HSPI The Open Access Publisher

J F S R JOURNAL OF FORENSIC SCIENCE AND RESEARCH
ISSN 2575-0186

Mini Review

# Forensic Perspectives on Human Chimerism: Identification Challenges and Detection Strategies

**Harsh Kumar[1] and Saumya Tripathi[2]***

[1]Student, M.Sc. in Forensic Science, Department of Chemistry, Banaras Hindu University, Varanasi, India

[2]Assistant Professor, Department of Forensic Science, College of Paramedical Sciences, Teerthanker Mahaveer University, Moradabad, India

**More Information**

***Address for correspondence:** Saumya Tripathi, Assistant Professor, Department of Forensic Science, College of Paramedical Sciences, Teerthanker Mahaveer University, Moradabad, India, Email: saumya.paramedical@tmu.ac.in

**Submitted:** August 22, 2025
**Approved:** September 08, 2025
**Published:** September 09, 2025

**How to cite this article:** Kumar H, Tripathi S. Forensic Perspectives on Human Chimerism: Identification Challenges and Detection Strategies. J Forensic Sci Res. 2025; 9(2): 150-154. Available from: https://dx.doi.org/10.29328/journal.jfsr.1001095



**Keywords:** Chimerism; SRY; Biological vestiges; HSCT; Genetic fingerprinting

**Abbreviations:** DNA: Deoxyribonucleic Acid; HSCT: Hematopoietic Stem Cell Transplantation; IVF: In Vitro Fertilization; STR: Short Tandem Repeat; SRY: Sex-determining Region Y (gene on Y chromosome); PCR: Polymerase Chain Reaction



## Abstract

Chimerism is a biological condition in which a single individual harbors two or more genetically distinct cell populations originating from different zygotes. This phenomenon may occur naturally due to errors during fertilization or early embryonic development, or it may arise artificially following medical interventions such as hematopoietic stem cell transplantation (HSCT) or *in vitro* fertilization (IVF). Chimerism is broadly categorized as natural or artificial, and its presence presents significant challenges in both clinical and forensic contexts. In transplant recipients, the coexistence of donor- and host-derived cells can generate misleading genetic test results and complicate post-transplant monitoring. In forensic investigations, individuals with mixed DNA profiles may be difficult to identify accurately, as standard genetic fingerprinting technologies can yield inconclusive or erroneous findings. These complications underscore the necessity of reliable detection methods capable of identifying and differentiating chimeric cell populations. This review consolidates current knowledge regarding the classification of chimerism and the available diagnostic techniques, emphasizing that improved understanding of this condition is essential for enhancing diagnostic precision, optimizing forensic identification, and minimizing the risk of misinterpretation that may adversely affect medical decisions and legal determinations.

## Introduction

### Chimerism

Chimerism is a rare and intriguing condition where one person's body carries two or more completely different sets of DNA [1]. In simple terms, not all cells share the same genetic code; some follow one genetic blueprint, while others follow a different one. For most people, every cell contains the same DNA they inherited from their parents. But in a chimera, the body is like a living patchwork quilt made from more than one genetic pattern [2].

### How does it happen?/ Mechanisms of Chimerism

There's more than one path to becoming a chimera, but one of the most common starts before birth:

- **Embryo fusion:** Very early in pregnancy, two embryos—often fraternal twins—can merge into one. The result is a single baby whose body carries cells from both embryos [1].
- **Cell sharing between twins**: In some twin pregnancies, a small exchange of cells happens through the placenta. Each twin ends up with a few cells from the other, creating a subtle form of chimerism [3,4].
- **Transplants later in life**: Even in adulthood, chimerism can occur. When someone receives an organ or bone marrow transplant, the donor's DNA can take up residence alongside their own, creating an acquired form of the condition [5].

Many individuals with chimerism remain unaware of the condition, with the discovery often occurring incidentally through DNA testing or medical investigations [6].

## Artificial chimerism (Man-made chimerism)

Artificial chimerism arises when a person receives donor cells through medical interventions such as organ transplantation, hematopoietic stem cell transplantation, or transfusion [5]. Post-transplant, the recipient harbors two sets of DNAs—both their own and the donor's— across different tissues [7] (Figure 1).

In forensic casework, Short Tandem Repeat (STR) profiling of such individuals can yield misleading results, especially if the donor and recipient are of different sexes [8]. Buccal swabs, fingernails, and blood samples may each reflect different genetic profiles, complicating individual identification.

