The constipation illness

Gabriele Bazzocchi, Mimosa Balloni

NeuroGastroenterology and Intestinal Rehabilitation Unit, Montecatone Institute Imola / Bologna, Italy

Abstract: Constipation is commonly described as a variety of symptoms including infrequent bowel movements and/or rectal evacuation disorders. Hard stools, excessive straining, bloating and abdominal pain are frequently associated. The several clinical pictures resulting by their combination are mostly due to a primary disturbance of colonic propulsion and/or obstructed rectal emptying, but the chronicity of these initially functional dysfunctions induce structural changes in the recto-colonic tract (such as dilatation, dolicoocolon, rectal prolapse, rectocele, hemorrhoids): constipation turns so in a condition of illness where primary and secondary disorders, functional and organic alterations are not no more clearly detachable and therapeutic priorities are a real challenge for primary care physicians and specialists. The recent knowledges indicate a pivotal role for the gut microbiota in the pathophysiology of colonic dysfunction underlying constipation, contributing to make it is a real “systemic” illness, and not a disorder of an organ, given that the impressive consequences which intestinal dysbiosis has on the Enteric, Autonomic and Central Nervous Systems.

Keywords: Chronic constipation; Intestinal microbiota; Colonic motility; Fecal microbiota transplantation

DEFINITION AND CLINICAL PICTURE

Constipation is traditionally defined as a symptom, not a disease, but today it is preferred to define it as a condition of suffering, an illness, a set of symptoms and clinical signs, which the patient can arrive in several ways to1-2. These ways are very different between themselves, but all of them converge towards a precise Syndrome defined by two clinical pictures. The first is characterized by a rarity and a reduced perception of the evacuative stimulus, followed by an easy defecation, after all satisfactory, even if frequently with the expulsion of small and hard stools. Apart from the long interval between two defecations, however spontaneous and normal, there are no other disorders, which clearly distinguishes this form of constipation from the symptomatic disorders that are typical of Irritable Bowel Syndrome (IBS): abdominal pain, swelling and abdominal distension, loss of appetite, difficult digestion and discomfort. The second “scenario” of constipation is instead characterized by a remarkable association of symptoms: first of all a difficult expulsion, with the perception of an obstacle to the discharge of stools, for which an intense “strain” and need to exercise an excessive abdominal pressure are required. Moreover, sometimes manual maneuvers for supporting stool expulsion are necessary, often with a residual sensation of not having completed bowel emptying. Although this is even more true if stools are scarce and hard, this picture may be present even if the fecal consistency is regular or even fluid. The two clinical pictures often succeed one another, usually the latter is added over time to the first, or they add up and alternate in the short term, creating the most diverse and complicated situations, also in relation to therapeutic attempts (laxatives, drugs, supplements, diets, etc.) which are carried out by patients 3-4. These altered defecation dynamics, the first identified as Slow Transit Constipation (STC), the second as Disordered Defecation (DD), are then associated with all those conditions that define IBS, above mentioned, in a way that a certain clinical and consequently pathophysiological distinction between the two pathological syndromes, constipation and IBS, is neither possible nor useful for therapeutic purposes. Further symptoms and signs may be associated, such as evidence of abnormal shape and stool (thin, “blocky”, fragmented, smelly), perineal pain, evidence of rectal prolapse or bleeding during and/or after defecation. It should also be considered that these two forms of constipation are further complicated by wrong patient behaviors rather than intestinal dysfunctions: people who think that defecation should be forced after lack of perception of the urge to evacuate for 48, 36, or even only 24 hours, use a whole series of measures to induce it (laxatives ingestion; positioning on the toilet trying to expel feces; introduction of suppositories or enemas), thus upsetting what would otherwise have been a regular interval between a spontaneous defecation and the next one. Other people would like to confine defecation at certain times of the day, when toilet is available at home, so that it does not happen during office hours, or for similar reasons: they position themselves on the toilet without having perceived any “need to evacuation” feeling, and “try” to defecate. In the very likely event of a failure or a shortage of intestinal emptying, they seek for treatment because they consider themselves suffering from constipation. This behavior is very often adopted to try to reduce bloating, meteorism or abdominal distension. It is clear that these behaviors, alone or superimposed on a real existing STC or DD, create such complex clinical pictures that their analysis requires an anamnestic investigation, mostly incompatible with the normal times of a medical examination, even in a specialized context. However, the lack of understanding of all the dynamics underlying the condition of constipation reported to the doctor, almost invariably affects the effectiveness of any treatment, even a surgical one, that is prescribed.

