Letter to Editor

Physiology and Anatomy of Hair in Drug Abusing Cases

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ABSTRACT

To interpret the results of hair analysis tests accurately and to understand the appropriate role of hair analysis in drug abuse testing and solve instances of poisoning, drug and substance abuse, a basic knowledge of the biology of hair is essential. In case of poising by heavy metals, the hair retains traces of poison for a considerable period. Chemical examination of hair in such cases will reveal the presence of poison in the living as well as exhumed whose biology is only partially understood. Hair grows from small organs (follicles-a skin organ which produce hair) located within the complex microenvironment of the skin which has multiple layers of tissue, three glands whose secretions bathe hair, and multiple vascular systems which are capable of transferring drugs to hair at many levels along the path of the hair shaft. The advantages and disadvantages of using pubic, scalp and beard hair as specimens for hair analysis are also considered. A more precise understanding of the mechanisms involved in the incorporation of drugs into hair is critical for forensic scientist in order to interpret the results of hair analysis properly.

►*Implication for health policy/practice/research/medical education:*
Physiology and Anatomy of Hair in Drug Abusing Cases

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1. Introduction:

To the casual observer, the hair appears to be a fairly uniform structure, differing in individuals only in color and amount. However, hair is a complex part of the anatomy whose biology is only partially understood. In order to interpret the results of hair analysis tests accurately and to understand the role of hair analysis in drug abusing test, some rudimentary understanding of the biology of hair is necessary. This communication offers a very brief review of the anatomy and physiology of hair with a view how drug enter and retained in hair. Examination of hair proved, Napoleons death to be due to chronic arsenic poising. A more complex treatment of this can be found in texts such as The Biology of Hair Growth (1), Human Hair (2), The Molecular and Structural Biology of Hair (3), and Chemical and Physical Behavior of Human Hair (4). However it must be clear that examination of hair is the province of the forensic biologist.

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Anatomy of hair:

Hair is an external appendage of skin that grows from hair follicles. It has a root, shaft, and a tip. In man, the diameter of individual hair shaft may range from 15 to 120 micrometer depending upon the type of hair and the region of the body the follicle is located. Hair contains a family of sulphur rich proteins and is basically made up of cystine containing protein called Keratin. In the hair shaft, keratin forms long fibres which become bound together very tightly through the replacement of SH groups with S-S bonds and through chemical cross-linking with other proteins. When the hair is in its normal unstretched state, it is referred to as A of alpha keratin. The original configuration of the hair is held in place by the bonding found in the cortex layers of the hair. As we stated earlier, keratin protein begins with an alpha helix building into protofibrils, microfibrils, macrofibrils, and then cortex layers. The bonds in the hair are located within each and every alpha helix.

Structure of the hair shaft:

Each hair shaft consists of three distinct types of cells: an outer cuticle which surrounds a central cortex which in turn may contain a central medulla (Fig.1). The cuticle is the outer covering of the shaft of the hair consisting of scales of keratin and forming a certain protein. Each cuticle cell is approximately 0.5 to 1 micrometer thick and approximately 45 micrometer long. Typical human hair has six to eight layers of cuticle. The function is to anchor the hair shaft in the follicle and to protect the interior fibres. However it may be damaged by chemicals, heat, light or mechanical injury. The cortex is like a hollow cylinder composed of fine fibres of protein material. Cortex consists of longitudinally placed non nucleated elongated cells. In human beings, the pigment is usually distributed near the periphery. The cortex contain abundant of keratin which is responsible for the repulsive smell when hair burns. Between the cells of the cortex are very small air spaces called Pusi. In the living portion of the hair root, these small spaces are filled with fluid but as the hair grows and dries out, air replaces the fluid. Melanin is the principal pigment of the hair as in eyes and skin. Melanin plays an important role for drug incorporation into hair. Melanin is synthesized in specialized organelles called melanosomes which is made from the amino acid tyrosine through the action of the enzyme tyrosinase. The method of incorporation of drugs into hair has also been one of much debate and is still uncertain. The simplest model proposes that passive diffusion of the drugs from the blood stream into the growing cells of the hair occurs. The drug is then tightly bound into the matrix of the hair shaft through keratogenesis, or binding to the keratin fibers of the hair. It is also believed that considerations must be given to incorporation through sweat and external adhesion. In human hair, medullar cells comprise only a small percentage of the mass or may be completely absent, continuous among the centre or discontinuous. Medullary index is the ratio of the diameter of the medulla to the diameter of the shaft. In human beard hair the medulla is quite complex and in some instances, a double medulla may be observed.

