barrier function…Though many studies have been performed to elucidate the interrelationships among actin stability, mucosal barrier function, and oxidant insult, the role of the actin cytoskeleton in intestinal disease such as inflammatory bowel disease (IBD) remains elusive... Microtubules provide a system for directing intracellular transport and secretion, as well as coordinating cytosolic organelle movement. Disruption of the microtubule cytoskeleton can severely limit cell function, and if not reversed, can adversely affect its integrity and viability. Microtubules maintain the overall shape and stability of the plasma membrane. These functions are based on the ability of the tubulin subunits to polymerize and on the ability of microtubules to resist depolymerization. We recently showed the crucial role of this structural component in the maintenance of mucosal barrier function… Tight junctions appear to be key regulators of intestinal permeability to macromolecules such as endotoxin and other bacterial byproducts. The physiology of this tightly regulated conduit is not fully known. However, this dynamic gateway is able to change its size under various physiological and pathological condition… transepithelial resistance and tight junction structure can be altered rapidly by osmotic load. Luminal osmotic load, especially when activated by sodium co-transport, can increase paracellular permeability to large molecules in rat jejunum. In addition, intestinal permeability increases following ingestion of hypertonic solution and meal-related solutes such as glucose. This change in intestinal permeability after meal ingestion should enhance the ability of the small intestine to harvest the maximal amount of nutrients, but it can also increase the risk of exposure to luminal proinflammatory compounds induced by various agents results in disruption of epithelial barrier function and hyperpermeability. For example, oxidant-induced mucosal barrier dysfunction is caused by the oxidation, disassembly, and instability of the actin cytoskeleton. In addition, disruption of microtubules by either oxidants, ethanol, colchicine or antimitotic agents can*

[50] Farhadi, A. et al. 2003. "Role of cytoskeletal structure in modulation of Intestinal permeability" *Archives of Iranian Medicine*, Vol 6, No 1, January 2003. http://www.ams.ac.ir/AIM/0261/0261049.pdf

severely limit cell function and the structural integrity of the intestinal barrier. The mechanism responsible for cytoskeletal damage in various settings is not fully understood…

Significance and perspective.

The intestinal barrier is the most important interface connecting man to his surrounding environment. It is now postulated that a breach in this barrier might be the primary event in the pathogenesis of several systemic and intestinal disorders including IBD. Indeed, it is now believed that IBD is a result of an abnormally exaggerated immune response to normal intraluminal proinflammatory factors such as bacterial byproducts [Author's addition: endotoxin is one] *in susceptible individuals with a dysregulated mucosal immune system. In this scenario, intestinal barrier integrity can play a key role since it can prevent exposure of the mucosal immune system to intralumuinal factors and thus prevent initiation and/or perpetuation of the inflammatory cascade in the presence of hostile luminal factors or in subjects with dysregulated immune systems. Thus, better understanding of barrier function can provide an opportunity for development of new therapeutic options for many systemic and GI inflammatory disorders. Potential agents are PKC mimetics,cytoskeletal stabilizers, and growth factor mimetics. Further studies are needed to explore these very promising therapeutic avenues.*

Dirty Tricks

Some prosecutors are determined to win cases even if evidence is not available. They will attempt to obtain what they want, even if doing this breaches all the rules of decency and fairness. Detective Philip Wheeler, from Scotland Yard, threw aside the sacred traditions of English law when he cooked up and set in motion a terrible plan.

In fact, there was ample evidence of innocence which was ignored. This involved a very important issue. The baby concerned was alive but extremely ill when admitted to hospital. Amongst other tests the ears were examined. They were reported to be *normal.*

Death followed quickly. During the autopsy the ears were reported to have mucopurulent material [pus] in both ears. I have published an article demonstrating how this is can be associated with endotoxin [51]. As stated in earlier pages of this book, endotoxin can lead to hemorrhages – including retinal, subdural hemorrhages' and subarachnoid hemorrhage.

So the caregiver who was alone with the baby when she collapsed, was charged with shaking.

However, Detective Wheeler had a problem. The evidence was not totally clear. Something more concrete was needed. Detective Wheeler was certain that the caregiver had shaken the baby and he was determined to prove it. He told the girl that the lungs (that had already been examined and declared to be normal) had been re-examined and he could prove that she had suffocated the baby as well as shaken her.

Obviously, he expected that the girl would confess and that he would win. She did not oblige.

He then offered the girl a 'deal: "plead guilty to a charge of manslaughter and we will let you go home. Plead innocent and you will go to jail for a long time."

[51] Kalokerinos, A. 1998. "Otitis Media -Towards a Final Solution." *Journal of the Australasian College of Nutritional & Environmental Medicine,* Vol. 17, No. 2, December pages 39-41.

Some choice! She had to accept or go through a form of hell that would destroy her.

I have been involved in cases worldwide, where prosecutors have offered deals like this. The real harm lay in the fact that they were then able to point to the pathologies and say, "we have confessions that prove that the pathologies are caused by shaking." Many innocent individuals have been wrongly convicted on the basis of such evidence.

As for Detective Wheeler? He toured widely while lecturing about the 'evils' of shaking babies. At a conference in Sydney he angered me immensely by stating things that were certainly not true. I approached him during a coffee-break. Although we had never met, my name tag was clearly visible. I asked him if he knew who I was. For a few seconds he looked at the tag – then turned and quickly ran away. Apparently he had heard about how I could react when angry.

Recently, much of his stagger has been blunted. Amongst a list of fallen idols (published on the internet) he was listed in:

Accusation: Detective Chief Inspector in charge of Brent and Haringey police child protection units. Accused of allowing his units to descend into chaos, with overworked frontline staff having to 'muddle through as best as they could' .His 'lack of supervision' was a 'crucial factor in teams being allowed to deteriorate'.

WHERE IS HE NOW? After being seconded to Her Majesty's inspectorate of Constabulary, he returned to Scotland Yard in January 2003 because it was felt 'inappropriate' to have him inspecting other officers.

Comment: Philip Wheeler, who supervised six police child protection teams in north-west London at the time of Victoria's death. He received a formal caution – a less serious punishment than a reprimand.

A Bloody Mess

Baby B was born to a mother who suffered from gestational diabetes and hyperemesis gravidarum (vomiting) during the pregnancy. A circumcision was carried out, during which there was heavy bleeding. Just how much was never documented. The procedure took some time. Vitamin K had been administered after the birth.

