

Regeneration of Human Scar Tissue with Topical Iodine: A Preliminary Report—Part 1 (Three Years)

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Abstract. Since Spallanzini first described salamander limb regeneration in 1769, there has been slow progress in understanding this process. Potential treatment benefits from regeneration are worth the effort. A hypothesis that topical iodine would regenerate human scar tissue is tested by applying Lugol's solution to four scars of various sizes, degree of damage, and location for variable lengths of time. Regeneration starts a few days after applying iodine and stops and forms adult scar if applications are discontinued. One face scar has completely regenerated. The wrist scar's terminal stages are being studied. The remaining two scars on the abdomen are behaving as if they are one and could take considerably longer to complete. Waiting for completion delays availability of this information for scientists, physicians, and patients.

For the past three years, Nikon Cool Pix cameras recorded regeneration changes. Regenerate material found under plastic wraps on the scars comes in two forms, snow-like and globular. Their function is unknown. Two black dots both 5 mm apart seen on the wrist and abdominal scar store iodine and appear to coordinate regeneration. Hair is the regeneration workhorse and does an amazing number of things. Amongst the hair activities are free movement to any cell within its range in any direction and self-amputation possibly to strengthen regenerating tissue. Hair delivers regenerate material and may be sending cell signals by touch, regenerate material, and electrical impulses. The hypothesis that topical iodine in the form of Lugol's solution regenerates human scar tissue back to normal is supported by these preliminary findings.

Keywords: Hair • Hair movement • Iodine • Regeneration • Scars • Self-amputation • Skin • Wound healing

Introduction

Regeneration and Wound Healing

Spallanzini in 1769 and Martin 230 years later expressed the same hope that a way is found to regenerate human tissue damage back to normal.^{[1][2]} Unfortunately, we are not yet close to unraveling either regeneration or wound healing. We do not understand regeneration and progress is limited.^[1] Wound healing is also complex.^[15] Cotran says, "The magic behind the seemingly precise orchestration of these events (wound healing) under normal conditions remains beyond our grasp. . . ." ^[3, p.109] On the other hand, Tsoni says, "The field of limb regeneration will prove to be one of the most important in the biomedical field."^[23, p.203]

Iodine

Elemental iodine discovered in 1812 by Courtois has been a universal antiseptic for 150 years,^[4] and its only established human body function is making thyroid hormones in thyroid glands from dietary iodine. Long term iodine intake levels dictate thyroid

gland function and pathology. Iodine is found in every body cell and fluid.^{[5][6][7]} In relation to regeneration, thyroidectomy makes it abnormal and excess thyroid hormone inhibits it.^{[1][8, p.149]}

In 1997 while treating patients with Lugol's iodine for fibrocystic disease,^{[9][10]} out of curiosity, the author applied Lugol's solution to a 50-year-old face scar that resulted from removal of a birth mole. Topical applications for three consecutive days did nothing. On the fourth day, the thin 2 cm white scar became red and hyperemic. Could this be regeneration? A hypothesis was formed: topical iodine in Lugol's form could regenerate human scar tissue back to normal. Eight years later, the author began iodine applications to test this hypothesis.

Materials and Methods

Lugol's Solution

Lugol's solution is made of 5% free iodine and 10% potassium iodide in water. Free iodine (elemental iodine) is only slightly soluble in water, but 200 years ago Henri Lugol, a Paris physician, discovered

that potassium iodide increased free iodine's solubility in water. Three chemical iodine species exist in Lugol's solutions: free elemental iodine, triiodide, and iodide.^{[11][12][13]} Free iodine reacts with water to make Lugol's solution brown, triiodide's weaker yellow color is not visible, and iodide is colorless.^[4]

Four Scars

During the 8 years between Lugol's solution scar applications, the author gained three new scars: two abdominal and one on the left wrist. (Figures 1 and 2.) An 18cm vertical abdominal scar was opened three times and accompanied by a horizontal colostomy scar. If we include the old one, there are four scars to study.



Figure 1. Photo of 18 cm abdominal scar which was opened three times. Note the abundance of hair growth, induced by iodine, around the scar. The two black dots are the coordinating centers (5mm apart) and are level with the colostomy scar seen on the right of the picture (left of the abdomen). The umbilicus disappeared for two months and reappeared in this form. Note that applications of iodine have been stopped, and the scars have reverted to the adult form. The coordinating centers have stayed in place.