Chemical composition of hair:

Hair is essentially a cross linked, partially crystalline, oriented polymeric network which contains a number of functional chemical groups (e.g. acidic, basic, peptide bonds) which have the potential of binding small molecules. Hair is composed primarily of proteins (88%). The principal protein is of a hard fibrous type known as keratin. The mineral content of human hair is from 0.25 to 0.95%. Both essential trace elements and heavy metals can be found in human hair. Human hair contains large amount of hydrocarbons side chain amino acids (glycine), hydroxyl side chain amino acids (threonine), primary amide side-chain amino acids (aspartic and glutamic

acid) dibasic amino acids (lysine), as well as disulphide (cysteine) and phenolic amino acids (tyrosine) (4).

The hair follicle:

A hair follicle is a skin organ that produces hair which is embedded in the epidermal epithelium of the skin, approximately 3-4 mm below the skins surface (Fig.1). Hair follicles are closely associated with two glands – sebaceous gland and apocrine gland. In most parts of the body, the hair follicle and the sebaceous gland are fused both anatomically and functionally into what is called a pilosebaceous unit. In the axillary and pubic areas, hair follicles are also associated with another type of sweat gland, apocrine gland. The ducts of apocrine and sebaceous glands empty into the follicle. The ducts of eccrine sweat glands, on the other hand, are located near the follicles, but do not empty into the follicle (5). The hair follicles are divided functionally into three zones along the axis of the hair shaft. The innermost zone, in and around the bulb, is the site of biological synthesis of hair cells. The next section, located directly above the bulb, is the site of the keratinisation, where the hair undergoes hardening and solidification. The final zone is the region of permanent hair. Here the hair shaft consists of dehydrated, cornified cells that have formed into fibrils fused by an intercellular binding material. Hair growth begins in cells located in the germination centre located in the base of the follicle. As the cell divide, increase in volume, and elongate, they become larger and move up the follicle into the keratogenous zone. Here the cells synthesize pigment and begin to keratinize. Long fibres are formed through the cross-linking of the sulfhydryl groups in amino acids like cystine. Gradually the hair cells die and decompose by eliminating the cell nucleus and releasing water. The cell contents coalesce into a dense horny mass.

Secretary glands:

Three glands are associated with the hair follicle - the apocrine, sebaceous and sweat glands. Because their secretions bathe the hair shaft, these glands may be possible source of trace elements in hair (6). It is possible that these secretions are also vehicles for the transfer of drugs into hair.

Sebaceous glands:

Sebaceous glands are present on the entire surface of the body except the palms, soles and dorsum of the feet. They are most numerous and large in the head region. They are located just below the surface of the skin and their ducts exit directly into the tunnel of the hair follicle. The secretion of the sebaceous glands is a waxy substance called sebum. A 10-cm 2 section of the forehead skin will secrete 0.7 to 2.4 mg of lipid during a 4-hour period (7).The composition of sebum depending upon the anatomical area from which it is collected. However, approximately one third of the non-aqueous material is free fatty acids, one third combined fatty acids, and one third unsaponifiable material like squalene, cholesterol, and waxes.

Apocrine glands:

In humans apocrine glands are located in the axilla and anogenital regions and in a modified form in the eyelids, breast and external ear canal. Apocrine glands are different from the type of sweat glands that are found on the scalp in that they secrete by the separation of the cytoplasm from the secreting cells. They secrete an oily, colourless and odourless substance and little is known about its composition or physiological function except that the body odour results from its bacterial decomposition.

Sweat glands:

Eccrine sweat glands are distributed over nearly the entire surface of the body. These glands originate in the dermal layer of the skin and their ducts exit near, but not connected to, the exit of the hair follicles. Eccrine sweat glands produce a fluid

secretion that does not result from the removal of cytoplasm from the secreting cells. Water salts such as Na^+ and K^+ are the principal ingredients of sweat along with urea, amino acids, lactate and pyruvate. Sweat has been shown to be a vehicle for the excretion of a number of drugs (8).