There is no doubt that a considerable amount of blood was lost during and immediately after the procedure. Obviously, the doctor had great difficulty controlling the bleeding. After the procedure 'the nappy was full of blood'. Just how much blood was lost is not known because, as far as I can gather from an examination of the notes, no blood was tested at the time.

The lack of information concerning this, is a serious issue.

Why was there difficulty controlling bleeding? It is not logical to assume that it was due to inept surgery. There must have been a coagulation/bleeding disorder at the time. This should have been apparent to the doctor. It is reasonable to assume (although the subject is complex) that a Vitamin K deficiency did NOT exist simply because an injection of Vitamin K had

been administered after birth.

A consultation with someone who specialized in the field of coagulation/bleeding should have been a part of the routine. This was not done.

This issue became even more important when, later, anaemia was detected and a transfusion was considered necessary.

A doctor stated that the mother and father told him later that the baby had a further episode of pallor associated with arching of the back, shaking his arms, rolling his eyes, and abnormal breathing sounds. They took B to hospital. He was fully medically assessed and had a chest X-ray. There was no reported abnormality on this assessment. The parents were reassured that B was well and he was discharged into their care.

In retrospect, this was an extraordinary decision. The history is typical of an intracranial disturbance. At the very least, further investigations should have been carried out, such as an immediate consultation with a Pediatric neurologist.

The circumcision area then got infected. The swab showed *'numerous gram negative bacilli'*. The culture showed *'staphylococcus aureus'*. It is difficult to assess this report because much depends on how a culture is carried out. A particular organism may be responsible for the bulk of the pus but another may dominate what is cultured. However, staphylococcus aureus produces an enterotoxin that can be very harmful.

When the circumcision became infected antibiotics were dispensed. This was a correct procedure, but there can be serious complications when antibiotic induced bacterial kill-off causes the sudden release of large amounts of endotoxin from the walls of the dead bacteria - with a resulting endotoxaemia.

Chronic subdural hemorrhages were found. A doctor stated: *'It is possible that chronic subdural haemorrhages could be the result of birth trauma. This is unlikely to be the case because the HISTORY OF HIS BIRTH does not suggest significant trauma'*.

This is not true - at least when chronic subdural hemorrhage is concerned; [52]

Chronic subdural hematoma in the infant ... in a significant number of infants there is no clear history of trauma. There may be, when the brain is examined visually, no signs of a previous subdural hemorrhage, but it can exist if great care is taken to examine the dura microscopically.

The following article[53] reinforces this issue.

Cranial dura maters of 36 consecutive infants with sudden infant death syndrome (SIDS) and 16 control infants coming to the Department of Coroner were examined microscopically to

[52] Behreman, R. E. et al. (eds) *Nelson Textbook of Pediatrics.* 11th edition, 1979. W.B. Saunders Company. ISBN: 072169019X , page 1789.

[53] Ribe, J.K. et al. 1993. "Blows to the maternal abdomen causing fetal demise: report of three cases and a review of the literature." *J Forensic Sci.* Sept;38(5):1092-1096. PMID: 8228881.

determine if subdural neomembranes are associated with cases submitted as SIDS...Overall prevelance of organising subdural neomembranes was 25% in the group examined. In all but two cases trauma could be excluded as a cause of head trauma by ageing neomembranes histologically. No association was found between type of delivery (vaginal or Cesarean) and presence of a subdural neomembrane.

In other words, in infants, subdural hemorrhages can exist in infants without any history of trauma of any sort, including birth trauma, and no clinical signs are present at any stage. This is another example, common in forensic medicine; showing, *'if you don't look, you do not see'*.

The diarrhea needs to be considered together with the article by Farhadi et al – already quoted at length.

The first indication that all was not well is recorded in the notes.

Baby has sniffle, running nose…

This might appear to be a trivial issue, but it is certainly not so. I spent many years studying reasons why infants developed running noses.

The extreme is to have a filthy, fly-infested running nose - Aboriginal style. This often persists to the age of eight or ten. Accompanying this long term persistent purulent nose, is an almost continuous bout of otitis media. The frequency of this is enormous. Even in the white community the incidence of otitis media is high - and has grown dramatically since I was born in 1927, for reasons that are only partially understood. Certainly, immune responses are of major importance. As children grow older, noses stop running and bouts of otitis media become less frequent as immune responses become normal.

That many infants have running noses, and do not suffer from serious disorders does not alter the fundamental truth.

There are reasons, therefore, to at least consider the relationship between the running nose that B had, with what was to happen later.

On Wednesday May 18: *"constantly running stool and lots of stool ('yellow in colour with white bits'). Changed formula from S26 to KARICARE."*

It is recognized that exclusive breast-feeding is ideal, although this cannot always be done. Failure to do this increases the risk of gastrointestinal disturbances in the form of infections and food intolerances.

The UNICEF UK Baby Friendly Initiative, Health benefits of breastfeeding, updated 3 March 2004, states: Artificially fed-babies are at greater risk of:

Gastrointestinal infection
Respiratory infections
Necrotising enterocolitis
Urinary tract infections
Ear infections

Allergic disease
Insulin dependent diabetes

This means that immune disturbances are more likely to develop in infants that are not breastfed. In many cases it can make the difference between good health and bad health, particularly in infancy. It is an *'insult'* that, from a health point of view, can be like the straw that breaks the camel's back.

The diarrhoea noted means that the gastrointestinal mucous membrane linings were disturbed. However, since (apparently) no cultures were done in attempts to identify particular viruses or bacteria, the pathogen responsible for the disruption will never be known.

In any event, it is safe to recognize that there was a gut disturbance. This involves a breakdown, to a degree, in the gut barrier and the absorption of endotoxin.

I have described in the earlier part of this report how endotoxemia can result in coagulation / bleeding disorders that *'can target the brain',* and this includes the dura and the retina (mechanisms previously detailed).

If thorough testing had been carried out, these issues may have been clarified. However, the presence of significant diarrhoea cannot be denied. This part of the case history has not been given suitable attention.

On June 15, 2005 the D-Dimer level was raised (0.4-0.8) normal is 0.9-1.2). This is a fibrin degredation product, indicating that a bleeding/coagulation disorder existed.

NOTE: *After admission to a teaching hospital stool cultures were performed and reported as:*

tridium difficile not Clos detected
C. difficile Toxin detected.

