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PHYSIOPATHOLOGY AND BIOMECHANISM OF WOUND HEALING AFFECTING PILONIDAL SINUS TREATMENT, PART ONE – FRISCH GEWAGT IST HALB GEWONNEN (WELL BEGUN IS HALF DONE)

***Om P. Sudrania, MBBS, MS, FRCS, FICS**

Ex Owner/Director Surgeon[1]; Emeritus Professor, Department of Surgery (Gastro) [2]; Senior Faculty Incharge (Retd), Department of Gastroenterology and Minimal Access Surgery[2]; Associate Professor and Unit Head (Retd); Department of Surgery;[2] Visiting Professor[3];
Madan Ganga Nursing Home, Sevoke Road, Siliguri 734001, West Bengal, India[1]
M G M Medical College and LSK Hospital, Kishanganj - 855107, Bihar, India[2]
Grant Medical College, Mumbai Central, Mumbai, India[3]

***Corresponding Author: Om P. Sudrania, MBBS, MS, FRCS, FICS**
Ganga Complex, Hospital Road, Kishanganj, Bihar, India.

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ABSTRACT

Background*:* Study of pathophysiological biomechanisms and biomechanics relating to sacral pilonidal sinus disease (SPSD) to improve its healing. Online search for research papers regarding SPSD, surgical anatomy, etiophysiopathology, wound healing (WH) and articles retrieved from reference lists and studied under these **subheads** – (**a**) Importance of physiopathology of WH mechanism in SPSD therapy. (**b**) Clinical relevance of WH mechanism by scar vis-à-vis regeneration. (**c**) Role of skin microbiota determining WH and infection (**d**) Applied surgical anatomy and layered concept of histopathology of SPSD. Chronic SPSD is two layered structure formed by deeper connective tissue layer paved superficially with endo/epithelial or granulation tissue besides detritus in lumen. Deeper connective tissue forms bedrock of final healing needing preservation. Acute SPSD has detritus with inflamed hyperemic wall of cavity. (**e**) Applied microstructure of fibrous connective tissue and scar. **Discussion and Conclusion:** SPSD is empirically treated variously, yet complications or recurrences are persisting, needing to address WH pathophysiological biomechanisms and biomechanics so that an optimum treatment can be formalised.

KEYWORDS: Sacral pilonidal sinus, wound healing mechanism, pathophysiology, surgical anatomy, histology.

INTRODUCTION

This innovative critique consists of reappraisal of physiopathological biomechanism and biomechanics to redefine and correlate evidence on wound healing (WH) process with layered concept of surgical anatomy of *sacral pilonidal sinus disease* (SPSD) aimed to cure without recurrences and complications. WH physiology restores tissue integrity limiting the process to wound repair.[1-8] Ideal treatment of SPSD should be economic, painless, easily reproducible, least loss of job, ambulatory technique need no hospitalisation; manageable by patient at home; hassle free from postoperative encumbrances, good *psychosomatic and quality of life* (PQOL); postoperative complications and recurrence free besides cosmesis. *Scalpelless Minimal Invasive Technique, 'least is best in All Weathers' for Sacral Pilonidal Sinus*, is dealt in *Part Two* and physiopathology of WH implicating SPSD is elaborated herein. A random online search for relevant research papers published under SPSD, histology, surgical anatomy, etiophysiopathology, WH, articles fetched through colleagues and reference lists. These have been methodically studied: (**A**) Importance of physiopathology of WH mechanism and SPSD therapy. (**B**) Clinical relevance of WH mechanism by scar vis-à-vis regeneration. (**C**) Role of skin microbiota determining WH and infection affecting SPSD (**D**) Applied surgical anatomy and layered concept of histopathology of SPSD. Chronic SPSD (CSPSD) is *two layered structure* of *deeper connective tissue layer* paved *superficially with endo/epithelial or granulation tissue* besides detritus in lumen. Deeper connective tissue forms bedrock of final healing needing conservation. Acute SPSD (ASPSD) has detritus with inflamed hyperemic wall of cavity. (**E**) Applied microstructure of fibrous connective tissue and scar.

