Scientific Research Publishing

Open Journal of Internal Medicine, 2023, 13, 181-208
https://www.scirp.org/journal/ojim
ISSN Online: 2162-5980
ISSN Print: 2162-5972

# Capacity Development of National Reference Centers (NRC) to Face the Challenges of Emerging Infections in Côte d'Ivoire

**Diané Kouao Maxime[1,2*], Adjogoua Edgard Valery[1,3], Coulibaly Ngolo Antoine Marie-David[1,4], Kadjo A. Hervé[1,3], N'guessan Kouassi Raymond[1,5], Sylla Yahaya[1,3], Anne Blessa Jean Claude[1,6], Beourou Sylvain[1,7], Guessennd-Kouadio Aya Nathalie[1,8], Dosso Mireille[1], Tiembré Issiaka[9]**

[1]Pasteur Institute of Côte d'Ivoire, Abidjan, Côte d'Ivoire
[2]Biological Resource Center, Abidjan, Côte d'Ivoire
[3]Epidemic Virus Department, Abidjan, Côte d'Ivoire
[4]Molecular Biology Platform, Abidjan, Côte d'Ivoire
[5]Mycobacterium Tuberculosis Unit, Abidjan, Côte d'Ivoire
[6]Clinical Bacteriology Unit, Abidjan, Côte d'Ivoire
[7]Department of Mycology Malariology, Abidjan, Côte d'Ivoire
[8]Antibiotics Unit, Abidjan, Côte d'Ivoire
[9]Department of Public Health UFR Medical Science, Université Félix Houphouët-Boigny, Abidjan, Côte d'Ivoire
Email: *dianekouao@yahoo.fr

**How to cite this paper:** Maxime, D.K., Valery, A.E., Marie-David, C.N.A., Hervé, K.A., Raymond, N.K., Yahaya, S., Claude, A.B.J., Sylvain, B., Nathalie, G.-K.A., Mireille, D. and Issiaka, T. (2023) Capacity Development of National Reference Centers (NRC) to Face the Challenges of Emerging Infections in Côte d'Ivoire. *Open Journal of Internal Medicine*, **13**, 181-208.
https://doi.org/10.4236/ojim.2023.133021

**Received:** July 9, 2023
**Accepted:** September 3, 2023
**Published:** September 6, 2023

Copyright © 2023 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Open Access

## Abstract

**Background:** Some national and international strategies for the detection and prevention of emerging infectious diseases have been established across sectors. The capacity to carry out these tasks varies from country to country, and that remains largely undervalued. The Pasteur Institute of Côte d'Ivoire has created and implemented the ***capacity of national reference centers*** to fight against emerging and other infectious diseases. **Objective:** Show on the one hand the strategies used to develop the National Reference Centers and the IPCI and on the other hand the results obtained by performing these strategies. **Method:** Datas collection by documentary analysis (published scientific articles and grey literature) was done on Google Scholar, PUBMED and institutional reference documents. The documentary research was carried out to have a better understanding of strategies used to create and develop the NRCs in microbiology of communicable diseases. **Results:** Seven integrated strategies were launched: 1-training and workforce development; 2-investigation of epidemics or public health events; 3-strengthening laboratory epidemiological research; 4-strengthening surveillance systems; 5-improving communication with partners and stakeholders; 6-building national and international collaborations; and 7-strengthening technical and technological platforms. In

two decades, the number of researchers has risen from 10 in 2004 to ninety (90) in 2021, with 12 senior researchers and 32 junior researchers. A number of health service staff had attended a qualifying training course, 27 investigations into outbreaks and other public health events had been carried out, 18 short-term research projects had been launched, major surveillance programs and epidemiological research efforts on vector-borne, food-borne and nosocomial infections had begun, and several scientific manuscripts had been published or were edited in the writting press. **Conclusion:** The Ivorian experience shows that, with concerted effort, considerable progress can be made in the development and implementation of an infectious disease control program.

## Keywords

Evaluation, Communicable Diseases, National Reference Centerorlaboratorie, Capacity Development, Côte d'Ivoire

## 1. Introduction

Microbiology laboratories play an important role in the management of infectious diseases in terms of national or global epidemiology [1]. The main objective of these medical analysis laboratories is to optimize the analyses which make it possible to improve the diagnosis and the prognosis and to make the therapeutic management of the patient more efficient.