ETIOLOGY

As far as the etiopathogenesis of constipation is concerned, it is advisable to immediately clear the field of those situations where constipation disorders are secondary to an intestinal disease whose onset may occur also, or only, with these conditions: tumors, complications of Diverticular Disease, inflammatory colitis, Celiac Disease and other pathological entities. The suspicion that bowel disturbances are a consequence of these pathologies may easily arise because, in addition to constipation, other symptoms and clinical signs, defined as “alarm features” are present, such as anemia, weight loss, stool blood in absence of anal pathologies, asthenia, fever, and alterations in laboratory test. “Acute” constipation, which suddenly appears in individuals with earlier regular and satisfactory evacuation habits, should be managed as potentially secondary to the above causes and therefore an appropriate diagnostic investigation should be performed. Even when constipation is chronic, it may be secondary to other pathologies, first of all to drug consumption. The intake of opioids, calcium antagonists, adrenergic agonists, dopaminergics, tricyclic antidepressants, neuroleptics and chemotherapeutic agents is often burdened by the progressive appearance of defecation disorders. Moreover, metabolic and hormonal disorders (hypercalcemia,
hypopotassemia, etc.) can cause constipation. The role of neurological pathologies is also very important: severe constipation can easily be classified as a consequence of a spinal or brain injury, due to trauma, hemorrhage, inflammation, and more. On the contrary, other neurological diseases can be the basis of constipation in a decidedly more subtle way: it is not so rare to find of a pathology such as Spina Bifida occulta, tethered cord syndrome and, more generally, pathologies of the cauda equina and sacral region (e.g. Currarino syndrome) after years and years during which the patient, as a rule in the pediatric age, but, from personal experience, even in adult age, reported a constipation which was particularly severe and refractory to any treatment.

The appearance of constipation in young women can be for many years the first and only disorder of Multiple Sclerosis, a disease that is then recognized when the typical neurological symptoms appear or are associated with disorders of a “neurogenic bladder”: retention and/or urinary incontinence. Even the great neurodegenerative diseases such as Parkinson’s or Alzheimer’s are almost invariably characterized by constipation, both with aspects of STC and DD. The role of neurological pathologies is also very important: hypopotassemia, etc.) can cause constipation.

Distension or stretch of the colon activates these sensory neurons to initiate polarized neural pathways that result in oral contraction and anal relaxation. These pathways do not require the mucosa but can be modulated by sensory nerve endings that project into the mucosa. Enteric neural circuitry can efficiently propel content with a wide range of physical properties. This content-dependent activity can be modified in terms of force of constriction and speed of propulsion depending upon consistency and volume of the colonic contents.

PATHOPHYSIOLOGY

Constipation is always a consequence of a dysfunction of the colon and rectum, given the transit time in the stomach and small intestine is measured in hours, compared to that in the large intestine in days. In a nutshell, we can identify two mechanisms that characterize the dysfunction of the colon at the basis of constipation: on the one hand a deficit, an inefficient propulsive motility of the colon that provides a propulsion depending upon consistency and volume of the colonic contents. The problem is, however, that anomalies are never present in all forms of functional constipation, so that, on one hand, the number of those with unknown etiopathogenesis is narrowed, and, on the other hand, it is possible to state that constipation is a Syndrome, almost never a Disease, but certainly an Illness.

The Central Nervous System (CNS) acts in the modulation of both mechanisms. Colonic dysmotility involves the Autonomic Nervous System (ANS), the Enteric Nervous System (ENS) and the smooth muscle of the colon, while the efficiency of evacuation is guaranteed by the peripheral somatic innervation of the striated diaphragm musculature, the abdominal wall, the pelvic floor including its myo-fascial structure and the anal sphincters.

Colonic Dysmotility is characterized by the reduction/absence of peristaltic contractions with propulsion effect of the colon: recent studies have found alterations of the complex regulation mechanisms of the ENS, a real “second brain” that is located in the intestinal wall and whose complexity, for the number of neurons and integrations between them, is comparable to the brain. Technical and ethical difficulties prevent us from conducting studies on healthy and sick people to understand the relationships between the anomalies identified in ENS functioning, and the behavior of contractility of the bowel muscles seen in patients with constipation, but there is no doubt that the abnormal transport of the endoluminal content through the colon, which is often long and twisted, plays a causal role in many constipations.