Best Method of Iodine Application

After medical discharge, Lugol's solution applied topically to scars began regeneration within several days. Daily scar application of iodine and covering with plastic to retain moisture and prevent

iodine evaporation worked best.

Documentation with Cameras

Scar regeneration monitoring with normal microscopic procedures is impossible. Several small Nikon Cool Pix cameras with 5-to-8 mega pixels recorded changes. A zoom lens and one camera with an enlarging attachment enabled magnifications of 3-to-20 times.

Photographing in order to learn what changes were occurring is unusual because there is no way of telling what you will find. New findings, stumbled upon, were automatically recorded. These findings were followed-up with a time-lapse photographic approach. Watching the regenerating area with a magnifying glass was like watching clouds—slow, and not helpful.



Figure 2. Wrist coordinating centers. They are dark because of the uptake of iodine for storage. They are 5mm apart. A partial trace of the residual scar in white is seen above the upper center. These two centers stayed in place during regeneration. This picture is taken 1.5 years after starting applications. The iodine stain is easily seen.

Results

Definitions of Regeneration Terms, Free Iodine, and Skin Behavior

Coordination Centers

As long as iodine is applied daily with a plastic cover, regeneration continues. Over three years of study, no two pictures of any scar are the same even when the second is taken only a few minutes later than the first. Two dots 5mm apart appeared on both wrist and abdominal scars. The dots seem to coor-

minate tissue activities and are named coordinating centers. (Figures 1 and 2.)

Regenate Material: Two Types

White Regenate Material. While under plastic wrap, a snow-like substance named white regenate material fell like snow onto scars, producing flat white layers. As topical iodine application levels increased progressively, the white regenate material became yellow, green, light brown, and then brown. Without plastic wrapping, regeneration was considerably slower and much less interesting photographically, and exhibited few signs of either kind of regenate material.



Figure 3. Abdominal scar below the umbilicus. A number of globular regenerating masses are shown clearly soon after removing the plastic wrap. There is no special shape or size. The dark color likely is stored iodine. Abundant hair is intimately involved with every aspect of regeneration. Some sense of the finger-like swellings that continuously bind the two sides together can be seen on both sides. The large round non-descript area at the bottom of the photograph is the partially formed umbilical hernia.

Globular (Masses) Regenate Material. Under plastic wrap—once regeneration was well under way—globular non-descript masses appeared on scar areas on both abdominal and wrist scars. These globular masses had no standard shape or size and changed shape frequently. Most globular masses had hair associated with them. (Figures 3 and 4.)

Free Iodine's Behavior on Skin

Lugol's free iodine stains skin brown and evaporates rapidly. A stain loses 50% free iodine within

two hours, 80% within two days, and by the third day 88% has evaporated. No further evaporation takes place. Therefore 12% of any one application gets into skin tissues as iodide. Covering with plastic minimizes evaporation and helps the regeneration rate. Iodide is also soluble in skin and would add to tissue levels.^{[12][21]}

Skin Response to Excess Iodine Application

If iodine applications were excessive especially on skin and not the scar, slight stinging resulted for a few minutes. This caused no ill effects, but may be a tissue signaling that iodine is not needed at that site, time, and dosage. Scars and scabs were much more iodine tolerant. Skin removes excess iodine triggering a few surface cell deaths (apoptosis).^[10] These dying cells in turn release more proteins for iodine to react with. This more heavily-stained dead tissue sloughs off, but when under wrap it recycles into regenerating scar.



Figure 4. Wrist globular mass (regenerating material) as seen through plastic wrap. There is yellow regenerating material (white with iodine in it). It was difficult to tell if globular mass shape changes or small movements were artifacts of body movement. Abdominal globular masses were mostly 5-10mm in size, and wrist masses 1-2mm. This mass is about 3mm long. It changed direction many times but did not move. It lasted about 2 days and then disappeared.