National and international strategies for the detection and prevention of emerging infectious diseases have been created in the civil and military sectors [2] [3] [4]. However, epidemiological capacity at national, regional or state and local levels is required to successfully implement many of these strategies. [3]. Health officials conduct increasingly complex outbreak investigations, implement and analyze new surveillance systems, and conduct sophisticated applied epidemiological research [3]. Unfortunately, the ability to carry out these tasks varies from country to country and remains largely undervalued. In 2006, Cote d'Ivoire set up National Reference Centers (NRC) and began to strengthen its epidemiological capacity to respond to emerging infectious diseases [5].

This article aims to report on the one hand the strategies used for the development of the national reference centers of the IPCI and on the other hand the results obtained.

## 2. Context

Côte d'Ivoire is a developing west African country with seaside resorts, tropical forests and a French colonial heritage with 27.48 million inhabitants [6]. Primary responsibility for public health rests with the state health ministry and approximately 33 regional health directorates and 101 local health departments.

The Pasteur Institute of Côte d'Ivoire (IPCI) is a health research institute un-

der the supervision of the ministry of scientific research and higher education. Although the IPCI has built a strong tradition of infectious disease epidemiology in Côte d'Ivoire since its creation in 1972, this tradition was largely unrecognized in the 1970s to 2000s.

Significant obstacles have hampered the further development of applied infectious disease epidemiology in Côte d'Ivoire. Almost all outbreak investigations have been conducted at the local level; however, local health officials had little or no training in applied infectious disease epidemiology. Little infrastructure existed to investigate outbreaks, and No microbiology laboratory was recognized as a reference in terms of diagnosis and microbiological monitoring.

In 2005, with the help of the PEPFAR project, IPCI and representatives from the Ministry of Health developed the concept of a network of collaborating laboratories, with the aim of intensifying epidemiological research and improving infectious disease surveillance. Within this context, in June 2006, inter-ministerial decree No. 393 of June 21, 2006, signed by the minister of higher education and scientific research and the minister of health and hygiene, designated the national centers for institute reference (**Table 1**). This text concretizes the recognition of the work carried out by the staffs of the establishment for many years. It's also a heavy responsibility that will require better organization and coordination of these centers starting in 2007.

This has made it possible to develop and define the missions and activities of national reference laboratories, train infectious disease epidemiology teams, and create laboratory and stakeholder networks able to collate existing public health data, identify deficiencies and collect additional data where necessary.

## 3. Program Objectives, Strategies and Results

### 3.1. General Approach

The overriding objective of the health authorities was to establish a sustainable national epidemiological capability in the fight against communicable diseases. The initial priorities of the NRCs were to develop the capacity to identify and respond to epidemiological emergencies, to conduct applied epidemiological research and to assist the Ministry of Health in carrying out its activities and developing their own epidemiological programs.

Six (6) missions [5] have been assigned to the NRCs and constitute their core business: expertise in the biology of infectious agents; contribution to epidemiological surveillance; alert by immediately informing the authorities of any finding that could have repercussions on the state of health of the population; microbiological monitoring of infectious agents; conservation and contingency of infectious agents; advice to public authorities and health professionals in this area.

The IPCI's NRC activities can be broken down as follows:

*Surveillance: Most NRCs are involved in epidemiological surveillance, resistance monitoring or epidemic investigations.

**Table 1.** Infectious agents and clinical syndromes important to health for which there are national reference laboratories in Côte d'Ivoire.

| bacteria | Virus |
|---|---|
| 1. Cholera and Shigellosis<br>2. Bacterial meningitis<br>3. Salmonella<br>4. Tuberculosis<br>5. Buruli ulcer | 1. Poliomyelitis<br>2. Influenza and respiratory virus<br>3. Measles<br>4. Yellow fever<br>5. Hemorrhagic fevers<br>6. Rage<br>7. Viral liverworts |
| Parasites and fungi | Diagnosis of pathogens |
| 1. Malaria drug resistant<br><br>Syndromes<br><br>1. Agents of sexually transmitted infections<br>2. Diarrhea virus | 1. Evaluation of microbiological diagnostic tests<br>2. Observatories of resistance of microorganisms in Côte d'Ivoire (ORMICI)<br>3. Biological control of antimicrobial vaccines<br>4. Ivorian Network for the Investigation and Surveillance of Nosocomial Infections (RIISIN)<br>5. Molecular typing of infectious agents |

*Expertise: IPCI NRCs are requested for their expertise in case confirmation, evaluation of new diagnostic tests, support for health programs, development of tools and guides, and microbiology training. All CNRs are equipped with conventional techniques and use molecular tools. So Expertise in molecular techniques makes the NRCs competitive at national level.