Clostridium difficile is a spore-forming bacteria that can be a part of the normal intestinal flora in as many as 50% of children under the age of two. It is the major cause of pseudomembranous colitis and antibiotic associated diarrhoea. It occurs when the normal intestinal flora is altered and produces a toxin that causes watery diarrhoea. An abnormal heart rhythm may occur. A positive culture alone is not sufficient to confirm a diagnosis. The presence of the toxin is necessary.

The following article provides more information [54].
Inhibition of p38 MAP kinase prevents toxin A-induced enteritis in mouse ileum. The p38 inhibitor SB203580 or SB202474, a control compound inactive on p38 kinase activity (100 µg/loop), was injected into the lumen of an ileal loop as described in Methods. After 30 minutes, toxin A (10 µg) was administered, and animals were sacrificed 4 hours later. Loops were cut out and fluid secretion was assessed by measuring the weight/length ratio (mg/cm). Enteritis severity was measured by histology, using scores to quantify neutrophil infiltration, congestion, and villus destruction. (a, b) SB203580 inhibited toxin A-induced fluid secretion

[54] Warny, M. et al. 2000. "p38 MAP kinase activation by Clostridium difficile toxin A mediates monocyte necrosis, IL-8 production, and enteritis." *J Clin Invest*. Apr;105(8)1147-56. PMID 10772660.

by 74% (a) (P < 0.001) and reduced enteritis severity by 78% (P = 0.005) (b), whereas the inactive analog SB202474 had no significant effect (means and SE are shown; 9-10 loops per group). (c-f) Histological features of toxin A-induced enteritis and their inhibition by SB203580. (c) Control ileum. (d) Toxin A alone causing destruction of villous architecture, neutrophil infiltration, edema, and ulceration. (e) SB203580 pretreatment preserved villous integrity, prevented neutrophil infiltration and ulceration, and partially inhibited edema. (f) SB202474 pretreatment was not protective.

There is another article[55] that describes some effects of toxins;

Experiments in intact animals exposed to enterotoxins demonstrate that neurons and immune cells of the lamina propria regulate toxin-induced diarrhoea and tissue damage. Clostridium difficile toxins cause profound diarrhea and acute inflammation by activating a complex cascade initiated by toxin binding to enterocyte receptors.

At this stage a full review of the case history should have been initiated. The importance of this is extreme. It is apparent that something serious was wrong with baby B before the final collapse. His parents were, quite rightly, concerned, and attempted to have the matter examined and explained. This is not the typical history of an intentionally shaken baby.

If the doctors interpreted the end symptoms as intentional shaking given the history, they were disobeying the first and most basic principle in the practice of medicine - to take a case history and consider its relevance. As a team, they had somehow convinced themselves that shaking was the cause of the problem - and that was that! Baby B had been through a series of potentially fatal illnesses that could explain what led to the final collapse, if properly considered as shown in earlier parts of this book. Had the doctors known the science I know, those pathologies, hemorrhages and fractures could have been scientifically explained with a completely different diagnosis from "inflicted trauma".

A summary of the case history:
Thursday May 19
Circumcision - severe bleeding

Friday May 20
Diarrhoea

Saturday May 21
Infected circumcision. Antibiotics

Monday May 23
Unsettled. Lots of small running stools (diarrhoea)

Saturday May 28
B 'very pale'.

Saturday June 4 to June 10
Still has loose stools

[55] Pothoulakis C., et al, 1998. ***"Nerves and Intestinal Mast Cells Modulate Responses to Enterotoxins."*** News Physiol Sci. Apr;13:58-63. PMID: 11390763.

Friday June 10
Vomited

Saturday June 11
High-pitched cry in morning
4.30pm very, very pale
Back arched
Taken to Hospital
Chest X-ray - normal
Allowed home

Sunday June 12
High-pitched cry

Monday June 13
Cried, unsettled

Tuesday June 14
Phoned doctor for appointment. Made for Friday afternoon. Later father said, 'I am going to take B to the doctor and I will sit and wait'. Apparently, he did not do this.

Wednesday June 15
3.00 am; twitching left arm
3.30 am; more twitching
Mother said 'something is not right'.
9.30 am; father phoned the hospital
Took B to hospital.
Arms legs and body shaking for 4 minutes
CT scan performed
Parents informed that there was a subdural hemorrhage

Conclusion.

This history is not compatible intentionally shaking a baby. All the symptoms can be explained by considering the references that I have detailed in this report. An alternative explanation, based on Munchausen syndrome, or Munchausen's by proxy, as proposed by Sir Roy Meadow, is no longer acceptable in such cases (New Scientist, 30 July, 2005).

The failure of the doctors to intensely investigate during the various problems faced by B is a serious issue. It is apparent to me that, when B collapsed, a diagnosis of 'shaking' was made and it was not considered necessary to investigate thoroughly. In this way, evidence that should have been available, was not obtained.

Postscript:

After a series of meetings/hearings during which an authority persisted in claiming that the retinal hemorrhages were diagnostic of shaking, the mother and father were handed the baby back. He is now well and responding like a normal infant. No charges were laid. The financial costs had to be borne by the parents. This was, indeed, huge. And Australia is

supposed to be a democratic nation!

Misleading Use of Complex Technical Jargon

A few years ago I was asked, by a law firm, to report on a particular case. It involved the death of an infant, who I will call 'Peter'. The consultant case management meeting includes the following statement:

'… the reported bone scan changes represent stress remodelling reactions of the posterior right 8th rib and right distal tibia, these changes do not occur spontaneously and represent a bowing effect from stress applied to the affected bones, that is, these changes are acquired. *The fact that repeat X-rays did not demonstrate any callus to suggest a healing fracture at these sites supports the finding that they are microtrabecular and are not frank fractures as such'.*

This explanation does not make sense. I cannot understand how microtubules could be specifically targeted by inflicted trauma without damage to surrounding tissues. Obviously, there had to be an alternative explanation for the pathologies. The medical literature was packed with information; much of which I had been studying for years, and I had accumulated a mass of clinical observations. This would need to be sorted out and presented as clearly as possible – not a simple task!

First: what are microtrabecular fractures?

The word *'trabeculae'* covers more than one tissue. In bone it refers to *'one of the various shaped spicules of bone in cancellous bone, which is a form of bone in which the matrix is arranged in a network of fine rods, plates, or tubes'.*

Details from the case history:

During labour the membranes were ruptured by the doctor.

