

The opioid epidemic. A new challenge for AIDS

La epidemia de opiáceos. Nuevo reto para el SIDA

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Intravenous drug use was the commonest means of contagion of HIV and thus of AIDS in Spain from the outbreak of the epidemic until 2010, although this had become a minority form of transmission in recent years. Hence, in 2015 there were 81 cases of AIDS in Persons who Inject Drugs (PID), in comparison with 205 by heterosexual transmission, 198 in Men who have Sex with Men (MSM) and 11 in the “others/N.A.” group. If on the other hand we observe the figures for newly diagnosed persons infected that same year, PID represent only 2.8% of the total in comparison with 53.6% for MSM, 25.4% heterosexual transmission (HT) and 17.6% in the “no answer” group.

In the U.S.A. however, a new phenomenon is occurring, with the appearance of a real epidemic in the use of opioids which kills 142 people a day and has led President Trump to recently declare a public health emergency, to last 90 days.

Only a few days ago a top-level conference was held, the “*America’s Opioid Epidemic: From evidence to impact*” summit, at the Johns Hopkins-Bloomberg School of Public Health last 30 October, where the importance of the crisis occurring in American society through the proliferation in opioid use was highlighted, with 64,000¹ dying from overdoses, a record which is increasing every year.

“If these figures are confirmed”, said ex-President Bill Clinton, who opened the Conference, “this would mean that last year more people died from overdoses than at the highest point in the AIDS epidemic, before we had any treatments available”. Opioids represent the primary cause of death for people under 50 years of age in the U.S.A. and since 2008 have caused greater mortality than car accidents. Today the epidemic means not only a public health

¹ Provisional data of the CDC.

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problem but is also affecting the economy and even entails a challenge to national security.

Prescription of opioids by doctors started to become widespread from the 1990s (Felter, 2017), as until that time these were used only for assuaging post-surgical pain or in cancer treatment. Since roughly 15 years ago, however, they started to be prescribed for other chronic ailments, such as back or articular pain or others, in spite of the problems associated with these. One must bear in mind that around 25 million people suffer chronic pain daily and 2 million Americans are opioid addicts.

The fight against this huge problem is mobilising the vast American research potential of the National Health Institutes, from basic science of the complex neurological pathways involved in pain and addiction, to models of treatment and service provision, integrating behavioural interventions with medication therapy, in an attempt to find treatments for pain that are not addictive (Collins, 2017).

To confront the epidemic with better prospects and tools, last year the American Senate passed a law, the Comprehensive Addiction and Recovery Act (CARA), signed in July by President Obama, who included a heading of 1100 million dollars in the 2017 budget for freer access to evidence-based practice, including treatment accompanied by medication, using methadone, buprenorphine or injectable naltrexone (Williams and Bisaga, 2016).

Although financing is highly important, it is not the only part of the fight against the epidemic. A review of regulations and services is needed in an attempt to connect marginal populations with the programmes and teams using modern methods to deal

with the serious problems generated by the use of opioids.

It should be borne in mind that treatment centres are often governed by outdated institutional ideologies which still uphold the idea of abstinence, the model of the mid-20th century based on alcoholism treatment. For this reason the authors conclude that the American system is ill-prepared to face up to the current epidemic. They stress the fact that in 40% of America's counties there is no doctor authorised to prescribe buprenorphine and that the authorised ones deal with few or no patients. For this reason they advocate an integration of the services for treating addictions at primary care centres, even while being aware that this will not attract marginal populations, who are totally disconnected from the healthcare system.

This dramatic situation affecting a large proportion of the rural population was already described a couple of years ago in the editorial written by us in this same journal, in which we referred to the HIV outbreak in Indiana.