*Alert: The IPCI was actively involved in the first detection of new viruses in the country, notably the avian flu virus and the first case of SARS COV2 in 2020.

*Consulting: IPCI has been asked to participate in the development of control measures for the Ministry of Health and Public Hygiene. Many practitioners turn to IPCI for advice on antibiotic therapy.

The study used two data collection methods: a documentary analysis and in-depth qualitative interviews, respectively, to achieve the study objective.

The data collection method of a literature review and an in-depth qualitative interview, respectively were done. The literature search was carried out to better understand the design and development strategies of NRCs in communicable disease microbiology. This enabled a global understanding of issues relating to the West African region and particularly the Ivory Coast concerning current NRCs. The literature review included published articles, national reports, organization reports and data and information sheets. These articles were consulted using search engines such as Google Scholar and Pubmed, using a snowball effect and including any reference documents and grey literature that would provide a better understanding of the situation. IPCI annual activity reports from 2006 to 2021 were consulted.

To further explore the points raised by the literature review, a follow-up semi-structured interview was conducted with IPCI management and heads of laboratories involved in the implementation process. This enabled the challenges

and enabling factors highlighted in the literature review and survey questionnaire to be explored in greater depth.

All data collection was carried out in French, the official language commonly used in Côte d'Ivoire. The two-stage process of survey and interview enabled better triangulation of data and guaranteed its quality. Data collection was carried out using Microsoft Excel.

The implementation of these missions was achieved through integrated strategies [3] by the IPCI: developing training programs for NRC staff, investigating epidemics or public health events and epidemiological research; strengthening surveillance systems; improving communications between the IPCI and its partners and stakeholders; and establishing international collaborations (**Figure 1**).

## 3.2. Strategies and Results

### 3.2.1. Training and Workforce Development

The lack of trained staff at the applied epidemiology of infectious diseases has made the training of heads of NRCs in the short and long term a key priority. The long-term program was to develop a group of biologists and epidemiologists (capable of carrying out outbreak investigations, epidemiological research and surveillance) who would later serve as trainers themselves [3].

The short-term training program was designed to equip NRC health staff with the practical skills and understanding needed to conduct and report laboratory activities during an epidemic, and to carry out more complex epidemiological research and surveillance activities in collaboration with national or international epidemiologists. The short-term training program aimed to equip health NRC staff with the practical skills and understanding needed to conduct and report laboratory activities during an outbreak and to conduct more epidemiological research and surveillance activities in collaboration with national or international epidemiologists. An annual short-term training plan consisted of a

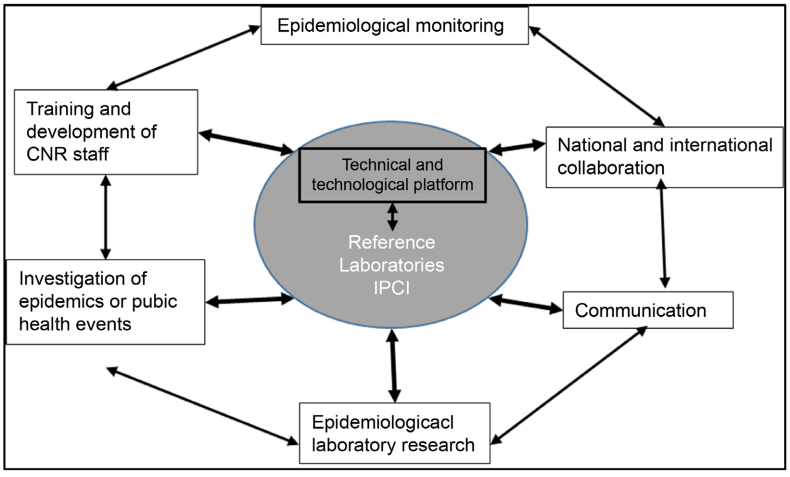


**Figure 1.** Strategic interventions used by the Pasteur Institute of Côte d'Ivoire for the development of the capacities of CNRs in the fight against infectious diseases (Source: Petersen L. R. *et al.* 2000 [3]).