## Microchimerism

When a pregnant women absorb some of the cells from their foetus, similarly, a foetus may also absorb some of the cells from the mother. Those cells travel through the blood of the mother and the foetus and migrate to different organs in the body [9]. These cells stay in the mother's and child's body for a long time [10]. This is known as Microchimerism. Microchimerism is classified into three categories [11] (Figure 2).

a) **Fetal microchimerism:** There is a pass-on of intact living fetal cells from the foetus to the maternal circulation. Up to 30 days in the maternal postpartum bloodstream, these fetal microchimeric cells can be detected.

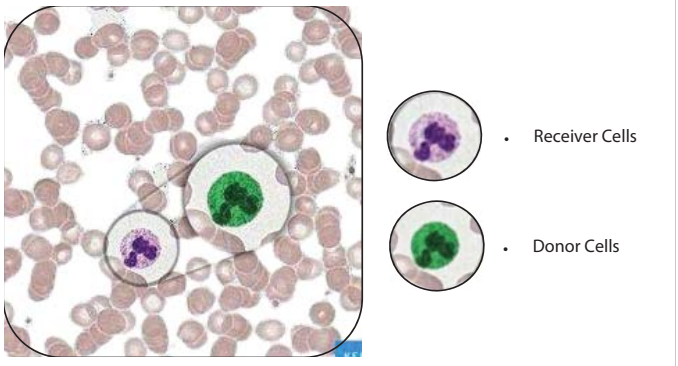


**Figure 1: Artificial Chimerism: Donor Cell Integration after Transplantation.**

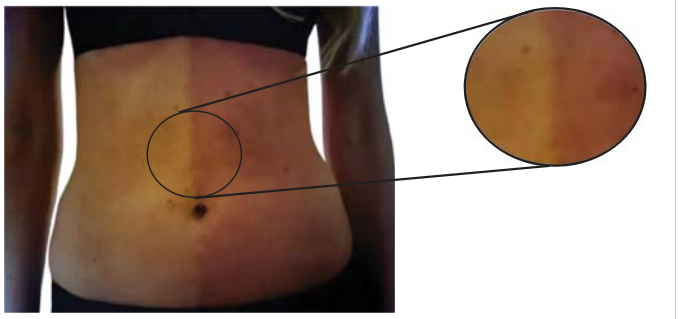

**Figure 2:** Maternal–Fetal Microchimerism.

b) **Maternal microchimerism:** This is a bidirectional process, and the transfer of intact living cells from maternal to fetal circulation takes place.

c) **Microchimerism in twins:** Exchange of cells between multiple fetuses, including from a "spectral twin" that does not survive to birth [12].

## Blood transfusion chimerism or twin chimerism

When a woman is pregnant with twins and one of the embryos dies in the mother's womb. A surviving fetus in the womb can sometimes take in a few cells from a twin that has passed away during pregnancy. After this, the surviving foetus consists of two different sets of DNA, one of its own and another one of its deceased twins. This situation is known as Fusion chimerism or Twin chimerism [13]. In this situation, twins may exchange blood through the shared placenta. Because of blood transfusion, the monozygotic twins become dichorionic and the dizygotic twins become monochorionic [4] (Figure 3).

## Tetra-gametic chimerism

Tetra-gametic chimerism happens when two sperm cells fertilize two different eggs, and the resulting embryos merge into one very early in development [14]. The person who grows from this fusion carries two complete genetic blueprints, with different DNA markers showing up in different parts of their body (Figure 4).

In very rare situations, one of the embryos is genetically male and the other is genetically female. When they combine, the individual may end up with both male- and female-specific