Delivery, on 26.7.05, was performed with the aid of forceps. This was not simple. Two doctors pushed on the stomach to assist the forceps extraction. It is known that this form of delivery can result in intracranial haemorrhages. It is also known that the existence of these haemorrhages may not be clinically apparent – even when examinations are carried out by specialist paediatric neurologists. And routine Apgar scores (a system used to quickly evaluate a newborn's physical condition after delivery) can be absolutely normal.
Vitamin K and Hep B vaccine were administered after birth. Vitamin K helps to prevent one form of bleeding in new-born and young babies.
It is known that Hep B vaccine can 'cause' central retinal vein thrombosis. This is a coagulation/bleeding disturbance.
On 27.9,05 , DPT vaccine and Hep B were administered by injection, and HIB (Ped Vax) with Polio (Sabin) and Phenmecc (Prevenor), given orally.
On 27.10.05 Peter vomited.
On 28.10.05 Peter vomited and was 'a little lethargic'.
On 29.10.05 at 5.45 am Peter vomited.
9.45 am, was unsettled, given panadol. Temperature taken - normal
1.50 pm, while in the care of mother Peter started gagging. Vomited again.

30.10.05, 6.30 am, twitching left arm and left leg for about 10 seconds.
7.30 am, would not take water or other fluids. Slight twitching again.
9.30 am, mother rang Tresilian. Advised to contact her doctor, but could not contact him. Peter vomited a little. Mother rang hospital and began to take Peter there in the car. Peter began to twitch again, in the car and while waiting to be seen in the hospital. Mother was asked if there were any bruises or rashes. No CT scan was performed. Given various medications. Transferred by road to city hospital More seizures.
31-10.05, More seizures. Phenytoin given
1.11.05, Full body X-ray. Eye examination. . MRI/MRA under anaesthetic. Haemorrhages reported in both eyes, and subdural haemorrhage
2.11.05, Seizure. EEG. Report to DOCS.
9.11.05. Peter to go into care until age 18 years.

Some Pathology Investigations

A report from The Children's Court states:

'Full blood count (FBC) initially demonstrated the same increase in platelets, mild anaemia and lymphocytosis (increased number of lymphocytes suggestive of viral infection).

This detail is highly significant because a viral infection, including one that is apparently mild, can precipitate problems involving endotoxin, and what is reported as *'Liver function tests demonstrated marginally elevated alanine transaminase and gamma-glutamamyl, thought to be of no clinical signifance'*, could signify entotoxin-induced liver disturbances.

This matter could have been clarified, but only if tests for endotoxin were carried out early. Furthermore, the possible presence of *'toxic strains'* of gastrointestinal E.coli organisms should have been checked.

Heightened sensitivity to endotoxin needs to be remembered. Doughty[56] et al, state;

'Underlying viral infections can heighten sensitivity and worsen cytokine-mediated disease following secondary inflammatory challenges. Mechanisms for this are poorly understood…These data demonstrate that early viral infection can enhance sensitivity to bacterial products, and that this sensitisation can occur in part as a result of IFN- .'

More to consider [57]

'Viral infections in humans or mice can result in increased sensitivity to challenges with bacteria, bacterial products, [Author's addition: endotoxin is one] *or cytokine administration…Taken together, the data show that during viral infections, the normally protective immune responses can profoundly modify reactions to secondary heterologous challenges, to result in dysregulated cytokine expression.*

[56] Doughty, L. et al. 2001. "A Role for IFN-alpha beta in Virus Infection-Induced Sensitization to Endotoxin." *J Immunol.* Feb 15;166(4):2658-64. PMID: 11160329.
[57] Nguyen, K.B. et al., 1999. "Synergism for cytokine-mediated disease during concurrent endotoxin and viral challenges: roles for NK and T cell IFN-gamma production." *J Immunol.* May 1;162(9):5238-46. PMID: 10227998.

Going back to the case of Peter, it is necessary to revise the paper written by Emery[58] and noted fully in early parts of this book. It explains how some of the features noted in shaken baby cases can develop without the need for diagnosing inflicted trauma.

The costochondral junction (where the ribs articulate with the sternum) *normally appears* (under the microscope) *as a series of columns of cartilage cells between strands of cartilaginous matrix and these strands continue into the bony trabeculae. This has a rather rigid and static appearance. The costochondral junction, however, is an extremely active structure. A fully distended cartilage cell is about 14 . Thick. When the size of the cartilage cells is taken into consideration together with the increasing length of bone (0.43 mm or 430 a day), we find that at least the length of a column of the ballooned cartilage cells must be replaced every day. If we were able to look at the living costochondral junction, the actual blowing-up of the small cartilage cells into the large ballooned cells is so rapid that it could almost be seen occurring. The costochondral junction is thus not a static structure at all, but much more like a series of small rockets, or a sort of slow-firing multi-barrelled jet; the cartilage cells distend and burst into the cartilage cavity so that the cartilage receeds from the shaft, leaving a slip-stream of matrix behind.*

In the fixed section of the normal costochondral junction, the marrow ends of these rockets (columns of cartilage cells) are open. There is a progressive increase in size of the cells as the marrow cavity is reached and each column of cells leaves behind at its side, a thin film of matrix.

The amount of energy required to feed this powerhouse is huge, and it must be immediately available – just as the heart must always be supplied. This is achieve through a huge blood supply, which utilizes vitamin C and glucose transporters. If anything interferes with these mechanisms, biochemical disarray can quickly develop. Endotoxin is one substance that often initiates pathologies. There are others -such as chemotherapeutic agents. Endotoxin, in particular, has the power to act with remarkable rapidity. Scurvy, of course, is the classical cause of bone disturbances, often involving subperiosteal hemorrhages that quickly ossify. Different bones can become involved at different times, giving rise to the impression of multiple acts of inflicted trauma at different times. It is necessary to re-stress that *'classical'* signs of scurvy do not need to exist in every case of scurvy.

The name of scurvy is unfortunately not ideal. Often, by the time the symptoms manifest, many other factors have hitched a free ride, and the resultant vitamin C problems can be masked by all sorts of seemingly unrelated pathologies. Endotoxin, in particular, not only *'causes'* scurvy by eating up vitamin C, it also produces pathologies in its own right – mostly by using mediators.

A book by Henrik Friis et al [59] contains some relevant information:

Vitamin C (ascorbic acid) deficiency causes scurvy. Scorbutic guinea pigs may show decreased T-cell percentages in blood, delayed dermal hypersensitivity responses to injected antigens, and humans that a lack of vitamin C has major effects on the immune system components of NAIDS. There are no reports of lymphoid tissue atrophy in scorbutic guinea

[58] Emery, J.L.1967. "Evidence from bone growth that most of the infants dying in the neonatal period had been ill before birth." *Acta Paediatr Scand.* Suppl 172:55-9. PMID: 4961921.