12- to 24-week laboratory applied epidemiology course for public health laboratory managers, designed to impart practical skills (Table 2). This 6 to 12 month training program, known under the name of "cours Pasteur" at the Pasteur Institute in Paris, started in 2005 for the first generation of the IPCI with an intern. Then the heads of NRC each began their training between the years 2000 and 2015.The profile of all these heads of laboratories showed that they are medical biologists and two were biologists. All of these physicians also held a specialized study certificate in medical biology, microbiology option (virology, bacteriology, parasitology) and PhD and PhD biologists. All had to complete at least one outbreak investigation, one surveillance project and one research project, as well as present their work at a scientific conference, participate as trainers in epidemiology courses and write at least one article each in a peer-reviewed scientific journal and in national and international communicable disease journals. To date, 20 heads of laboratories and departments have been trained between 2006 and 2021.

Table 2. Training received by CNR staff reported by the IPCI, 2006-2021.

| Year | CNR | Training site | Training theme |
|---|---|---|---|
| 2009 | Flu | IP Paris | Antiviral resistance testing and sequence analysis |
| 2011 | Flu | IPCI, Abidjan | Laboratory management and virological diagnosis of influenza |
| 2011 | Viral hepatitis | Johannesburg; South Africa | BIOSAFETY training course |
| 2011 | Agents of sexually transmitted infections | IPCI, Abidjan | Preparation of the list and quantification of laboratory needs |
| 2011 | Bacterial meningitis | Center Pasteur Cameroon | Training on antibiograms of the bacteria responsible for meningitis |
| 2011 | Tuberculosis | Algeria | Training of African executives on the diagnosis of tuberculosis |
| 2012 | Flu | Clemenceau Medical Teaching Hospital, Caen (France) | Training on viral respiratory infection diagnosis by molecular technics using respifinder kit, Virology laboratory |
| 2012 | Flu | Pasteur Institute of Paris (France) | Training on influenza virus sequencing |
| 2012 | Flu | WHOCC London (UK) | Training on antiviral susceptibility testing |
| 2015 | Poliomyelitis | South Africa | Biorisque Management/Global Action plan III (GAPIII) Workshop (final phase of poliomyelitis eradication) |
| 2015 | Hemorrhagic fevers | Abidjan, Ivory Coast | Training in molecular techniques for viral hemorrhagic fevers. |
| 2015 | Hemorrhagic fevers | Abidjan, Ivory Coast | Training in quality management in a medical biology laboratory and in biosafety |

Most of the staff in the units that house NRCs work full time as public officials for these activities, in particular case confirmation activities.

The diversification of skills materialized during 2006. The IPCI welcomed health practitioners (doctor, pharmacist, dental surgeon) general practitioner or specialist in public health and epidemiology, technicians specialized in quality control, in Sanitation. This made it possible to implement the epidemiology and clinical research department and to strengthen the capacities of the units, to create cross-functional units: molecular biology platform (PFBM), laboratory input production unit (UPIL), biological resource center (CeReB), training department. The activities of these departments and units have gradually been put in place. It is beginning to assist the Biology teams in developing projects and managing data.

During the second IPCI Scientific Council held from 22 to 23 September 2006, the members of the Scientific Council noted "significant progress with regard to the 2005 recommendations and a better awareness reflected in an internal dynamic within a more motivated and therefore much more committed team".

The efforts undertaken by the researchers and their collaborators have begun to bear fruit, but it is the year 2007 which will truly be a year of progress thanks to the facilities which were put in place in 2006 and at the begining of the year 2007, namely offices, a conference room, an internet connection and internship grants in high-performance laboratories: Canada, France.