Deaths due to overdoses, according to preliminary studies (O'Donnell et al., 2016) as already mentioned, represented a total number of 60,000 in 2016 partly being caused by a five-fold increase in synthetic opioids, soaring from 3105 deaths from overdoses in 2013 to 20,000 in 2016. This rapid increase was mainly due to illegally produced fentanyl² and also to fentanyl analogues, such as acetyl fentanyl, furanylfentanyl and carfentanyl³, which are increasingly being related with overdose deaths.

2 Fentanyl is a synthetic opioid 50 to 100 times more powerful than morphine.

3 Carfentanyl is estimated to be 10,000 times more powerful than morphine.

This information is collected by means of the State Unintentional Drug Overdose Reporting System (SUDORS), the component of CDC's Enhanced State Opioid Overdose Surveillance (ESOOS), designed to monitor deaths by opioid overdose and in this case the data is from the ten states participating, but is being extended this year 2017 to 33 States and the District of Columbia.

Fentanyl and its analogues are highly powerful and fast-acting synthetic compounds which can lead to unconsciousness and death, thus requiring immediate treatment with high doses of naloxone. They are so potent that even when administered other than intravenously, inhaled or smoked, these are responsible for one fifth of the deaths caused.

It should also be remembered that although we have described the problem in the U.S.A., this should be seen as part of an international setting. Opioid consumption has increased worldwide from 1980. For example, from 2000 to 2010, consumption rose 400% in the U.S.A. in comparison with 65% in Great Britain and 37% in Germany. In Spain, according to García del Pozo et al. (2008) from 1992 to 2006 the increase was fourteen-fold.

The U.S. population consumes roughly 80% of the world production of opioids (Manchikanti and Singh, 2008). Hauser et al., 2016) estimate that 90% of the world's production of morphine, fentanyl and oxycodone was consumed in the U.S.A., Canada, Australia and New Zealand in 2009 and that in those same years, the U.S.A. consumed from 83 to 99% of the oxycodone⁴ and hydrocodone⁵ available.

4 Oxycodone is an analgesic opioid, effective when taken orally, very powerful and potentially addictive. It is synthesised from thebaine.

5 Hydrocodone is an opioid derived from codeine, which is used as an oral analgesic to treat moder-

COINFECTION WITH HIV AND HEPATITIS C (HCV)

It is quite clear that the huge epidemic of drug addicts which has been increasing over the last 15 years entails a great risk of infections such as HIV and HCV, as the most important of these.

According to the WHO there are estimated to be 2.3 million persons living infected with HIV and HCV, over half -1.3 million- of whom are people who inject drugs, meaning that people infected with HIV are six times more likely to be infected by HCV than those not infected.

In all there are estimated to be 37 million people in the world infected by HIV and 115 million with HCV virus antibodies (Platt et al., 2016). The high prevalence of HCV infection becomes specially significant in PID, coinfection. Hence, if this reaches 2.4% in the general population of the sample, it rose to 6.4% of MSM and 82.4% of PID, being particularly high in Eastern Europe and Central Asia.

The HIV and HCV outbreak mentioned above, taking place in the small area of Scott County, Indiana (U.S.A.) took place when a large number of people in this small rural area started to inject themselves with opioids, sharing the injection equipment. This led to an outbreak of HCV, which at first went unnoticed but which was followed by another outbreak of infection by HIV. The situation went from involving 5 infections of HIV per year in the period from 2004 to 2013 to 181 cases in a single year

ate to severe pain and as an antitussive. It can be found in tablets, syrups or capsules and is a narcotic which may produce dependence and serious withdrawal symptoms.



and furthermore over 90% of the people infected with HIV during the outbreak were also infected by HCV. This outbreak was the factor triggering off reflection on the close relationship between the use of opioids and HIV and HCV. It led to considering the need to have a system for early detection of an increase in the frequency of HCV infections as a marker of what could then prove to be an HIV outbreak. In this respect the CDC carried out a study using data from different sources to evaluate other rural locations which could be at a similar risk to that of Scott County and managed to individualise 220 counties in the U.S.A. (5% of the counties would be vulnerable) which could undergo similar outbreaks if preventive measures are not taken.