Wrist Scar Details

The wrist scar was a source of detail because it was easy to photograph. Two weeks post injury the

wound became infected. Antiseptic iodine applications cleared the infection. When the scab fell off, in the middle of the 2cm scar were two dark dots 5mm apart straddling the radial artery. In retrospect, these two dots indicate that regeneration starts during antiseptic iodine applications. The dots remain in place during regeneration (3 years). Time-lapse photography suggests that they coordinate regeneration. During regeneration, it appears as if everything moved except coordinating centers and hair follicles. Wrist coordinating centers were composed of one cell storing iodine. The centers continuously changed appearance within two minutes—for three years. There was also a palpable subcutaneous ridge between the wrist centers (this did not happen with the abdominal scar).

Because nearby wrist hair interfered with photographing the coordinating centers, only once—early in the process—were hairs shaved away. Better coordinating center pictures resulted, but the shaving slowed regeneration. As we learn below, hair is a regeneration workhorse.



Figure 5. This is a picture of the top of the abdominal scar about a month after starting applications of iodine. Note the large number of new hairs adjacent to and in the crevasse. At the end of the crevasse there is a tiny black dot. This was the first sign of the coordinating centers for the abdominal scars.

Face Scar Regeneration

The face scar was the easiest to regenerate. No coordinating centers appeared at any time. As surgery was done by a plastic surgeon, there was minimal tissue damage and it was gone in 6 months.

Abdominal Scars (Laparotomy X3 and Colostomy)

During the initial healing process, the scar below the umbilicus had an obvious tissue deficit and thus was healing with secondary intention. Whereas, above the umbilicus scar edges were apposed and healing was by primary intention.

The two scar areas above and below regenerated differently. At any time, either the upper or the lower half of the scar was active while the other half was quiet. The halves switched roles at about 6-month intervals. The top half scar formed crevasses with abundant regenerate material and hair. (Figures 5 and 6.)



Figure 6. This picture is also of the upper part of the scar closer to the umbilicus. The umbilicus is the round white mass on the right hand side. The umbilicus was on its way to disappearing at this point. There is abundant regenerate material and hair around the central crevasse. Picture is taken through a plastic wrap. In the middle, some regenerate material can be seen sticking to the plastic wrap. More of a brown color regenerate material is sticking to the wrap on the lower left side of the scar. The white glistening is an artifact from the wrap.

Below the umbilicus regeneration was interesting. The two scar sides had a significant deficit gap. The walls approached each other acting somewhat like two hands with fingers extended pointing at each other as they came together. (Figure 3.) One or more “fingers” on one side would slide over the gap and attach to the other side. Then the opposite side would do the same thing. These swellings (like fingers of the hand) just welled up from tissues, and might not take longer than a couple of hours to cross over and complete. The (finger-like) swellings were thick until

later stages of regeneration, when they thinned. This went on for years.

Three Hernias: Umbilical, Left Side Abdominal, and Colostomy Muscle

The umbilicus exhibited various appearances during the first year. At one point the umbilicus disappeared. A couple of months later umbilical tissue reappeared (Figure 1), and a year later it formed an umbilical hernia to aid regeneration.

Two Other Hernias. Two other hernias, one a small abdominal hernia opposite the umbilicus and another, a colostomy muscle hernia, moved medially (each towards the middle) towards and began merging with the umbilical hernia. In Figure 1 where the scar has been regenerating for over a year, there is still no sign of either the abdominal hernia or the colostomy hernia (which become prominent a year or so later).



Figure 7. The two abdominal coordinating centers in one of their many types of appearances. Viewing on the back camera screen, it was easier to see that they were made of numerous cells. It was not possible at the time to capture this impression. The multicolor is real; no artificial stains except for iodine have been applied. In most cases, each color represented a different cell. Remember that everything in the picture is alive, even hair—when viewed as a functional follicular unit.

Abdominal Coordination Centers

For about a year there were two much larger coordinating centers centrally placed on the big scar 5mm apart and consisting of more than 50 cells. (Figures 1, 5, and 7.)

Wrist centers remained in place from beginning to end. Each center in both pairs was independent and acted differently. The wrist centers had a palpable subcutaneous ridge between them while the abdominal centers had no such connection. Both pairs of centers took up iodine avidly after staining, and stored it.



Figure 8. This is not hair #1, but the image shows the same type of kink that hair #1 did just prior to self-amputating at the kink site. A pair of hairs in the foreground emanate from the same follicle.