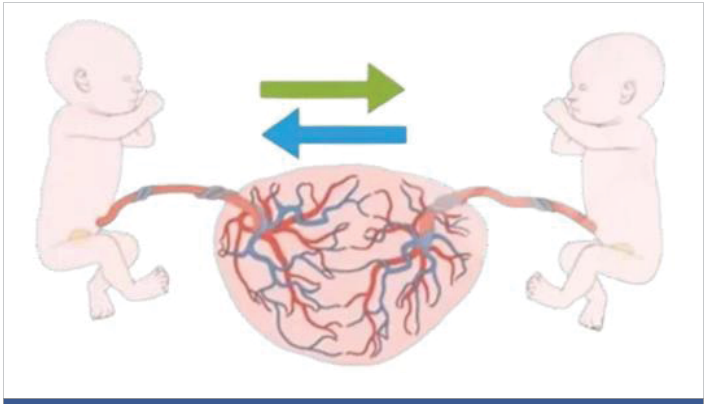

**Figure 3:** Zygotic Exchange Chimerism.

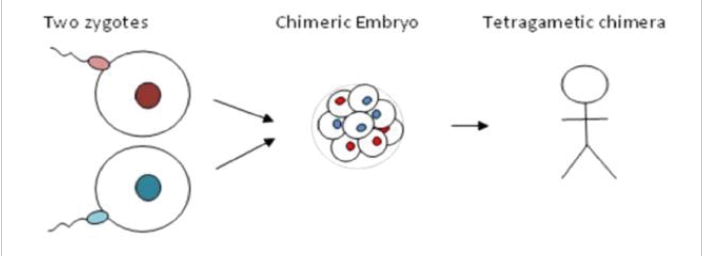


**Figure 4:** Tetra-gametic Chimerism: Fusion of Two Zygotes into One Embryo.

genetic markers, which can sometimes result in intersex traits [15]. The chances of tetragametic chimerism are slightly higher with *in vitro* fertilization (IVF), since multiple embryos are often implanted, increasing the likelihood that two might fuse.

## Symptoms of chimerism

Chimerism can reveal itself in many different ways, and the signs are not always obvious. The exact symptoms depend on how the condition developed and how widely the extra genetic material is distributed in the body. Some people may have:

- **Two differently colored eyes:** A striking condition known as heterochromia, where each eye has its own distinct shade [1] (Figure 5).
- **Irregular skin pigmentation:** Areas that are noticeably darker or lighter than the surrounding skin. These patches might be small and subtle, or they could cover larger parts of the body, sometimes affecting only one side (Figure 6).
- Hair exhibiting contrasting shades or textures, such as naturally growing in two distinct colors or showing visible streaks.
- **Variations in sexual characteristics:** Including the presence of both male and female reproductive traits or other intersex differences.
- **Genital appearance that is not clearly male or female:** Sometimes referred to as ambiguous genitalia [15].
- More than one genetic profile in the blood, where testing reveals two or more sets of DNA in red blood cells [2].

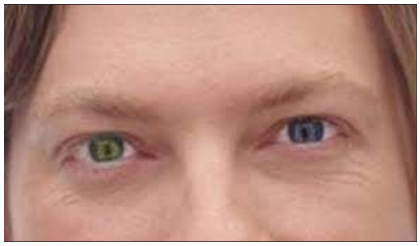

**Figure 5:** Ocular Chimerism

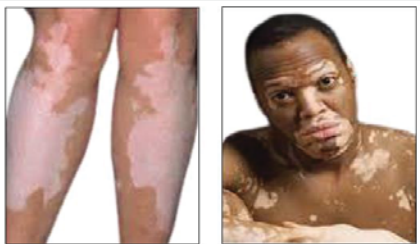

**Figure 6:** Pigmentary Chimerism.

These features alone do not confirm chimerism, but when several are present, they can guide medical professionals or forensic experts toward deeper genetic investigation.

## Methods to detect the chimeric condition

- In forensic investigations, accurate sex determination is a critical DNA-based tool for individual identification [16]. However, chimerism presents unique challenges that can compromise the reliability of standard genetic analysis. In cases of artificial chimerism—such as post-transplant patients—not all sampled cell types yield accurate genetic profiles; hair root cells often remain the most reliable source of genetic material [7].
- One key genetic marker that scientists often search for is the SRY gene, located on the Y chromosome. Think of it as a biological "on-switch" that kickstarts the development of male traits very early in life. By reading, or sequencing, this gene, researchers can confirm a person's biological sex—even in complex cases like chimerism, where the body may carry more than one genetic blueprint [17]. This becomes especially important when someone has both male-specific signals, such as an SRY-positive result, and female-specific markers scattered in different parts of their body.
- Such scenarios can lead to discordant results in sex determination, especially in forensic contexts where biological samples may originate from a tissue that does not represent the individual's predominant genetic makeup. For instance, an individual with tetragametic chimerism might present male genetic markers in blood but female genetic markers in buccal cells, potentially leading to misinterpretation in criminal investigations or identity verification [14,18].
- Recent studies emphasize the importance of multi-sample, multi-locus genetic testing— combining autosomal STR profiling, sex chromosome-specific markers, and targeted sequencing—to reduce misclassification risks in chimeric individuals [19,20]. Forensic laboratories are increasingly advised to implement confirmatory protocols that account for possible chimerism when encountering atypical or inconsistent DNA profiles (Table 1).