Today, several heads of laboratories are experts and consultants of the World Health Organization and other international organizations. The number of researchers has increased from 10 in 2004 to ninety (90) in 2021 with 12 senior researchers and 32 junior researchers 46 junior researchers. Table 3 gave an overview of some of the national and sub-regional training courses that reference laboratory managers have been able to provide on the basis of their expertise.

**Table 3.** Training given by NRC staff reported by the IPCI, 2006-2021.

| NRC | Year | Training site | Training theme |
|---|---|---|---|
| Agents of sexually transmitted infections | 2006 | IPCI, Abidjan | Quality Management in HIV Laboratories for Laboratory Professionals |
| Rage | 2009 | INHP, Treichville of the Communal branch of Yopougon and Port Bouet | building the capacity of technical officers from the National Institute of Public Hygiene (INHP) in the care and monitoring of people exposed to rabies. |
| Buruli ulcer | 2011 | Alepe, Ivory Coast | Training and awareness on clinical diagnosis, collection and delivery of samples to the CNR, |
| ORMICI | 2011 | IPCI, Abidjan | Organization of the regional course for level 1 antibiogram on "Phenotypic techniques for determining antibiotic resistance in bacteria" |
| Poliomyelitis | 2015 | Abidjan | Training of regional health directors, district chief medical officers, district surveillance officers and EPI officers in the methods of collecting and transporting samples to the laboratory |

### 3.2.2. Investigation of Epidemics or Public Health Events

The benefits of developing National Reference Laboratory (NRL) capacity on outbreaks were filling a public health gap in the ability to respond to epidemiological emergencies; develop relationships between the IPCI and its partners, such as clinical health and research laboratories and health departments responsible for surveillance; formulate hypotheses and bases for future research; provide training opportunities; and recognition of public health, epidemiology [3].

In 2006, the first avian influenza viruses in Abidjan were diagnosed at the Pasteur Institute in Côte d'Ivoire from samples sent by the veterinary services. This also testifies to the collaborations that exist with our colleagues in the veterinary services. There is no doubt that this enabled Côte d'Ivoire to take measures very quickly in order to avoid human cases.

Twenty-two (22) investigations of disease outbreaks or public health events requiring field trips were completed, increasing from five (5) in 2006 to three (3) in 2009; 2010 and 2012 then at 1 the other years (**Table 4**). Each survey was carried out at the request and with the approval of the departments responsible for monitoring the National Institute of Public Hygiene (INHP) of the Ministry of Health.

Eleven (11) of these outbreaks were of vector origin: seven (7) were traditional outbreaks due to mosquitoes (**Table 4**, event number 8; 21; 31; 35; 36; 37; 38) and three (3) came from waterborne products (event no. 3; 23; 27). The other outbreaks were due to a diverse group of agents and modes of transmission and covered areas as large as Africa (**Table 4**).

Among the conclusions of these investigations were the recognition of N meningitidis as a potentially common pathogen of human origin (epidemic 2; 10; 15; 28; 32; 40) and the emergence of *N meningitidis W135*, the recognition of multi-resistant bacteria (MRB) infections as an emerging pathogen in Côte d'Ivoire (partly due to the urbanization in the immediate vicinity of farms or grazing areas, the unsanitary conditions of hospitals, the overload of work and use of hospital services, insufficient hospital infrastructure; events 26; 30) and the human rabies virus in localities in Côte d'Ivoire (events 18, 32). Cote d'Ivoire's new epidemiological capacity enabled it to participate in two multinational outbreaks among returnees from overseas travel COVID-19 and Ebola (event 35, 39) as well as communicable disease surveillance organized by the world health organization and the ministry of health (event 7, 9, 11, 13, 16 - 18, 22).

### 3.2.3. Epidemiological Research in the Laboratory

Research activities have been better organized since 2006, there is no doubt that the start of the department of epidemiology has contributed to the drafting of innovative and collaborative projects.