(A)IMPORTANCE OF PHYSIOPATHOLOGY OF WOUND HEALING MECHANISM IN SPSD THERAPY -

Surgeons are a faculty who create and deal with wounds, yet mostly nescient, not abhorrent, of WH physiopathological biomechanism observed in attitudes and the way of dealing with skin wounds. Thus WH is stressed as SPSD is a wound and its treatment involves iatrogenic injury that patient expects for healing and succour.[9] In long-term PQOL satisfaction only recurrence-free survival matters.[10] Sentience of WH physiopathology is paramount to attain desired results and ignorance may be sine qua non for despair. Patey[11] in 1970 stated, "...after the plethora of scholarly theses on the origin of pilonidal sinus, to reduce it therapeutically to the level of the humble stitch sinus smacks of lèse-majesté". He[11] maintained, "If simpler forms of treatment are effective, the question arises as to what advantages, if any, the operation of excision and leaving the wound open to granulate has to compensate for its obvious disadvantage of prolonged healing." Patey is often quoted for his jeer: 'Don't take a hammer to swat a fly'.

(B) CLINICAL RELEVANCE OF WOUND HEALING MECHANISM BY SCAR VIS-À-VIS REGENERATION

Skin WH is highly regulated dynamic process beginning instantly after injury and may take years.[12] Skin WH involves molecular and cellular function with mechanical forces acting at wound edge, unique in nature involving interaction of several cells, growth factors and cytokines. It is highly complex process occurs by scarring and fibrosis vis-à-vis regeneration that is lost before third trimester (week 24 of gestation) in humans except epidermal/dermal wounds not involving reticular dermis.[2] Craniofacial and oral wounds heal at an accelerated rate compared to other cutaneous wounds.[6-8] Ireton et al[13] observed, "...healed skin only reached 80% of the tensile strength of unwounded skin"; after full remodelling and maturation of collagen fibres from type III to type I in skin that takes years.[14] *Tensile strength* is indicator of tissue strength and its gain depends on collagen production and organization, which is intimately related to *mechanical stress*. Tensile strength is the breaking strength of a material divided by its cross-sectional area and is therefore most accurate physiologic measure for assessing wound's ability to withstand tension.[13] Collagens are important component in all phases of WH, formed by fibroblast-myofibroblast differentiation; impart integrity and strength to all tissues and play key role, especially in proliferative, remodelling, maturation phases of repair. Collagens form base for intracellular matrix formation in the wound.[5] Neutrophils, macrophages, proliferating fibroblasts-myofibroblasts and vascularized stroma, together with collagen matrix, fibrinogen, fibronectin, hyaluronic acid and cyto-chemokines constitute acute granulation tissue replacing fibrin-based provisional matrix.[15,16, 17,18, 19]

Mercandetti[20] noted that not only do authors vary number of phases, they also denote differences in phase descriptors used. Therefore, certain phases have more than one name, such as remodeling or maturation and proliferation or granulation. As our understanding of WH progresses, further phases and subphases may well be delineated. WH by primary intention is arbitrarily divided in three or four phases.[1, 3-6] First phase viz. bleeding, coagulation-hemostasis, inflammation (early and late phase[5]) starts soon after injury, marked with arrival of neutrophils in 24-48 hours and lasts 4 to 6 days. It is heralded by multiplication of endothelial cells, growth of new blood vessels and duplication of smooth muscle cells. Huang and Ogawa[21] exclaim, "It is likely that this inflammation promotes excessive local angiogenesis, endothelial dysfunction, and vascular hyperpermeability that in turn facilitate the continued influx of inflammatory cells and factors, thereby setting up a vicious cycle of inflammation and abnormal vascular activities". Bigger the wound and injury, austere is inflammatory reaction and bigger is chance of infection and delayed healing-nonhealing. Proliferation/granulation usually lasts 3-24 days occuring in three stages: (1) Filling the wound (2) Contracting wound margin (3) Grows new skin over wound or re-epithelialization. Collagen accumulation diminishes density of blood vessels and granulation tissue matures towards remodelling and scar.[5] Scar tissue forms final seal of healing with epithelialisation by keratinocytes. This decrees us to save existing scar and normal skin tissue in treating SPSD. Prolongation of inflammatory phase is marked by granulations and hampers proliferation phase, thereby entire healing process is arrested.[21] Hypergranulation prevents epithelialisation and arrests further WH.[22] Mechanisms and molecular pathways of WH still need elucidation to achieve complete understanding of remodeling system.[23] *Remodelling* phase starts with deposition of collagens (scar tissue) and *Maturation* increases conversion of type III into type I collagen in skin and lasts from 21 days to 2 years or so. Unwounded dermis contains 80% type I collagen and rest is type III, while wound granulation tissues express 40% type III collagen.[5] Earlier these phases were viewed as distinct steps occurring sequentially; newer insights suggest that healing phases overlap; even occurring simultaneously inside wound.[24,25]