Blood supply to the follicle:

Hair follicles are surrounded by two dense capillary networks, the pattern of which is different in active and in quiescent follicles. The lower third of an actively growing follicle is surrounded by a rich vascular plexus composed of long parallel vessels connected by cross shunts. There is a second dense network of vessels located at the level of the sebaceous gland which extends to the surface of the skin. These two networks are connected by a simpler, parallel system of larger vessels that descend along the side of the follicle. The follicles of velus hairs or in bald scalp are surrounded only by a very simple capillary system. In the quiescent follicle (telogen phase) the dermal papilla contains no capillaries and the lower plexus form a loose bundle of vessels at the base of the hair while the upper plexus remains the same. The dermal papillae are part of the uppermost layer of the dermis, the papillary dermis, and the ridges they form greatly increase the surface area between the dermis and epidermis. Blood vessels in the dermal papillae nourish all hair follicles and bring food and oxygen to the lower layers of epidermal cells. The degeneration of the blood vessels in the dermal papilla during catagen seems to be a secondary effect and not the primary cause for the cessation of hair growth (9-10).

The hair growth cycle:

Hair grows in cycles of various phases, anagen is the growth phase; catagen is the involuting or regressing phase; and Telogen, the resting or quiescent phase (11-12). Each phase has several morphologically and histologically distinguishable sub-phases. Prior to the start of cycling is a phase of follicular morphogenesis (formation of the follicle). There is also a shedding phase, or exogen, that is independent of anagen and telogen in which one of several hairs that might arise from a single follicle exits. Normally up to 90% of the hair follicles are in anagen phase while, 10–14% are in telogen and 1–2% in catagen. The cycle's length varies on different parts of the body. For eyebrows, the cycle is completed in around 4 months, while it takes the scalp 3–4 years to finish; this is the reason that the eyebrow hairs have a much shorter length limit compared to hairs on the head. Growth cycles are controlled by a chemical signal like epidermal growth factor.

Anagen phase- Anagen is the active growth phase of hair follicle: The root of the hair is dividing rapidly, adding to the hair shaft. During this phase the hair grows about 1 cm every 28 days. Scalp hair stays in this active phase of growth for 2–7 years. The amount of time the hair follicle stays in the anagen phase is genetically determined. At the end of the anagen phase an unknown signal causes the follicle to go into the catagen phase. It is thought that drugs and trace elements are incorporated into hair (perhaps complexed with protein) at this time of intense metabolic activity (13). For example when radioactive compounds like ^{35}S-labeled cystine are administrated to experimental animals, appreciable radioactivity is seen shortly thereafter in the keratogenous zone but little seen in the follicular bulb (14). Conversely when radio-labelled glucose is administrated, the densest radioactivity is seen in the bulb. This suggest that hair follicles may receive nutrients from the vessel surrounding the bulb but other chemicals are incorporated into hair at the level of the keratogenous zone and do not pass up from the bulb. Therefore finally formed hair shaft may contain not only those drugs present in the capillaries nourishing the bulb but also any drugs

present in the surrounding tissue, lymph, or intercellular fluid surrounding the lower part of the follicle.

Catagen phase- The catagen phase is a short transition stage that occurs at the end of the anagen phase. It signals the end of the active growth of a hair. This phase lasts for about 2–3 weeks while the hair converts to a club hair (15).

Telogen phase- The telogen phase is the resting phase of the hair follicle (16). When the body is subjected to extreme stress, as much as 70 percent of your hair can prematurely enter a phase of rest, called the telogen phase. Then hair begins to fall, causing a noticeable loss of hair. This condition is called telogen effluvium (17). The club hair is the final product of a hair follicle in the telogen stage, which is dead and fully keratinized hair. Fifty to one-hundred clubbed hairs are shed daily from a normal scalp (18).

Rate of growth:

It is usually stated that hair grows at a rate of 1 cm/month or 0.5 inches /month but drug of abuse affect the rates of hair growth as it may be half an inch/month. However this is an oversimplification. Precise value for hair growth rates in humans are difficult to obtain because all the hairs are not growing at any one time and the percentage of growing follicles is dependent on the anatomical location and age. The range of hair growth rates are given below - Average length and growth rate per day (19-22). Hairs on the head-70cm/0.35mm, Eyebrows-1cm/0.15mm, Moustaches (beards or whiskers) - 28cm / 0.4mm, Armpit hairs-10-50mm/0.3mm, Pubic hair - 10-60mm / 0.2mm, Scalp hair in woman grows faster than in men. Hair growth rate generally decreases with age. Experimental data on hair growth rates can be found in texts by Montagna and Ellis (1), Chatt and Katz (23).