[59] Friis, H. 2001. *Micronutrients and HIV Infection*. Published by CRC, 272 pages (September 14) ISBN-10:0849300851.

pigs or humans. Scorbutic guinea pigs respond to vaccines as effectively as their controls. One the other hand the major effects of vitamin C deficiency in humans are on the non-specific host defences, particularly those involving phagocytic cells. Scurvy is accompanied by markedly impaired functions of phagocytes in blood and tissues, and by greatly reduced generalized host –defensive mechanisms that protect against infectious diseases. The random mobility of neutrophils and monocytes is depressed, their phagocytic capability is reduced, and their chemotactic ability to migrate into areas of inflammation becomes problematic. Reductions in chemotaxis may be due to an abnormality in contractile element functions, possibly involving abnormal assembly of microtubules within these phagocytic cells. It must also be noticed that that infectious diseases reduce the content of vitamin C in phagocytic cells. A depressed content of vitamin C in polymorphonuclear cells is also a common finding in leukemias, other hematologic diseases, diabetes, scurvy, pregnancy, and in aged individuals.

Under these circumstances, isolated pathologies are not the norm, because disturbances in one tissue/organ affect many other tissues/organs.

One study by Lukic examines the limits of mechanical stress in microtubules:[60]

Three types of protein polymers, thin and weak acting filaments, thick and stiff microtubules and intermediate filaments, build a cytoskeleton - a meshwork of proteins present in every eucariotic cell. Very complex mechanical behavior of the cell is the result of interplay between these polymers of very different mechanical properties, which are further influenced by other proteins or drugs. Several important processes depend on them, like mitosis, transport of organelles, organisation of contents in the cell, and cell movements.

However, knowledge of their mechanical behaviour is still incomplete. Only recently it has been shown that cylindrical microtubules are not isotropic polymers, structurally, energetically or mechanically. The principal aim in this thesis was to see what kind of behaviour microtubules show under large stresses and strains. Such answers could provide a clue to some processes in the cell. For example, microtubules are usually connected to organelle centrosome, but in cells like neurons, many are free and are accumulated in the axon. Do they break away from the centrosome mechanically and what kind of forces would be needed for it?

Atomic force microscopy (AFM) was used in this thesis due to its ability to measure forces at the nanoscale. Microtubules (25 nm in diameter) are first deposited on a porous surface, and they occasionally lie over holes that are around 200 nm in diameter. AFM tip is then brought into contact and microtubules are pressed in the middle. By measuring both applied force and vertical deflection of the tube, one can estimate bending modulus. Experiment is done in real time, with AFM tip connected to a special interface - nanomanipulator. This haptic device, conceptually similar to a computer joystick, allows real-time positioning of the AFM tip over the sample while letting the user feel the force exerted on the AFM tip. Scaling of forces and movements is in the order of 10^{6}-10^{7}. The whole experiment is similar to a macroscopic case when a bar is supported on two ends and pressed in the middle.

[60] Lukic, B. *Determination of the limits of mechanical stress in microtubules.* Awarded the Annual Prize for Best Diploma Thesis in 2003, by the Croatian Medical and Biological Engineering Society. http://www.crombes.hr/ifmbe-news/ifmbe-news.iee.org/ifmbe-news/jan2004/lukic.html

All in all, five microtubules were deformed, some of them several times. Fracture was not observed up to forces of 0.6 nN, and they seem to be linearly elastic material up to stresses of 13 MPa. Linearity was checked by comparison of values of elastic modulus with those at smaller deformations, and elasticity by deflection of microtubules before and after deformation. These values are similar to those obtained for actin filaments, and still well below theoretical limit. But very high deformations (in one case, 66 nm in vertical deflection for a microtubule with suspended length of 125 nm) are quite surprising, given that no visible effect on the microtubule, no change in linearity and no fracture of the structure were observed. This could maybe point to an unknown biological function.

One could argue that stresses in the form of blows might produce fractures. In the case of Peter (now being examined) no bruises or hemorrhages were noted in any of the areas adjoining the fractures. This makes a diagnosis of inflicted trauma, without other signs, very doubtful.

On the other hand, all the necessary features for hemorrhages caused by factors discussed in early parts of this book are present. Thus, a proper examination of the case history was not carried out.

Osteogenesis imperfecta can enter into the differential diagnosis of SBS. [61] However, it needs to be considered not just because of the fact that it causes bones to become brittle, but why they become brittle, and which parts become brittle. Osteogenesis imperfecta is connected with abnormalities in collagen formation.

Neri et al [62] describes a case *of reflex sympathetic dystrophy syndrome in a patient with osteogenesis imperfecta who had microtrabecular fractures.*

Paterson [63] notes that *several bone disorders may also cause fractures to occur, apparently spontaneously or with normal handling, and unexplained fractures of whose presence the parents were unaware may be found on routine radiology. This presentation will outline these disorders and indicate the diagnostic clues that may be helpful. One frequent feature common in all of these disorders is the finding that superficial evidence of trauma is not commensurate with the number or types of fractures found on x-ray.*

The principle disorders known to cause unexplained fractures and difficulty in diagnosis are:

Osteogenesis imperfecta
Temporary brittle bone disease
Bone disease of prematurity
Rickets due to vitamin D deficiency
Scurvy (vitamin C deficiency)
Copper deficiency

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[61] Gonzalez de Dios J. 2006. "Differential diagnosis between osteogenesis imperfecta and child abuse: a dilemma with legal implications in Neuropaediatrics." *Rev Neurol.* Jan 16-31;42(2):122-3. PMID: 16450326.
[62] Neri et al. *Pediatric Rheumatology in Clinical Practice.* Published by Springer London, ISSN 0770-3198 (Print) 1434-9949
[63] Paterson C., 2004. *Bone diseases that lead to false allegations of nonaccidental injury.* June 5, Lecture at the NCHR's symposium, Gothenburg, Sweden.
http://www.nkmr.org/english/bone_diseases_that_lead_to_false_allegations_of_child_abuse.htm

Here I need to deal only with temporary brittle bone disease and scurvy – items that many authorities refuse to accept even when confronted with cast-iron evidence.