Only recently, thanks to the works of the Australian group directed by the physiologist Marcello Costa, it has been possible to understand that propulsion in the large bowel is consequence of two neural mechanisms. The first is the content-independent spontaneous colonic migrating motor complexes that occurs cyclically. The second is a content-dependent, adaptable mechanism controlled by the mechanical activation of enteric neural activity. Mechanosensory enteric neurons (located in the myenteric plexus) have essential mechanosensitive nerve endings in the circular muscle. Distension or stretch of the colon activates these sensory neurons to initiate polarized neural pathways that result in oral contraction and anal relaxation. These pathways do not require the mucosa but can be modulated by sensory nerve endings that project into the mucosa. Enteric neural circuitry can efficiently propel content with a wide range of physical properties. This content-dependent activity can be modified in terms of force of constriction and speed of propulsion depending upon consistency and volume of the colonic contents.

In others words, bolus size and its consistency affects propulsion speed suggesting that propulsion is not a simple reflex, according to the classic theory about intestinal peristalsis, but rather a more complex process involving an adaptable neuromechanical loop. Consistency depends on the degree of fluidity of the intraluminal colonic contents, which in turn depends on the degree of absorption of fluids along the gut. But consistency is due also by the dry-component of the feces that, as for the 60-80% composed by alive microbial cells originating from the microbiota that dwell in the colon.

Based on recent revised estimates, the human microbiota comprises approximately 10^{13} prokaryotes (bacteria and archaea), as well as fungi and viruses with a contribution of 0.5 kg of the average adult’s body weight, but with an extraordinary metabolic capacity, far exceeding that of human beings. Of all these microbial components, bacteria have been the most thoroughly studied, but it is become increasingly clear that trans-kingdom interactions are just as important in influencing health and disease. Many if not all human cell structures coexist with a more or less rich microbiota: organs as the lung, or the bladder, not to mention the fetus, which until a few years ago were considered examples of “sterile structures and systems”, in fact turned out to have their own microbiota, and in many cases some of their pathologies have been associated with alterations of its composition. That applies for example to all recent works that describe the role of urinary microbiota in urinary tract and gynecological dysfunction. Not discounting a number of shortcomings in the available studies, even blood does not seem to be excluded, whereas the only exception,
to date, is represented by the CNS. There is no doubt, however, that the microbiota residing in our gastrointestinal tract is the hub upon which the modulation not only of all intestinal functions, but also of other organs, depends, including the CNS, even at the level of its “higher” functions such as mood and ideation. Harboring around 10–100 trillion prokaryotic cells at density of $10^{11}$ to $10^{12}$ cells/mL, the human gastrointestinal tract is one of the most complex microbial ecosystem on the planet Earth, comprising only a few phyla (Firmicutes and Bacteroidetes) but hundreds of species, thousands of strains, and millions of bacterial genes with specific assemblies for each subject, like fingerprints. Added to this is the high degree of plasticity, i.e. the microbiota ability to change in response to several endogenous and exogenous factors, such as age, diet, geography, lifestyle, intake of drugs and host inflammation.

So, when a relevant impoverishment of the microbial biomass occurs in the large bowel, that significantly influences colonic propulsion capacity. It should be noted that the action of fibers and prebiotics is not due to a “mass” effect resulting from a recall of water produced by the polysaccharide molecules of which they are made up, but their action, which favors evacuation derives from the fact that they constitute the main metabolic substrate for the colon microbiota, that, as we have seen, the biomass which constitutes the dry weight of the feces. Moreover, colonic dismotility may be the direct consequence of intestinal dysbiosis, independently by change in the intraluminal content volume, because function and neurolastility of the Enteric Nervous System are influenced directly by colonic microbiota: butyrate may affect neurochemical coding of myenteric neurons and the contractile activity in the rat colon upon long-term exposure, can speculate that a deficiency of butyrate in the gut lumen, inducing alterations in cholinergergic neurons of myenteric plexus, is only an example among many how colonic motility can be influenced by microbiome imbalance.