A piece of research performed by Joan Duwve⁶ (2015) based on interviews made by Public Health specialists on PID in Austin found that injecting drugs resulting from prescribed opioids had become usual practice in some families, including up to three generations of one family and with several members of the community injecting the drugs together. "The practices consisted in grinding and heating up 40 mg oxymorphone tablets. The syringes and the whole injection equipment were generally shared". "The drugs were dissolved in non-sterile water and transferred to insulin syringes which were normally shared with others". The daily number of injections ranged from four to fifteen and the number of participants in each session also varied from one to six.

6 Joan Duwve is the Associate Dean of Public Health Practice at the Richard M. Fairbanks School of Public Health at the University of Indiana - Purdue University, Indianapolis.

It should be considered that the vulnerable counties are made up of a mostly white population with very high unemployment and poverty rates and even higher rates of deaths from overdoses and without the minimum infrastructure required for facing up to an epidemic of this kind, which Michael Botticelli⁷ called "treatment deserts". We should be aware that in spite of the calls from the CDC to implement the required measures nationwide there are no federal or state plans indicating that work is being done in the right area (Ehley, 2017). Botticelli furthermore acknowledges that thanks to the Affordable Care Act of 2010, there has been an extension of Medicaid, which has enabled extending access to treatment of addictions.

Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases of the National Institute of Health, has remarked "we are very likely to be seeing the start of other similar outbreaks of HIV connected with the use of drugs, as there is no particular difference between the Indiana community and many others all over the country". The Director of the CDC, Thomas Frieden, has qualified the Indiana outbreak as a "sentinel event", since it only represents the tip of the iceberg of the drug abuse problem.

It is worth remembering that the current Vice-President of the United States, Mike Pence, was the Governor of Indiana when the outbreak described took place, and opposed getting under way the programmes for exchanging syringes recommended by the CDC to prevent the spread of HIV and HCV infections among patients who inject drugs (PID). Though it may appear unreal, even now, after

7 Michael Botticelli was the Director of the White House Drugs Policy during President Obama's administration.

the Scott County experience, programmes for exchanging syringes are not generally accepted. There are two counties in Indiana, Lawrence and Madison which have decided to close the programmes since, according to the members of the Local Council, these schemes “promoted the use of drugs”. In Kentucky, 54 of the 120 counties are on the list of the ones considered as being high-risk for outbreaks of HIV and only 20 allow needles to be exchanged.

And yet, when the right measures were implemented to contain the outbreak, the response was very positive. It was quickly halted, by getting under way a coordinated measure of the Indiana State Public Health department and the local authorities: treatment, laboratory tests for HIV and HCV, education for health, antiretroviral medication for treatment and prevention and syringe exchange programmes, all not previously available.

All this led to starting up a plan, the National Viral Hepatitis Action Plan 2017-2020 as a strategic framework able to facilitate cooperation between different sectors. This involves extending the programme which was carried out in the aforementioned outbreak in Scott County to a federal scale in order to stop the epidemic of opioid use, the outbreaks of HIV and HCV along with the disease, the misery and deaths occurring in the U.S.A..

There were 34,000 new annual cases of HCV in 2015, three times the ones seen in 2010, and yet the new HIV cases went from 45,000 in 2008 to 37,000 in 2014 and PID represent approximately 10% of the new cases annually. Nevertheless, and in view of the characteristics described, in many communities, especially in the rural environment, there is great scepticism about these figures and there are probably quite a lot more HIV

infections as there are no facilities to carry out the proper analyses and on the other hand there are a lot of people who do not make it easy to have the research carried out on them. For all these reasons, these critical voices such as that of Hiram Polk, Kentucky State Health Commissioner, indicate that the test is implemented on a very limited scale and that the figures of those infected are not thus very credible.