Hair (Workhorse of Regeneration): Hair Types

Hair activities were central to regenerating scars. Time-lapse photography helped tease out details of hair’s multiple activities. There are many types of hairs such as long, short, small, fine, thick, flat, and occasionally hollow. Hairs occur sometimes in groups of two or three. This is a summary of some of the findings on hair activities.

Some of Hair’s Activities:

- Hairs on their own move accurately to any cell location within reach in all directions. Sometimes wrist movement aided the hair movement.
- Hair movements were by short rapid jerks.
- Self-amputation is a repeating continuous property of hair in regenerating tissue.
- Hair stubs with follicle, after complete self-amputation, may disappear completely for weeks and then reappear and grow back.

- Hair carried regenerate material to cells, coordinating centers, and to tissues in general.
- Hair follicles appeared to be the source of white regenerating material.

Hair cell and tissue signaling:

- Hair may have multiple methods of cell signaling such as touch, electrical, regenerate material, and inter-hair communications.

Hair Study Methods and Hair Movement.

Wrist field hairs were numbered. Hair #1 is flat, making direction changes easier. (Figures 8-12.) All hairs are capable of moving on their own in short rapid jerks. Wrist movement aids hair movement sometimes. Destination changes occur as many as 6 times per day and more at night. Only once did the author see hair #1 move. Staring at the hairs for an hour was useless and mind-numbing.



Figure 9. A photograph of hair #1 down the center with some regenerate material on it. This is about 1/3 its actual size. The two coordinating centers are easily seen and present in a multitude of different forms all the way through regeneration. They are 5mm apart and there is a firm palpable subcutaneous ridge between the two centers not visible in this picture.

Hairs also went to new destinations by rising up above skin vertically and then coming down at their destinations an hour or two later. These destinations appear to be exact, as the hairs return to the same

spots numerous times. All these movements may be controlled by iodine, but arrector pili muscles near hair follicles also cause moving.^[14, p.355]

Source of Snow-Like Regenerate Material.

In the first year it took many photographs to arrive at the conclusion that white regenerate material forms in follicles and then transports up the hair. The mechanism of regenerate material movement on hair is unknown. Most times white material is flat on the hair. The white material on hairs is discontinuous, raising the possibility of coding by another signaling system.



Figure 10. Photograph of hair #1 and the two wrist coordinating centers. Hair #1 is delivering regenerate material to the coordination center on the ulnar side of the wrist. Hair #1 is shortened even further in this picture. Regenerate material can be seen on hair #1 and around the other coordinating center. Discontinuous regenerate material shows on the hair curving over the top coordinating center in an almost code-like manner. The thinness of hair #1 near the follicle is related to this hair's flatness. Depending upon how the hair is photographed along its length, it can go back and forth between thick and thin.

Hair Self-Amputation Multiple Methods.

While watching hair #1, a kink formed about 1/4 of the way up the hair from the follicle to the point the kink touched skin. (Figure 8.) Within a few hours hair #1 self-amputated at that point. The cut-off hair end sank into regenerating tissues. The proximal short hair end continued as if nothing had happened, sending regenerate material to nearby tissues. About a week later hair #1 self-amputated again near the follicle leaving only a short stub. (Figure 12.)

Then, approximately a month later, hair #1 re-

grew again to normal size. On two occasions stub and follicle disappeared completely only to return again several weeks later. Self-amputation is a general hair phenomenon during regeneration. (Figure 12.)

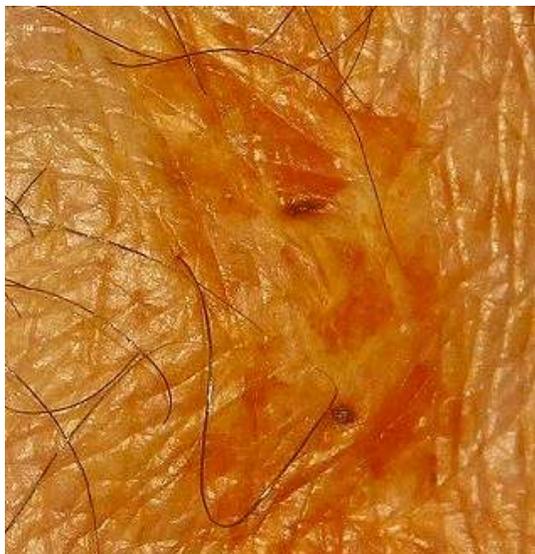


Figure 11. Hair #1 making contorted moves, when it is longer, to deliver regenerate material and/or signals to the lower center area. It's length is considerably longer than in the previous photograph. There are two small areas of regenerate material on hair #1. Other hairs also show white regenerate material.