In summary, for the same “contractile” capacity of the bowel, when the content is made up of Scarce and fluid fecal material, the efficiency of the oro-aboral transit is profoundly different, if compared to a voluminous content with pasty consistency. It can be said that an empty colon has no motor activity and this is very important for explaining many cases of constipation in patients where disturbances of defecation came after profound imbalance in diet habit or antitonic consumption. Intestinal evacuation, which is necessary to eliminate metabolic products that would otherwise be harmful and toxic for the body, is nothing but the mechanism, necessary but not sufficient, to maintain a balance of microbiota that dwells and develops in our gut, as a result of a real production process, a sort of “anaerobic bioreactor” contained particularly in the large bowel. It follows that the primary objective of every therapy for constipation is certainly to achieve defecation but not di per sé, but as a way of rebalancing the ecosystem in the intestinal lumen. In an our study, we demonstrated that in a population of patients with severe functional constipation it was enough to restore a regular colonic content using a symbiotic product for improving defecation disturbances. An efficient intestinal evacuation requires a total coordination between effort and relaxation of the pelvic floor muscles and anal sphincters. It is not surprising to verify how is frequent a disorder of this area when considering that the ability to control bladder and bowel emptying is the last function that the Homo Sapiens “cub” learns: children start walking and talking before being able of avoiding micturition and defecation at inappropriate times and before diaper weaning. Acquiring this ability means having the encephalic and medullary centers of both the CNS and the ANS well organized in order to control the same muscle-fascial structures of the abdominal wall and of the pelvic floor, so that they can first be effective at “retaining”, containing urine, feces of various consistency, gas, and then efficient at expelling them at chosen times, thus ensuring a complete emptying. An Obstructed Defecation can derive from a paradoxical contraction of the puborectalis muscle and/or an abdominal-perineal dyssynergy, so that the pressure increase indispensable to expel is not achieved; or it can derive from structural alterations that mechanically hinder the expulsion of fecal content: a bulging of the wall of the rectum (rectocele), a pathological descent of the perineal plane, or a rectal prolapse or intussusception are the conditions that hinder efficient evacuation, sometimes up to completely prevent it. Hence derives the need to “open” the way to the expulsion of fecal content with suppositories, enemas, manual maneuvers and the assumption of particular postures. Continuous vicious circles exist between functional and structural alterations, so that the onset of one worsens the second and so on.

ASSESSMENT

A meticulous clinical history and a proctological evaluation, better if complete with an anoscopy, make it possible, in most cases, to gather all necessary elements for a correct framing of the constipation form. The execution of a rectal exploration, first digital and then with a disposable rectoscope, without any preparatory cleaning, is very useful in these cases because it allows to identify the presence of feces in the rectum: knowing the time from the last evacuation, it can be deduced if the rectal coprostasis is a consequence of incomplete emptying, if this has happened in a short time. Or it can signal a problem of visceral sensitivity if the last evacuation has taken place previously, at a considerable distance, and the presence was not perceived by the patient. The clinical and anamnestic evaluation is sufficiently precise when the “alarm” symptoms/signs mentioned above are not present. In the presence of one or more signs, a specific clinical and laboratory diagnostic pathway is necessary to exclude the aforementioned pathologies and other possible organic causes of the evacuative disorder.

Other forms of investigation that allow acquiring further elements of distinction between the physiopathological mechanisms at stake in a constipation are certainly the defecography and the ano-rectal manometry. They provide useful elements only if carried out by expert hands and according to specific execution protocols which, unfortunately, are almost never the “standard” ones in Radiology and Gastroenterology units, not dedicated to this pathology. A clear example is the ano-rectal manometry performed with a technique that does not allow recording the pressure increase that occurs in the upper rectum during the abdominal pressure, the evacuative effort. The lack of this element does not allow recognizing and classifying the type of dissynergic defecation. Other investigations are the rectal balloon expulsion test and the perineal and anal sphincter electromyography, but the same applies: they provide useful elements only in expert hands and when the indication is very clear. Investigations such as the study of the intestinal transit time using radiopaque markers are not of widespread use because their clinical value depends on the technique used, on a documented bowel diary and on the inclusion in a very specific therapeutic program.