The type of temporary brittle bone disease that interests me is a form of scurvy. It is precipitated, as I have already described, by endotoxin. This disturbs vitamin C and glucose transporters. The onset can be dramatic because of the ever present need for vitamin C and glucose in certain rapidly growing tissues, including bone growth plates and the brain. It is known that one of the main features of scurvy is collagen disturbances, so not all tissues are affected at the same time. Otherwise, in scurvy, ***all*** parts of the body would be affected at the same time. This does not happen.

Furthermore, as I have already detailed, spontaneous cures can occur. That is, without the administration of bigger doses of vitamin C, orally or by injection. That can be when the trigger for scurvy in such cases is an infection. If the body can muster its immune functions, and enough vitamin C is provided, infections can vanish and the scurvy disappears. Permanent scars, known as *Harris Lines,* may be left in the epiphyseal areas affected.

But when there is a problem due to endotoxin/vitamin C utilization, there is a rapid onset of collagen disturbances in the epiphyseal areas involved. This is a form of acute temporary brittle bone disease in the areas involved. .

The existence of temporary brittle bone disease was not accepted as an entity for many years. This was most likely due to a failure to note that it was not a generalized form of brittle bone. Microtrabecular fractures can accompanying temporary brittle bone disease, which opens a new aspect of so-called SBS.

It is not surprising to find pathologies similar to scurvy in pediatric oncology patients. Roebuck[64] documents *growth plate injury*, and *the radiographic findings are similar to those in scurvy: osteopenia…pathologic fractures…The same syndrome has been described in children with brain tumors…treated with methotrexate.*

Antonacci et al [65] provide more facts;

Microtrabecular fractures and endplate fractures were commonly seen in osteoporotic vertebral bodies, often in vertebrae that appeared to be uninvolved on specimen radiographs.

Gilsanz [66] details:
Ascorbic acid (vitamin C) and ascorbic acid oxidase, a copper dependent enzyme, are needed for the synthesis of normal collagen, and their deficiency manifests with similar radiographic and clinical features. Scurvy, which , as a consequence of improved nutrition, is now extremely rare, occurs in children 6 months of age and is depicted radiographically by severe osteoporosis. Characteristically' there is atrophy of trabeculae just beneath a well-preserved zone of provisional calcification, leading to a lucid band, the 'scurvy line'.

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[64] Roebuck, D.J. 1999. "Skeletal Complications in Pediatric Oncology Patients" *Radiographics.* Jul-Aug;19(4):873-85. PMID: 10464796.

[65] Antonacci, M.D. et al. 2002. "A histologic study of fractured human vertebral bodies." *J Spinal Disord Tech.* Apr;15(2):118-26. PMID: 11927820.

[66] Favus, M. J. (Ed) 2006. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* American Society of Bone and Mineral Research' 6th Edition, ISBN-10 0977888207. Quoting Gilsanz (initials please) page ???

At this stage it is important to note (as I have documented earlier) that the presentation of scurvy varies enormously, from mild, to moderate to severely life-threatening.

Bone growth is very easily disturbed by infections, as the following article by MacRae et al[67] shows:

Childhood chronic inflammatory disease can be associated with transient and permanent growth retardation. This study examined the potential for spontaneous growth recovery following pro-inflammatory cytokine exposure. Murine ATDC5 chondrogenic cells and postnatal metatarsals were exposed to interleukin (IL)-1ß, IL-6 and tumour necrosis factor-α (TNFα), and their growth and proliferative capacity were determined following recovery. TNFα and IL-1ß reduced chondrocyte proliferation and aggrecan and collagen types II and X expression at minimum concentrations of 10 ng/ml and 0.1 ng/ml respectively. TNFα but not IL-1ß exposure led to increased caspase-3 activity and altered cellular morphology, consistent with reduced viability. Cytokine exposure particularly inhibited proteoglycan synthesis. This effect was dose and duration dependent. Compared with the control, IL-1ß and TNFα led to a 71% and 45% reduction in metatarsal growth after 8 days of exposure respectively (P < 0.05). An additive effect of IL-1ß combined with TNFα was observed (110% decrease; P < 0.05). Metatarsals exposed to IL-1ß or TNFα individually for a 2-day period, and allowed to recover spontaneously in the absence of cytokines for a further 6 days, showed normal growth trajectories. In combination, growth was 59% lower (P < 0.01) compared with control metatarsals at the end of the recovery period. Exposure to the combination for 4 days followed by a 4-day recovery period resulted in 87% decrement compared with controls (P < 0.05). IL-6 did not alter any parameter studied. IL-1ß and TNFα exert diverse inhibitory effects on ATDC5 chondrocyte dynamics and metatarsal growth. The extent of recovery following cytokine exposure depends on the duration of exposure, and may be incomplete following longer periods of exposure. … TNFα but not IL-1ß exposure led to increased caspase-3 activity and altered cellular morphology, consistent with reduced viability. Cytokine exposure particularly inhibited proteoglycan synthesis. This effect was dose and duration dependent. Compared with the control, IL-1ß and TNFα led to a 71% and 45% reduction in metatarsal growth after 8 days of exposure respectively (P < 0.05). An additive effect of IL-1ß combined with TNFα was observed (110% decrease; P < 0.05). Metatarsals exposed to IL-1ß or TNFα individually for a 2-day period, and allowed to recover spontaneously in the absence of cytokines for a further Childhood chronic inflammatory disease can be associated with transient and permanent growth retardation. This study examined the potential for spontaneous growth recovery following pro-inflammatory cytokine exposure. Murine ATDC5 chondrogenic cells and postnatal metatarsals were exposed to interleukin (IL)-1ß, IL-6 and tumour necrosis factor-α (TNFα), and their growth and proliferative capacity were determined following recovery. TN and IL-1ß reduced chondrocyte proliferation and aggrecan and collagen types II and X expression at minimum 6 days, showed normal growth trajectories. In combination, growth was 59% lower (P < 0.01) compared with control metatarsals at the end of the recovery period. Exposure to the combination for 4 days followed by a 4-day recovery period resulted in 87% decrement compared with controls (P < 0.05). IL-6 did not alter any parameter studied. IL-1ß and TNF exert diverse inhibitory effects on ATDC5 chondrocyte dynamics and metatarsal growth. The

[67] MacRae, V. E. et al. 2006. "The restricted potential for recovery of growth plate chondrogenesis and longitudinal bone growth following exposure to pro-inflammatory cytokines." *J Endocrinol*. May;189(2):319-28. PMID: 16648299. http://joe.endocrinology-journals.org/cgi/reprint/189/2/319

extent of recovery following cytokine exposure depends on the duration of exposure, and may be incomplete following longer periods of exposure.