Oral Iodine and Regeneration

Oral iodine had no detectable influence on regeneration. Even high doses did not stop adult scar formation when topical iodine was discontinued.

What About Controls?

Normal controls were not possible. Multiple scars of different types, sizes, and severities—along with stopping and starting regeneration numerous times for variable periods—provided the only possible controls.

Discussion

The Hypothesis

The results of this case report support a hypothesis: Topical iodine in the form of Lugol's solution regenerates human scar tissue back to normal. Checks of result validity were put into methods and results. The procedure, as described, is harmless. So,

physicians, scientists, and patients (with their physicians) can examine regeneration themselves. Regeneration is both unbelievably marvelous and at the same time mysterious because so many questions arise as it progresses.

Total Time of Regeneration

Because abdominal and colostomy scars act as if they are one big scar, when considered together, regeneration may take longer. Waiting for completion seems unnecessary. Regeneration attended to properly without stopping should be considerably faster. But as this was an exploratory experiment and there was no hurry, stopping and starting regeneration was repeated many times, sometimes for as long as 4 months.



Figure 12. Picture of wrist regenerating area (radial artery runs under this area and between the two coordinating centers). The hand is to the right of the picture. The arrow points to what is left of the stub of hair #1. Including hair #1, there are 15 hair stubs in this picture. This illustrates the magnitude of hair self-amputation.

Two Types of Regenerate Materials (Snow-Like and Globular Mass Type)

A by-product of regeneration is regenerate material. There are likely more unidentified regenerate materials. Because of their reactions with iodine (changing color), regenerate materials may turn out to be a host of new proteins with therapeutic potential. Tsoni^[1] states that a salamander's blastema formation is characterized by synthesis of more than 130 unique proteins; during dedifferentiation 26 new proteins are made. These are two hallmarks of salamander regeneration. Globular masses could be another

form of regenerate proteins. More recent DNA studies show several hundred genes are involved with blastema formation when compared to normal limbs.

Plastic Wrap Effects on Regeneration Rate

Covering scar tissue with plastic definitely accelerates regeneration. It also makes photography more interesting. Two other benefits may come from covering regenerating areas: retaining moisture (similar to a fetal skin regeneration environment)^[22] and preventing free iodine evaporation.^[21]

Hair Self-Amputation

The finding of purposeful hair movement is startling. The only movement we are aware of is hair erection when a person is emotionally upset.

Self-amputation of hair was another unexpected finding. But hair is strong and could add to tissue strength. We know scars are 70% as strong as intact skin, thus hair imbedded within regenerating tissues would strengthen it.^[15, p.35]

How much cell signaling hair does is unclear. Many methods using hairs, from touch to electrical signals, could be passing information to cells and coordination centers.^[16]

Antisepsis and Regeneration

In a committee report to decide on the merits of reintroducing iodine for antisepsis, it was emphasized that iodine may be doing more in wound healing than just antisepsis.^[17] This agrees with the findings of this case report.

Sponges (Porifera)

Sponge iodotyrosine content reaches 14% of total sponge amino acids, but the percent of iodothyronines (thyroid hormones) have not been reported. Sponges have possibly the greatest ability to regenerate of any animal; small pieces of tissue regenerate whole animals.^{[18][19]}

Flatworms (Platyhelminthes)

Even with complex internal structures, flatworms regenerate when cut in half. Flatworms lack a circulatory system (a network of vessels carrying fluids, oxygen, and food molecules to parts of the body). Consequently, all flatworm cells must be within diffusion distance of oxygen and food. This relationship is possible because flatworms have thin bodies and highly-branched digestive cavities. This

structure would encourage access to ocean iodine at all times.^{[19, p.420, p.428][20, p.499]}

Treatment Potential and Verification

If verified, regeneration induced by topical iodine could be a treatment approach with significant potential. But even before that potential is realized, scientists, patients, and physicians should examine regeneration. As results reported here have taken three years and are still incomplete, further results may take some time to examine.

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