PHARMACOLOGIC THERAPIES FOR CONSTIPATION

Supplements, drugs, devices, dietary schemes, behavioral indications, rehabilitation programs, psychological treatments or treatments with water could fill up an endless list.
Perhaps no other condition boasts as many "cures" as constipation. Many of these approaches have never been subjected to a rigorous scientific evaluation, but are spread by word of mouth about constipation therapy and, maybe even more, about desperate search for solution, since defecation disorders, along with scarcity of integrated, competent and dedicated responses by public hospital facilities, may cause such an incredible impairment of Quality of Life.

The medical "arsenal" is very wide, even if restricted to products and devices supported by evidence of effectiveness. Certainly macrocol 3550 or 4000 products are useful: at high doses to resolve "blocks" and important fecal retentions; in small doses to guarantee optimal fecal consistency and easy evacuation. Also the stimulant laxatives are useful: picosulphate, senna products, cascara, etc. may effectively stimulate the propulsion of the colon. However, entrusting the solution of constipation exclusively to these drug intake does not make sense, but their use can be beneficial and irreplaceable, when in combination with other strategies. It is difficult to understand why laxatives from herbalist's shops, markets, or "natural" product stores, are preferred to the products which are proposed by pharmacies and so subjected to strict tests of tolerability, definition of the right dose and reliability of the preparation technique. The alleged "naturalness" of the non-pharmacy product often hides big problems of bioavailability, purity, dose-dependent efficacy, presence of additives and other substances with counterproductive effects.

There are also products based on soluble dietary fiber (psyllium derivatives, glucosammins and many others): the axiom that constipation equals fiber deficiency and, therefore, requires a diet rich in fruit, vegetables and bran supplements, has persisted for too long and is only based on common myths, although there is no doubt that these treatments can have positive effects in many forms of constipation, particularly when an impoverishment of colon microbiota occurs so compromising a regular "stool production", as we have already discussed. The same goes for products based on alive bacteria, the probiotics, and prebiotics such as FOS, inulin and others. Systematic review and meta-analysis still struggle for finding clear evidence of efficacy of probiotics in chronic constipation, but this may be due to the methodological approach of the studies since the rationale for its beneficial action is too strong. The best is probably their combination with other strategies (laxatives, prokinetic drugs). It is already possible to distinguish between toxic and non-toxic products, so permitting to reduce them. If oral therapy is ineffective, many people with constipation often use enemas, rectoclysis, or colon hydrotherapy sessions. Even these approaches are often not decisive, but they are undoubtedly useful to remove stagnant contents from the large intestine and to allow the colon to bear a poly-therapy specifically aimed at rebalancing the intestinal microbiota, which, in the early stages, may be burdened by swelling, pain, irregular evacuation frequency and persistent obstruction symptoms. These disorders lead the patient to suspend therapy before time, since the effects are possibly beneficial, but often unbearable, in the long term. Hence derives the usefulness of guaranteeing an "artificial" evacuation through different Trans Anal Irrigation (TAI) approaches that make use of sophisticted "constant and controlled positive pressure" systems: water is introduced by positive pressure, unlike the atmospheric one (as used for rectoclysis), not intermittently (as for enemas and washing syringes) and adapted to the single patient. TAI with these devices, initially exclusive for patients with forms of constipation secondary to neurological pathologies, is proving to be useful also in the most severe functional forms and in forms arising after destructive operations of the pelvic organs.

WHAT ABOUT DIET, REHABILITATION OF PELVIC FLOOR, BIOFEED-BACK, SURGERY?

Patients are more and more confused about "nutrition", and so are the therapists who prescribe restrictions that are often unbearable and meaningless. As regards constipation di per sé, when not associated with the symptoms of other functional diseases, such as Irritable Bowel Syndrome, or allergies and intolerances well documented by laboratory and instrumental tests, the diet regime to follow is the mediterranean diet. Eliminating components from our traditional diet, for fear of other pathologies (off with harmful fats!) or increasing others in the hope of relieving constipation (eat more fruit and vegetables!) results in an imbalance of the intestinal microbiota and an impoverishment of its richness and stability, with a higher prevalence of certain bacterial groups and pathological consequences, including constipation and abdominal discomfort: whenever this approach could be therapeutic for the same disorders? Pelvic floor rehabilitation techniques and biofeedback, in experienced hands and for well-selected forms of constipation, are unquestionably useful. The same applies to surgical operations aimed at resolving the pathologies that cause mechanical obstruction to stool passage and expulsion. There is no doubt indication for surgical repair in a woman with a rectal prolapse/intussusception or a large anterior rectocele, which formed over time after difficult childbirths, and after years of food errors and evacuation effort due to hard stools is correct. But also in this case, operation will not be so succeed if not preceded and followed by restoration of a normal stool consistency and volume, since hard stools are expression of dysbiosis and dysmotility of the colon, as well as pathological stagnation in the sigmoid due to the incomplete evacuation.