## Case studies related to chimerism

- A well-documented case that demonstrates how chimerism can cause serious misinterpretation in forensic and legal investigations is that of Lydia Fairchild (2002, USA). DNA testing conducted during her application for public assistance indicated no biological link between her and her children. The STR results were so conflicting that authorities suspected fraud, and she faced the terrifying prospect of losing

**Table 1:** Detection Techniques and Forensic Applications.

| Technique | What it Targets | Why it Matters in Forensics |
|---|---|---|
| STR Profiling | Autosomal short tandem repeats | Helps identify individuals; reveals mixed profiles in chimeras |
| SRY Gene Test | Y-chromosome marker | Resolves sex determination issues in ambiguous cases |
| Multi-locus Genetic Testing | Combination of STR, mtDNA, and sex-linked markers | Avoids misclassification when DNA sets conflict |
| Tissue-specific Sampling | Hair roots, buccal swabs, blood, nails | Cross-checks samples to confirm suspected chimerism |

custody. It was only after further investigation that doctors discovered she was a tetragametic chimera—carrying two different genetic profiles in different parts of her body. The initial cheek swab results showed no match, but further testing of cervical tissue provided the proof that she was their biological mother [6]. This case vividly illustrates how overreliance on a single DNA sample can lead to life-altering misinterpretations.

- A similar challenge was reported by van Dijk, et al. [14], where an individual showed different DNA profiles in blood and buccal swabs because of tetragametic chimerism. Such discrepancies could easily cause investigators to draw the wrong conclusions about identity if the possibility of chimerism is not considered.

- Another example comes from the work of Yu, et al. [7], who proved cases involving people who had experienced hematopoietic stem cell transplantation. In one case, a biologically female individual appeared to have male DNA markers in her blood due to the presence of donor cells. If interpreted without context, such results could mislead investigators and even point toward the wrong person.

## Ethical challenges of DNA misidentification in forensics

The involvement of chimerism in forensic science introduces a number of ethical challenges that extend far beyond the laboratory. One of the most serious risks is the possibility of wrongful conviction. When DNA from a crime scene comes from a tissue carrying a donor or alternate genetic profile instead of the individual's main genotype, investigators could mistakenly associate evidence with the wrong person [2,7]. Such errors can compromise justice, undermine the credibility of forensic science, and cause significant harm to individuals who are falsely accused.

Chimerism also raises difficult questions about the dependability of DNA evidence in courtrooms. While DNA profiling is often presented as nearly infallible, cases of chimerism demonstrate that results can sometimes be inconsistent. For instance, tetra-gametic chimerism may produce different genetic signatures depending on the tissue sampled [14]. This creates uncertainty over whether such evidence satisfies the high standards of reliability demanded by legal systems, including the *Daubert* standard in the United States and similar frameworks elsewhere.

Equally important are concerns about privacy and informed consent. Detecting chimerism often requires analysis of multiple tissue types, which can unintentionally reveal deeply personal information—such as intersex traits or underlying medical conditions [18,19]. The release or misuse of such findings could stigmatize individuals, expose them to discrimination, or compromise their right to control their own genetic information. This places a strong ethical responsibility on forensic professionals to weigh investigative needs against respect for human dignity and autonomy.

Ultimately, these issues highlight the urgent need for clearer safeguards and guidelines in forensic practice. Approaches such as cross-checking DNA from different tissues, independently verifying conflicting results, and ensuring that courts are fully aware of the complexities posed by chimerism are essential. Beyond scientific accuracy, such measures ensure that justice is upheld, privacy is protected, and the humanity of those involved remains at the center of forensic work [21].

## Conclusion

From a forensic perspective, the most crucial goal is accurate identification of a person. Chimerism complicates this process because the presence of two or more genetically distinct cell types in one individual can mislead genetic fingerprinting results. Forensic experts may face unexpected challenges when a person's DNA profile does not match in the way it should. Chimerism, whether it occurs naturally or as a result of medical procedures, is both intriguing and complex. When someone carries more than one set of DNA, it can lead to unusual physical characteristics, puzzling medical findings, and DNA test results that tell only part of the story. Variants such as artificial chimerism from organ or stem cell transplants, microchimerism during pregnancy, twin or fusion chimerism, and tetragametic chimerism each arise differently, yet all share the same forensic challenge — they blur the lines in determining biological identity and even sex. In forensic investigations, conventional DNA profiling can be unreliable in such cases, particularly when both male and female genetic markers are present. This is where advanced approaches, like SRY gene sequencing and careful tissue-specific sampling, become essential. Recognizing chimerism is not just a matter of scientific interest — it is key to avoiding misidentification, ensuring justice, improving medical outcomes, and deepening our understanding of the extraordinary complexity of human biology.