(C) ROLE OF SKIN MICROBIOTA DETERMINING WOUND HEALING AND INFECTION -

SPSD is de novo potentially or frankly infected wound depending on clinical stage, patient status and other factors; locally or systemically and intrinsically or extrinsically. Patey[11] reckoned, "Infection is concomitant feature of the active phase of pilonidal sinus." Skin is exposed to milieu interior and extérieur and harbours many agents on its surface.[26] Grice and Segre[27] explain, "The skin is the human body's largest organ, colonized by vast and diverse milieu of

microorganisms called microbiota, most of which are harmless or commensal to the host. Colonization is driven by the ecology of the skin surface, which is highly variable depending on topographical location, endogenous host factors and exogenous environmental factors. The cutaneous innate and adaptive immune responses can modulate the skin microbiota, but the microbiota also functions in educating the immune system." Chen et al[28] decipher, "...how host–microbe interactions depend heavily on context, including the state of immune activation, host genetic predisposition, barrier status, microbe localization, and microbe–microbe interactions." Skin microbiota play important role in *shaping* postoperative problems irrespective of technique employed in SPSD management.

(D) APPLIED SURGICAL ANATOMY AND LAYERED CONCEPT OF HISTOPATHOLOGY OF SPSD -

Surgical anatomy of CSPSD is two layered format of *deeper connective tissue* paved *superficially with endo/epithelial or granulation tissue layer* facing lumen, containing debris. *Deeper connective tissue* forms *bedrock* of final healing that needs preservation. ASPSD has inflamed hyperemic wall of cavity with debris only. Possibly SPSD originates from so-called pit or external opening of putative acquired SPSD. It is distinct spot in natal cleft varying in size and numbers in different people, e.g. 11 pits in one case of Lord and Millar[29]. Sinuses may vary in number and location depending on time lag (Doll et al[30]), younger age, softer skin texture, host defence, degree and virulence of infective agents and other factors. Disease duration in long-standing symptomatic chronic disease is not correlated with higher number of sinuses nor correlated with higher number of complex fistuli systems.[30] Pits are supposedly keratin plugs by Søndenaa and Pollard[31], hair follicles by Bascom & Bascom[32] or result of hairs by Doll et al[33], Karydakis[34]. Some pits may lead to well defined sinus tracts from epidermis to subcutaneous tissues where it may end in a cavity or blindly with varying degree of inflammation in and around SPSD.[13] Brearley[35] (1955) observed that secondary sinuses when present are lined with granulation tissue. It is regarding wall of primary sinus and relation to it of hairs in the track that accounts vary. Granulation tissue is usual in distal part and squamous epithelium proximally near surface. He[35] also indicated *diverse accounts* by different authors. *Primary sinus/es* develop from *outside-in*, i.e. starting from natal skin and burying *in* becomes partly epithelialized tube near skin surface in variable length and rest by granulation tissue.[11,31,32] *Secondary sinus tracts*[32] usually develop *inside-out*, i.e. starting from deep cavity with pent up products blowing out in areas of least resistance paramedially; ejecting effluents on skin surface by destroying tissues on its way *out* and such tracts are *lined by deeper fibrous and superficial granulation tissue*. Kooistra[36] stated, "As a result of the infection much of the lining epithelium of the cystic part was destroyed, and granulation tissue and scar tissue was seen replacing it." Lord and Millar[29] disputed Kooistra[36] for cavity lined by squamous epithelium with hair follicles and stated, "In the midline and deep to the pits is a cavity lined with granulation tissue." Scar tissue forms deeper layer matured over years of CSPSD must be bien entendu. Søndenaa & Pollard[31] depicted variable pictures of epithelialisation in 77%, granulation tissue in 94%, but *fibrosis* was seen in 100% cases of sinusoidal cavity; their description is equivocal regarding hair follicle origin. Davage[37] (1954), Brearley[35] (1955), Coll[38] (1960), Lord and Millar[29] (1965), found no evidence of epithelium lining the cavity and even primary tract was lined by epithelium in few millimeters near skin surface. Patey[11] reechoed, "Apart from the epithelial pits the sinus is lined throughout by granulation tissue and typically contains hairs." Cavity can be termed pseudocyst often described incorrectly as cyst, pilonidal cavities are not true cysts (Davage[37]) and lack epithelialized lining; however, fibrous tracts of sinus may be epithelialized in variable length (Kooistra[36]) in few millimeters. *Pilonidal sinus disease* is therefore correct term.[39] Brearley[35] stated, "The cysts in question are lined with cuboidal epithelium resembling ependyma and not skin."