Types of hair:

There are three basic types of hair on the human body which differs in length, texture, colour, diameter and shape. Vellus hair is very fine, short, non-pigmented hair with a small cross sectional area that is found on the seemingly hairless parts of the body such as eyelids, forehead and bald scalp. Terminal hair is the coarse, long, pigmented hair with a large cross sectional area that is located in the hairy areas of the body such as scalp, beard, eyebrow, eyelash, armpit and pubic area. Intermediate hair is the hair that is intermediate in length and shaft size and is found on the arms and legs of adults. These different types of hair are produced by three different kinds of follicles. Non sexual hair follicle produce intermediate hair which is found both in male and female and which is not change after puberty and also not influence by any hormones. Ambo-sexual hair follicles are found in the axilla, the pubic area and in the temple area of the scalp. Male sexual hair follicles are unique to males and are found in the beard area, ear, nose, chest, on the top of the head and abdomen. These follicles respond to the high androgen levels found after puberty, at this time hair from these follicles changes from fine vellus hair to coarse terminal hair.

Hair patterns:

There is no considerable difference in hair patterns, colour, texture, and hair diameter and hair growth rates. Hair can grow in a variety of patterns such as rows, clusters or whorls and within any cluster the individual shaft can be extremely variable in size. The diameter of scalp hair increase from birth until about the age of 12, after that it remains constant. Hair grows in a predictable patterns, lengths and texture on specific body areas such as scalp, temple and crown of the head, beard, pubic area, chest, armpits, abdomen, nose, ears, arms and legs. These hair patterns are the results of (i) the distribution of different types of hair follicles, (ii) The type of hair shaft

growing from the hair follicle which in turn is dependent upon age.

Scalp hair versus beard versus pubic hair as a specimen:
The difference in the biology of each of these types of hair should be considered when interpreting the result of hair testing.

Scalp hair- Scalp hair is easiest to collect but the considerable variation in growth rate in various regions of the scalp makes choice of the sampling area an important variable. In addition because the duct of the sebaceous glands discharge directly into the hair follicles, the hair shaft is exposed directly to sebaceous secretions before it emerges from the skin. Scalp hair is also exposed to sweet secretions as well as contaminants in air, water or dust. Finally the chemistry and physiology of the scalp hair may be modified by cosmetic treatments whose impact on hair analysis has yet to be determined.

Beard hair- Beard hair is thick, have relatively enormous follicles and have the slowest growth rate. The follicles of beard hair are distinctive in that the hair shaft and sebaceous gland duct exit from the skin in two separate channels. Thus beard hair may be somewhat less contaminated by sebaceous secretion than scalp hair. On the other hand when beard hair is obtained by shaving the specimen is likely to be contaminated by pieces of epidermis. Like scalp hair beard hair may be subject to environmental contamination. Also the distribution of medullary cells in beard is quite varied and unusual.

Pubic hair- Pubic hair has advantage as a specimen in that it is always available when scalp hair is not and may be less contaminated through environmental exposure or cosmetic treatment. However pubic hair may be contaminated by urine and less suitable as a specimen for other reasons. Hair in the axillae and pubic region is curved rather than straight which makes segmental analysis difficult. Pubic hair will be exposed to sebum and sweet secretions and in addition the secretions of apocrine glands which are present in significant numbers only in the axilla and pubic area. Like the sebaceous glands, apocrine glands discharge their secretions directly into the hair follicles.

2. Conclusion:
Hair is a tough, biochemical inert material produced from small organs composed of cells known as follicles that are quite similar, anatomically and physiologically. Hair consists of an inner cortex and a cuticle, and is basically made up of cystine containing keratin protein. Within this protein many bonds are present, the most important of which is a disulfide. Even on the body of the single individual hair can be found in an amazing array of lengths shapes, colour and textures. The cross section of the hair may be round or oval, triangular or kidney shaped. Hair does not grow continuously but undergo precise periods of growth and quiescence which are controlled by process which are partially understood. Although the growth rate of hair is generally reported to be 1 cm/month. Hair formation begins in the third month of fetal life and follows a cyclic pattern of growth. This hair growth is influenced by a number of factors such as nutrition and hormones. Finally to understand the functional anatomy and physiology of hair it should be viewed as an appendage of the skin. The complexity of hair biology should be understood and appreciated by all forensic scientists attempting to use hair as a specimen for the detection of drug of abuse.

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