## References

1. Madan K. Natural human chimeras: A review. Eur J Med Genet. 2020;63(9):103971. Available from: https://doi.org/10.1016/j.ejmg.2020.103971

2. Arcabascio C. Chimeras: Double the DNA–double the fun for crime scene investigators, prosecutors, and defense attorneys. Akron Law Rev. 2007;40(2):435–64. Available from: http://nsuworks.nova.edu/cgi/viewcontent.cgi?article=1037&context=law_facarticles

3. Waszak M, Cieślik K, Wielgus K, Słomski R, Szalata M, Skrzypczak-Zielińska M, et al. Microchimerism in twins. Arch Med Sci. 2013;9(6):1102–6. Available from: https://doi.org/10.5114/aoms.2013.39212
4. Tavares L, Da Costa DC, Batschauer APB, Jobim LFJ, Ewald GM, de Mello C, et al. Blood chimerism in twins. Immunohematology. 2018;34(4):151–7. Available from: https://pubmed.ncbi.nlm.nih.gov/30624949/
5. Khan F, Agarwal A, Agrawal S. Significance of chimerism in hematopoietic stem cell transplantation: New variations on an old theme. Bone Marrow Transplant. 2004;34(1):1–12. Available from: https://doi.org/10.1038/sj.bmt.1704525
6. Darby A. The case of Lydia Fairchild and her chimerism (2002). The Embryo Project Encyclopedia. 2021. Available from: https://embryo.asu.edu/pages/case-lydia-fairchild-and-her-chimerism-2002
7. Yu J, et al. Detection of chimerism in forensic samples: Challenges and case studies. Forensic Sci Int Genet. 2022;60:102717. Available from: https://doi.org/10.1016/j.fsigen.2022.102717
8. George R, Donald PM, Nagraj SK, Idiculla JJ, Ismail RH. The impact of chimerism in DNA-based forensic sex determination analysis. Malays J Med Sci. 2013;20(1):76–80. Available from: https://pubmed.ncbi.nlm.nih.gov/23785258/
9. Mahmood U, O'Donoghue K. Microchimeric fetal cells play a role in maternal wound healing after pregnancy. Chimerism. 2014;5(1):40–52. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4199806/
10. Klintschar M, Schwaiger P, Regauer S, Mannweiler S, Kleiber M. Persisting fetal microchimerism does not interfere with forensic Y-chromosome typing. Forensic Sci Int. 2004;139(2–3):151–4. Available from: https://doi.org/10.1016/j.forsciint.2003.10.011
11. Sandhya S, Naik R, Suryawanshi H, Gupta N. Microchimerism: A new concept. J Oral Maxillofac Pathol. 2019;23(2):311. Available from: https://doi.org/10.4103/jomfp.JOMFP_85_17
12. Johnson BN, Peters HE, Lambalk CB, Dolan CV, Willemsen G, Ligthart L, et al. Male microchimerism in females: A quantitative study of twin pedigrees to investigate mechanisms. Hum Reprod. 2021;36(9):2529–37. Available from: https://doi.org/10.1093/humrep/deab170
13. Marin S, Fernandez S, Alvarado A, Bermejo C, Martinez P, Mansilla E, et al. A case of blood chimerism and twin-to-twin transfusion syndrome in monochorionic dizygotic twins. Obstet Gynecol Rep. 2020;4(1):1–3. Available from: https://doi.org/10.15761/OGR.1000142
14. van Dijk E. Tetragametic chimerism in forensic DNA casework. Int J Legal Med. 2016;130(2):383–90.
15. Yunis EJ, Zuniga J, Romero V, Yunis EJ. Chimerism and tetragametic chimerism in humans: Implications in autoimmunity, allorecognition, and tolerance. Immunol Res. 2007;38(1–3):213–36. Available from: https://doi.org/10.1007/s12026-007-0013-3
16. George R, Sriram G, Saraswathi TR, Sivapathasundharam B. Isolation of epithelial cells from acrylic removable dentures and gender identification by amplification of the SRY gene using real-time PCR. J Forensic Dent Sci. 2010;2(1):32–6. Available from: http://dx.doi.org/10.4103/0974-2948.71055
17. Sharma S. SRY gene analysis in complex sex determination cases. J Forensic Sci. 2020;65(3):849–57.
18. Shao H. Complex sex chromosome mosaicism in chimeric individuals: Forensic implications. Forensic Sci Int Genet Suppl Ser. 2021;8:144–6.
19. Alghafri R, Al Saeedi R, Al Lawati Z, Al Balushi F. Multi-locus approach for accurate sex determination in chimeric individuals. Forensic Res Criminol Int J. 2023;11(1):45–52.
20. Sato T. Genetic profiling strategies for identifying chimerism in forensic casework. Leg Med. 2022;58:102099.
21. Drobnič K. A new primer set in the SRY gene for sex identification. Int Congr Ser. 2006;1288:268–70. Available from: https://doi.org/10.1016/j.ics.2005.08.020