In recent years doubts have arisen over the indication of major surgery, such as total colectomies or extensive resections, without any detailed documentation of ENS alterations. These interventions are usually a last resort when previous surgery was not useful. It is probably too early for including the Fecal Microbiota Transplantation (FMT) among the therapeutic options for chronic constipation, even if this approach has been already tested. We have seen that the human gut microbiota is not a mere assembly of microorganisms, but a highly organized integrated network of cells interacting intensely with each other as well as with the host, which could be thought of as an additional organ within the human body. Based on the available literature, the possibility of transferring this organ from a healthy individual, i.e. endowed with a high-diverse intestinal microbiota, to an individual whose microbiota is impoverished, unbalanced and unable to oppose the action of pathogens, has proved to be highly effective and statements on FMT indications, donor selection, preparation of
fetal material, clinical management and fecal delivery, and basic requirements for implementing an FMT centre are already well established\(^1\). The first and most documented clinical application of FMT is recurrent Clostridium difficile infections (rCDI) in which it is currently used as a last-resort treatment after failure of multiple courses of antibiotics\(^2\), but beyond rCDI, FMT has been explored in a treatment option in a variety of gastrointestinal diseases, such as Inflammatory Bowel Diseases\(^3,4\), non-alcoholic steatohepatitis, alcoholic hepatitis, hepatic encephalopathy\(^5,6\). The evidence that FMT can be useful in the treatment of disorders as Irritable Bowel Syndrome\(^7\) and constipation is very interesting, confirming what we have discussed, i.e. in this disorder intestinal dysbiosis and altered interaction with gut mucosa are pivotal. Moreover, extremely interesting it is that manipulation of gut microbiota through FMT seems to disorder intestinal dysbiosis and altered interaction with gut mucosa are pivotal. Since it is clear that intestinal dysbiosis may contribute to the pathogenesis of many diseases, FMT is increasingly being explored as a potential treatment that aims to optimize microbiota composition and functionality\(^8,9\).

CONCLUSIONS

Constipation, it is a syndromic condition, not life-threatening unlike other diseases of the digestive system, such as cancer, inflammatory diseases, hepatitis, peptic ulcer, etc., but it causes suffering and undermines Quality of Life often more than these. It is common and burdened by entails huge social costs for treatments, examinations, hospitalizations and work capacity impairment, especially in countries with high standards of living. It recognizes a very complex etiopathogenesis in which both underlying pathophysiological mechanisms and therapeutic approaches - that are attempted, assumed and then abandoned, in inextricable cause-effect circles - play an equally important role. Constipation is not considered a significant health problem, so there are no specifically dedicated centers in Italian hospitals. In order to seek solutions, the patient has to contact a specialist, who, even if he/she is the right choice in terms of cultural knowledge and clinical experience, will hardly be able to work with a team that integrates all the skills needed for diagnostics and a global approach to the patient with constipation illness.

REFERENCES

17. Sant’Anna MSL, Ferreira CLLF. Can intestinal constipation be modulated by probiotics, prebiotics and Symbiotics? Food and Nutrition Sciences 2014; 5: 1106-1113.
18. De Giorgio R, Blandizzi C. Targeting Enteric Neuroplasticity;

Acknowledgments
The Authors are indebted to Dr. Cecilia Baroncini, Scientific Office of the Montecatone Rehabilitation Institute, for the secretarial assistance.

Disclosure
There were no conflicts of interest and the authors of the publication did not receive any financial support by any grant/research sponsor

Correspondence:
Prof. Gabriele Bazzocchi, MD, Ph.D, AGAF
gabriele.bazzocchi@unibo.it
Dr. Mimosa Balloni, MD mimosa.balloni@montecatone.com
NeuroGastroenterology and Intestinal Rehabilitation Unit, Montecatone Rehabilitation Institute S.p.A., via Montecatone 37 Imola, BO, Italy