The CDC itself, as acknowledged by Debra Houry, Director of the National Centre for Injury Prevention and Control, which has designed programmes for exchanging syringes, connected with treatment based on therapeutics, laboratory analysis programmes for HIV and HCV and naloxone administration, admits that these programmes are not available on a widespread basis, there only being 221 programmes for swapping syringes.

There is a need for programmes integrated on a federal scale, assumed by the States that cover the following in a combined effort:

- Syringe exchange programmes.
- Substitution therapies, such as methadone or buprenorphine.
- Programmes for teaching users about safe injection practices and preventing overdoses.
- Making naloxone available.

It should finally be mentioned that this interrelation between the use of opioids and HIV and HCV infections has been called an “opioid syndemia”. The syndemic theory was introduced by anthropologist Merrill Singer over one decade ago to explain how epidemics interact with each other, increasing the risk of several of these.



RECENT PROGRESS

The recent publication (Wadman, 2017) of the development of “biased opioids” as safer drugs to fight pain brings in a new way to counter mortality from overdoses, resulting from either medication or drug addiction. These deaths take place through breathing suppression (apnoea), which tends to lead to death. The drugs act on neuronal receptors to relieve pain which also control breathing, slowing this up and even halting it. The idea for fighting against the problem of overdose deaths would involve developing medications able to act with the analgesic power of opioids but reducing their effect on breathing. In this respect last 2 November a firm known as Trevena from Chesterbrook in Pennsylvania presented the Food and Drug Administra-

tion (USA) with a product called Oliceridine, (trade name, Olinvo) an intravenous opioid for hospital use (Figure 1). Other products in the same line are also currently being developed (Schmid et al., 2017).

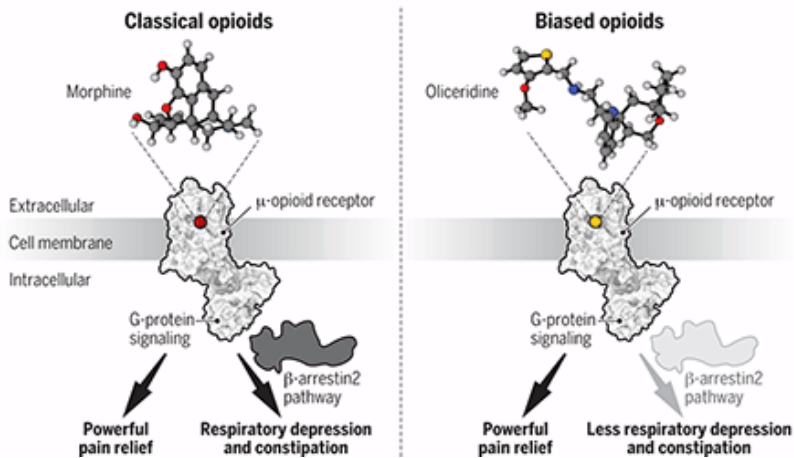
CONCLUSION

This whole problem is bringing to light the situation of medical care and Public Health in the U.S.A., where the most advanced medicine in the world coexists with the dearth of medical care or very mediocre medical care in a large part of the country, mainly in the rural environment. It is associated with a mostly unemployed population in these areas, with the poverty, lack of healthcare infrastructure, discrimination and social abandonment characterising the many towns and villages

Figure 1. New opioids with less respiratory depression, oliceridina (Olinvo, of Trevena)

Bias toward breathing

A new generation of opioids aims to stall the signaling that is thought to shut down the lungs during overdoses.



Source: *Science* 358 (6365), page 848, 17 November 2017. Reprinted by permission of *Science* magazine.

abandoned from the healthcare and social standpoints, where the measures for fighting addiction, based on outdated and reactionary concepts, are furthermore jeopardising the very structure of Public Health in the country.

In Spain we fortunately have a universal medical care system and a Public Health system which in theory extends to the whole population. We should not however overlook the existence of marginal populations where a similar phenomenon could arise, which should make us conceive and implement surveillance systems specially addressing marginal populations.

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