Bone growth disturbances can also follow infections due to meningococcal meningitis. This is to be expected because meningococcal meningitis involves endotoxin in a big way – as demonstrated in an article[68] by Belthur et al;

Between 1990 and 2001, 24 children aged between 15 months and 11 years presented with late orthopaedic sequelae after meningococcal septicaemia. The median time to presentation was 32 months (12 to 119) after the acute phase of the disease. The reasons for referral included angular deformity, limb-length discrepancy, joint contracture and problems with prosthetic fitting. Angular deformity with or without limb-length discrepancy was the most common presentation. Partial growth arrest was the cause of the angular deformity. Multiple growth-plate involvement occurred in 14 children. The lower limbs were affected much more often than the upper. Twenty-three children underwent operations for realignment of the mechanical axis and limb-length equalisation. In 15 patients with angular deformity around the knee the deformity recurred. As a result we recommend performing a realignment procedure with epiphysiodesis of the remaining growth plate when correcting angular deformities.

To understand how growth plate disturbances occur, it is necessary to consider some mechanisms involving microtubules. This enters into the world of electron microscopes, as the particles involved are too small to be seen under light microscopes. However, it is not wise to concentrate only what is observed with the aid of electron microscopes because each structure depends on many other structures.

Baas et al [69] details some fascinating information.

Microtubules cut and run.

There is broad agreement that cells reconfigure their microtubules through rapid bouts of assembly and disassembly, as described by the mechanism known as dynamic instability. However, many cell types have complex patterns of microtubule organization that are not entirely explicable by dynamic instability. There is growing evidence that microtubules can be moved into new patterns of organization by forces generated by molecular motor proteins. Studies on several cell types support a model called 'cut and run' in which long microtubules are stationary, but relatively short microtubules are mobile. In this model, cells mobilize their microtubules by severing them into short pieces, using enzymes such as katanin and spastin that break the lattice of the microtubule polymer. After being reorganized, the short microtubules can once again elongate and lose their mobility. Microtubule severing is also crucial for a variation of 'cut and run' in which the severed microtubules are reorganized by means of treadmilling.

Microtubules are prominent cytoskeletal elements that undergo dramatic alterations in organization and distribution during important cellular events such as mitosis, migration and the outgrowth of processes. *Dynamic instability is a potent mechanism whereby cells can try*

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[68] Belthur, M.V. et al. 2005. "Late orthopaedic sequelae following meningococcal septicaemia. A multicentre study." *J Bone Joint Surg Br.* Feb;87(2):236-40. PMID: 15736750.

[69] Baas, P.W. et al. 2005. "Microtubules cut and run." *Trends Cell Biol.* Oct;15(10):518-24. PMID: 16126385.

out various configurations of microtubules through rapid microtubule assembly and disassembly before selectively stabilizing the most suitable option [1,2]. However, this mechanism is not sufficient to explain the entirety of microtubule behaviors observed in cell as the reconfiguration of microtubules that have already been stabilized by factors that bind to the surface or the ends of the microtubules. Recent studies on a variety of cell types some of which have highly specialized microtubule arrays, provide evidence for another pathway by which microtubules change their configuration during morphogenesis. This pathway, which can be explained by a model we call 'cut and run,' involves the breakage of microtubules into short pieces that are highly susceptible to movement. The crux of this model is that long microtubules are relatively immobile, whereas short microtubules are quite mobile. Thus, in order for a cell to transform its microtubule array from one type of organization to another, the long immobile microtubules are severed into short pieces that rapidly move into a new configuration, after which the short pieces once again elongate and lose their mobility.'Cut and run' involves the breakage of microtubules into short pieces that are highly susceptible to movement. Terminal differentiation of growth-plate chondrocytes is accompanied by the acquisition of a spherical morphology and a large increase in cell volume. These changes are likely to be associated with rearrangement of the cytoskeleton, but little information on this aspect of chondrocyte hypertrophy is available. We report a role for microtubules in the control of chondrocyte maturation and hypertrophy hypertrophy was observed, although collagen type X immunoreactivity was noted within the interstitial matrix.

Some vital issues[70] about scurvy have been raised by Rajakumar;

Bone involvement is typical for infantile scurvy…The bone changes occur at the junctions between the ends of the diaphysis and the growth cartilage. Osteoblasts fail to form osteoid (bone matrix), resulting in cessation of endochondral bone formation. Calcification of the growth cartilage at the end of long bones continues, leading to the thickening of the growth plate…Pereexisting bone becomes brittle and undergoes resorption at a normal rate, resulting in microscopic fractures…

These are microtrabecular fractures - claimed by the expert witness in the Peter case to *'not occur spontaneously'*. Obviously, he had not read the literature in a proper way. Witnesses in the case would have been very impressed by his statement – and ignored what I had to say.

Hess describes these pathologies involving osseous trabeculae in his book on scurvy, page 129;

The bone trabeculae on which they abut are not well formed or of equal length, and do not present an even transverse plane, but are misshapen, small, so that the line of junction with the cartilage is zigzag. In cases of marked scurvy the junction may be entirely disorganized and deformed, showing fractures of the rarefied bone and hemorrhages in the neighborhood.

On page 128 Hess states;

These changes (in the trabeculae) *are not found in every specimen, so that in order to be able to exclude scurvy definitely, it is necessary to examine a considerable number of ribs; several may be normal, only one or two showing the characteristic microscope changes.*

[70] Kamaravel Rajakumar. 2006 "Scurvy" E Medicine from WebMD <http://www.emedicine.com/ped/topic2073.htm accessed 11 August 2007.> Assistant Professor Department of Pediatrics, Children's Hospital, of Pittsburgh.

Walter Scott[71] was another early author who documented microtrabecular fractures in scurvy cases;

High power photomicroghraph of the scorbutic lattice, showing the salient pathologicical features of scurvy, - highly calcified bony trabeculae with many fractures, connective-tissue invasion of the marrow spaces, and the absence of normal cellular elements.

One must note that, where endotoxin is a strong factor, some details of the pathologies may differ to a degree, from what is considered to represent *'pure* scurvy', where the onset of pathologies is slower and often more widespread and distinct.