Stone[40] (1924) like Kooistra[36] (1942) made divergent observations. Stone's version appear self-contradictory from his observations. He[40] stated, "The inner portion of the wall was of many layers of stratified cuboidal epithelium with-only slight cornification adjacent to the lumen, but with imperfect and rudimentary papillae in certain areas. Hair follicles were seen and also sweat glands. Outside of the epithelial layer was a dense corium-like sheath, and beyond this loose fat and areolar tissue. Some of the sweat glands lie in the fat at quite a distance from the lumen of the sinus. In short the sinus is a slightly modified invagination of true skin. None of its elements were fully developed –even the characteristic hair is thin, fine and scanty in pigment, somewhat like lanugo." He[40] starts the para, "The writer was fortunate enough to discover and remove cleanly, a typical sinus which had never been actively inflamed." This confers that the specimen might be case of congenital sacrococcygeal dimple than a case of SPSD. It should be borne in mind that 1923-4 era was a period when debate between congenital and acquired origin was at peak and knowledge of tissue histology was still in nascent state. No wonder, Kooistra[36] (1942) with vast experience illustrated cavity lined by squamous epithelium with hair follicles.

(E) APPLIED MICROSTRUCTURE OF FIBROUS CONNECTIVE TISSUE OR SCAR -

The term connective tissue (German – Bindegewebe) was introduced in 1830 by Johannes P Müller and is composed of collagen fibers as the tissue it replaces, but fiber arrangement is different. In fibrosis, collagen crosslinks form an alignment in one direction instead of random dense basketweave pattern of collagen fibers in normal tissue. This collagen scar tissue alignment is of

inferior functional quality and strength than normal collagen randomized alignment, e.g. scars in skin are less resistant to stress and ultraviolet rays. Skin adnexae like sweat glands and hair follicles etc do not grow within scar tissue. Scar doesn't have stretch, mobility and range of motion that normal skin does and may limit joint mobility. Collagens serve within body to large extent for maintenance of structural integrity of tissues and organs denoting major unit of interstitial matrix, basement membranes and connective tissues.[35] Chronic inflammation with or without infection ignites formation of scar and its maturation progresses with time; be it physiological or pathological. Thus aim should be to conserve existing tissue; be it scar or skin at any cost and do not destroy them.