Infections can precipitate scurvy. Hess documents this in page 218 of his book;

A few years ago the author reported an epidemic of scurvy in connection of an outbreak of grippe (influenza) *in an infant asylum…The signs were atypical- an undue degree of hemorrhage occurring at atypical sites.*

This approaches what is found in some SBS cases – where infections/endotoxin play a major role.

Returning to the case of Peter, some interesting details emerged during the hearing. After Peter collapsed a series of errors were generated.

The possibility that injuries were precipitated by the 2-month immunizations was raised by the parents. This involved a vitamin C deficiency due to a vitamin C depletion, and the enhanced effects of a 'minor' infection. This was dismissed by the doctors because vitamin C levels tested *high.* No attention was paid the possibility of problems with vitamin C transporters and glucose transporters, so that even during what appears to be a simple infection, vitamin C transporters and glucose transporters in some tissues may not be functioning correctly. Endotoxin is a prime causal agent of glucose transport derangement, so one should look for factors involving endotoxin. At the same time, what I have documented about endotoxin in earlier parts of this book, should be reconsidered.

On 30/10/05 the hospital notes included the word *'mottled'*. This can be caused by endotoxin , also known as *'sepsis'*. I have already noted that this does not always mean that live bacteria are in the blood stream. Furthermore, endotoxemia may appear to be mild in nature but the introduction of another factor, such as a mild viral infection or a vaccine, can precipitate a more serious clinical state that can be fatal.

Underlying viral infections can heighten sensitivity and worsen cytokine-mediated disease following secondary inflammatory challenges. Mechanisms for this are poorly understood. The impact of the innate response to lymphocytic choriomeningitis virus (LCMV) infection on sensitivity to endotoxin (LPS) was investigated. Compared with uninfected mice, infection with LCMV for 2-days-sensitized mice to LPS by 2-fold for lethality and by 2- to 6-fold for serum TNF levels. Priming for LPS-induced TNFwas also seen with splenic and peritoneal leukocytes isolated from infected mice and challenged with LPS ex vivo. The effect on TNF

[71] Walter Scott, 1941. "Epiphyseal Dislocation in Scurvy." J Bone Joint Surg. 23 (2):314-322. http://www.ejbjs.org/cgi/reprint/23/2/314 Page 314.

production was present in the absence of IFN, its major producers NK and T cells, and the major pathways for its induction through IL-12 and the signal transducer and activator of transcription 4 (STAT4), and therefore was IFN independent. Early LCMV infection induces high concentrations of the type 1 IFNs, IFN. Administration of recombinant IFN alone heightened the TNF- response to LPS. Innate IFN and IFN- responses to LCMV exist in a delicate balance. To reduce priming for LPS-induced TNF during LCMV, deficiencies in both the IFN and IFN receptors or STAT1, a transcription factor downstream to both IFNs, were required. These data demonstrate that early viral infection can enhance sensitivity to bacterial products, and that this sensitization can occur in part as a result of endogenously expressed IFN. This work also raises issues about potential complications associated with IFN- therapies [72]

Induction of the antiviral cytokine interferon [alpha]/[beta] (IFN-[alpha]/[beta]) is common in many viral infections. The impact of ongoing antiviral responses on subsequent bacterial infection is not well understood. In human disease, bacterial superinfection complicating a viral infection can result in significant morbidity and mortality. We injected mice with polyinosinic-polycytidylic (PIC) acid, a TLR3 ligand and known IFN-[alpha]/[beta] inducer as well as nuclear factor [kappa]B (NF-[kappa]B) activator to simulate very early antiviral pathways. We then challenged mice with an in vivo septic shock model characterized by slowly evolving bacterial infection to simulate bacterial superinfection early during a viral infection. Our data demonstrated robust induction of IFN-[alpha] in serum within 24 h of PIC injection with IFN-[alpha]/[beta]-dependent major histocompatibility antigen class II up-regulation on peritoneal macrophages. PIC pretreatment before septic shock resulted in augmented tumor necrosis factor alpha and interleukins 6 and 10 and heightened lethality compared with septic shock alone. Intact IFN-[alpha]/[beta] signaling was necessary for augmentation of the inflammatory response to in vivo septic shock and to both TLR2 and TLR4 agonists in vitro. To assess the NF-[kappa]B contribution to PIC-modulated inflammatory responses to septic shock, we treated with parthenolide, an NF-[kappa]B inhibitor before PIC and septic shock. Parthenolide did not inhibit IFN-[alpha] induction by PIC. Inhibition of NF-[kappa]B by parthenolide did reduce IFN-[alpha]-mediated potentiation of the cytokine response and lethality from septic shock. Our data demonstrate that pathways activated early during many viral infections can have a detrimental impact on the outcome of subsequent bacterial infection. These pathways may be critical to understanding the heightened morbidity and mortality from bacterial superinfection after viral infection in human disease. [73]

To vaccinate an infant who is suffering from an infection (even a mild one) is highly risky. I first observed this in the 1960's, and efforts to point this out to colleagues were unsuccessful. The result was not pleasant to watch.

When pathologies are initiated, various pathways may be followed. Often, the immune system functions properly and spontaneous cures result. Unfortunately, sometimes this does not happen. Endotoxin can take over in one or more ways. Hemorrhages of various sorts can occur, including subdural and retinal hemorrhages. Vitamin C transporters can be affected, so fractures and/or other scurvy-like disorders can appear with considerable rapidity. Epiphyseal

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[72] Doughty, L.A. et al. 2001 "A role for IFN-alpha beta in virus infection-induced sensitization to endotoxin." *J Immunol.* Feb 15;166(4):2658-64. PMID: 11160329.

[73] Doughty, L.A. 2006. et al. "Activation of common antiviral pathways can potentiate inflammatory responses to septic shock." *Shock.* Aug;26(2):187-94. PMID: 16878028.

bone growth, in one or more places, may be affected, with cessation of proper collagen formation and osteoporosis in affected areas.

That is how I believe Peter developed microtrabecular fractures. He will carry scars in his bones resulting from this for the remainder of his life. His parents will carry mental scars. The baby they loved and cherished will not be allowed to be alone with them until he has grown almost fully.

Worse still (if that is possible) are the parents who unjustly sit in jails, waiting in death row.

Something terrible has infected my medical colleagues – or a considerable number of them.

The time has come to end this form of abusive diagnosis. The time has come for doctors to look squarely at what is there for all to see in the medical literature, and to consider the unjust errors of gigantic proportions which have been made, and to correct them.