DISCUSSION

Lately there are lot of developments in physiopathology of WH and its good understanding shall help surgeons in managing SPSD better. All wounds are not equal as there is wide range of wounds encountered in surgical practice. Coll[38] stated, "Various methods of treatment have been proposed, which is testimony to the fact that no one procedure is outstandingly successful in avoiding morbidity and recurrences." He[38] continued, "It is extraordinary that so simple a lesion should tax the surgeons' ingenuity, but it is *about time to admit* the fact that what it taxes is not the adequacy of the method employed, but how well, how carefully, and how gently the surgeon executes it". Rogers and Hall[41] (1935) alluded, **"**It has been commonly believed that the presence of a recurrent or persistent sinus after excision implies that some of the diseased tissue must have been left behind. This belief has naturally led to increasingly radical excisions in an attempt to remove all the diseased tissue at one operation." Thompson et al[42] (2010) muttered, "Over the past 70 years some surgeons have avoided wide en bloc excision because of the risk of debilitating complications,..." Saikaly and Saad[43] (2020) grumbled, "...treatment should not be disabling more than the disease itself..." Bascom and Bascom[32] (2002) quoting an English surgeon, "There comes a time in the treatment of surgical disease when conventional methods are no longer improving the outlook for the patients and a paradigm shift in our concepts of aetiology and hence surgical treatment is required. The author has given us this opportunity by not only challenging convention but also providing us with a lucid alternative thesis and compelling arguments for changing current surgical practice." Brearley[35] (1955) made two points for effective treatment, "First, the prevention of drilling (?by hairs as etiology); and secondly (more important for treatment), the cure of an established sinus by the methods applicable to sinuses anywhere in the body." Brearley's both points being logical but fail to deliberate on method to deal with 'sinuses anywhere in the body' that may prove paradigm shift. Idiz et al[44] stated, "There are articles in literature, *mainly curettage studies*, advocate that removal of the sinus tract is unnecessary; otherwise, the generally accepted view is to remove all granulation tissue." They[44] made three points – (1) mainly curettage studies (2) removal of sinus tract is unnecessary (3) generally accepted view is to remove all granulation tissue; though their advocacies are highly relevant but ignored. Patey[11] made two points, "...first, that sacrococcygeal pilonidal sinus is pathologically, irrespective of origin, a foreign body granuloma, and that excision is therefore not essential to achieve a cure; secondly, that excision destroys a functional anatomical mechanism important in healing, and that it should therefore only be practised if clear advantage can be demonstrated." While his first point appears laudable but second point of 'functional anatomical mechanism important in healing' is inexplicable. He[11] went on, "I suspect that one factor limiting wider adoption of this simple treatment is a subconscious feeling that, after the plethora of scholarly theses on the origin of pilonidal sinus, to reduce it therapeutically to the level of the humble stitch sinus smacks of lèse-majesté." It shows that prior accounts muddled physiopathological WH biomechanism resulting in unphysiological fecundity. Most such studies fail to deliberate on their reason to initiate particular study, i.e. *why* has it been designed, instead dwell on *what* or *how?*[45,46]

Surgical Site Infection has profound clinical impact on WH but difficult to quantify for its therapeutic relevance. Doll et al[47] concluded in their study, "The suggested positive effects of topical gentamycin application on long term recurrence rate could not be confirmed. Astonishingly though, surgical infection does not seem to alter long term recurrence rate." Brebbia et al[48] also echoed in study of seven patients treated for pilonidal cyst with wound left open, swab specimens were taken because of persisting local pain and host of bacteria were found, yet no antibiotic therapy was given and local wound care led to complete recovery. It imputes better cognition of physiopathological parameters for incriminating indolent wounds for infection and needs redefinition to make it pathognomonic for surgical relevance. Thus mere bacterial counts on culture are irrelevant to overall wound care in inducing such reports without clinical *signs of acute inflammation* when skin is a mine of commensals and pathogens. This Author's case referred in 'Part Two' section of the article, copious wound discharge was sterile, yet WH failed indicating factors other than infection are operative in WH.

Surgeon factor affecting wound healing quality – Coll[38] (1960) indicated earlier on surgeon factor, which is recognised as risk/prognostic factor. Allen- Mersh[49] observed, "Some treatments are operator-dependent and, to achieve the best results, junior surgeons must be correctly trained and supervised." Idiz et al[44] observed, "Inexperienced surgeons may excise only blue areas stained by MB, whereas experienced surgeons may insist on excising inflamed areas macroscopically visible even if such tissue is not stained by MB. Only excising blue-stained areas (particularly in complicated cases) may cause a false sense of confidence even for experienced

surgeons." Thus surgical incompetency will lead to poor surgical technique reflecting finally in poor WH and consequent complications. **Surgical techniques** should be carefully executed, viz. gentle tissue handling; diligent use of electrosurgical units in cutting or coagulation; type of sutures and their application; wound closure in layers or mass stitching; obliteration of dead space in wound; simple or *mattress sutures* with/without *tension stitches* (are unphysiological by biomechanical factors for tissue tension); use of various drains, length of time left in situ, suction or simple drains; antiseptic or aseptic operation theatre technique; forced tissue retraction during surgery, are some issues that influence outcome of surgical procedures.

CONCLUSION: Knowledge of biomechanism, biomechanical processes and physiopathology of WH shall go long way to craft treatment policies that will ultimately give long lasting cure of SPSD which mostly afflicts youth in productive life.

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