The objective is to create a self-sustaining laboratory applied epidemiological research program focusing on foodborne and diarrheal diseases; AIDS and other sexually transmitted diseases, including hepatitis; vaccine-preventable diseases;

**Table 4.** Epidemics or public health events reported by the national reference centers (NRC) of the Pasteur Institute de Côte d'Ivoire (IPCI), 2006-2021.

| No. | Year | CNR | Range/Extended | syndromes | Pathogens | Number of cases | Commentary (publication reference) |
|---|---|---|---|---|---|---|---|
| 1 | 2006 | Malaria drug resistant | national | Diagnostic test | Plasmodium falciparum | 6 tests assessed including 4 retained | BCP Malaria, CareStartTM Malaria pLDH, Acurate Malaria Test, SD Malaria Antigen: could be used in the diagnosis of malaria (Report 2006 (Unpublished data). |
| 2 | 2006 | Bacterial meningitis | Regional epidemic (Séguela, Bouna, Bouaké, tengrela, dabakala, daloa, soubre, boundiali) | Meningeal syndrome | N, meningitidis A<br>N, meningitidis W135<br>N, non-typeable meningitidis<br>S, pneumoniae | 49 cases | These data enabled the Ministry of Health and Public Hygiene via the National Institute of Public Hygiene to carry out a vaccination response in the health districts affected by the epidemic (Report 2006; Unpublished data). |
| 3 | 2006 | Cholera and shigellosis | epidemic in 3 health districts (Abidjan and 2 in western Côte d'Ivoire (Danané and Zouan Hounien). | Gastroenteritis syndrome | Vibrio cholera | 21 cases | The age group most affected by cholera is between 16 and 45 years old. Children were the least affected (Report 2006 [14]). |
| 4 | 2006 | Agents of sexually transmitted infections | national | Diagnostic test | Human Immunodefi-ciency Virus (HIV) | 3 tests assessed including 1 retained | Chek plus HIV 1 - 2 sensitivity and specificity 100%, report 2006 (Unpublished data). |
| 5 | 2006 | Measles | National epidemic: 37 health districts | Nasopharyngeal syndrome | measles virus | 11 cases | (Report 2006; Unpublished data). |
| 6 | 2006 | Influenza and respiratory virus | LANADA (animal sample) | surveillance | Influenza viruses | 22 cases | 7 positive (including 5 H5N1) (Unpublished data). |
| 7 | 2006 | Influenza and respiratory virus | Sentinel site and national investigation | Human nasopharyngeal syndrome | Influenza viruses | 46 cases | 23 positive<br>3 positive (ELISA)<br>10 Flu M gene positives<br>(Unpublished data). |
| 8 | 2006 | Yellow fever | Epidemic | hemorrhagic fever | yellow fever virus | 376 cases | 2 sera from Côte d'Ivoire which proved positive for IgM-type anti-yellow fever antibodies were confirmed by the regional laboratory, IP Dakar. |
| 9 | 2006 | Poliomyelitis | surveillance | AFP | wild poliovirus | 1570 cases | 0 wild poliovirus after cell culture,<br>181 non-polio enterovirus<br>14 vaccine-derived polio virus<br>(Unpublished data). |

**Continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10 | 2007 | Bacterial meningitis | National epidemic | Meningeal syndrome | *N.meningitidis A*<br>*N.meningitidis C*<br>*N.meningitidis W135*<br>*N.meningitidis sp.*<br>*S.pneumoniae*<br>*H. influenzae B*<br>*Streptococcus agalactiae* B | 98 cases | Three techniques are used at CNR level. These are culture, the search for soluble antigens and PCR. The interest of PCR in the detection of bacteria in CSF is undeniable given the results (Report 2007; Unpublished data). |
| 11 | 2007 | Poliomyelitis | surveillance | AFP | Non-polio enterovirus<br>vaccine-derived polio virus | 1626 | 0 wild poliovirus after cell culture,<br>163 non-polio enterovirus<br>16 vaccine-derived polio virus<br>Unpublished data). |
| 12 | 2007 | Influenza and respiratory viruses | surveillance | flu syndrome | RSV<br>Parainfluenza virus | 425 cases | Each sample was tested simultaneously by the ELISA technique for the identification of type and B influenza viruses and inoculated on MDCK cells for viral isolation. Secondarily, the search for the viral genome of influenza A, B and C, Metapneumovirus, RSV, Parainfluenza 1, 2, 3 and 4, rhinovirus, and Coronavirus OC 43 and 229E viruses was carried out by molecular biology.<br>Of the 425 samples, 40 were positive for influenza, i.e. a prevalence of 9.41%. 13 cases or 3.06% of RSV infection were confirmed. The search for Parainfluenza viruses was carried out on 94 samples from the Pediatrics department of the University Hospital of Treichville and made it possible to highlight 9 cases of infection by Parainfluenza viruses. Unpublished data. |
| 13 | 2007 | Measles | surveillance | Naso-pharyngeal syndrome | Anti-measles specific IgM | 348 cases | Measles confirmation: For all suspected cases based on sera: 13.1% (Unpublished data). |
| 14 | 2008 | Tuberculosis | Slaughterhouse | Tuberculosis in cattle | Mr bovis | 104 cases | the first time in Côte d'Ivoire, that Mycobacterium bovis was isolated from cattle slaughtered at the slaughterhouse, to confirm the existence of animal tuberculosis (Cissé *et al.* 2008; CISSE *et al.* 2008). |
| 15 | 2009 | Bacterial meningitis | Epidemic | Meningeal syndrome | S.pneumoniae<br>*H. influenzae b*<br>*Neisseria meningitidis 3*<br>*N.meningitidis. VS*<br>*N.meningitidis. B*<br>*S. agalactiae*<br>*Cryptococcus neoformans* | 29 cases | the emergence of NmW135 in Côte d'Ivoire, as well as the simultaneous disappearance of NmA (Soumahoro *et al.* 2018). |

**Continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 16 | 2009 | Poliomyelitis | surveillance | Acute flaccid paralysis | wild-type poliovirus Non-polio enterovirus vaccine-derived polio virus | 102 cases | After treatment, inoculation and intratypic differentiation, 102 cases of poliovirus were isolated, i.e. 15%, of which 53 were type 1 wild type poliovirus. 47 were of vaccine origin including 40 type 1, 6 type 2 and 1 type 3 (2007 Report; Unpublished data). |
| 17 | 2009 | Measles | National outbreak | Nasopharyngeal syndrome | Anti-measles specific IgM | 762 cases | 64 health districts were affected by positive cases of measles with recrudescence in the districts of Abidjan (2007 report; Unpublished data). |
| 18 | 2009 | Influenza and respiratory viruses | sentinel surveillance, pandemic influenza investigation | flu syndrome | influenza A and B viruses virus type A, type H3N2 virus type A, type H1N1 untypeable virus | 1360 samples 456 positive cases | Influenza virus types A and B circulated. Type A viruses, 167 (50.45%) were of the H3N2 subtype and 37.46% were non-typeable. Two cases of influenza A (H1N1)2009 have been diagnosed in patients from the United States. Antigenic characterization of circulating strains was performed at the WHO collaborating center, Atlanta). All A (H3N2) viruses were antigenically close to the A/BRISBANE/10/2007-LIKE (H3N2) strain. The A (H1N1) virus strains were antigenically close to the A/California/07/2009 (H1N1)v strain (Report 2009; (Unpublished data). |
| 19 | 2009 | Rage | surveillance | animal bite | Lyssavirus | 32 samples | 2 confirmed human cases of rabies (Report 2009; Unpublished data). |
| 20 | 2010 | Measles | National outbreak | Nasopharyngeal syndrome | Anti-measles specific IgM | 913 suspected cases | 461 cases have been confirmed with an annual prevalence of 50.49%. The prevalence for the year 2009 was 24.27% with 185 confirmed cases out of 713 samples taken from suspected cases. This situation was linked to measles outbreaks in the districts of Abidjan West and Abidjan East (Report 2010; Unpublished data). |
| 21 | 2010 | Yellow fever | yellow fever and dengue fever epidemic | Hemorrhagic fever | Dengue virus Yellow Fever Virus | 964 suspected cases | Epidemiological, biological and entomological investigations around confirmed cases of dengue fever and yellow fever in the Montagnes, Sud Comoé and Worodougou health regions, particularly in 04 health districts The entomological component consisted of capturing adult mosquitoes (135 batches of mosquitoes, Séguéla/Man/Zouan-Hounien/Aboisso), (Report 2010; Unpublished data). |

**Continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 22 | 2010 | Influenza and respiratory viruses | sentinel surveillance, pandemic influenza investigation | flu syndrome | influenza A and B viruses type B virus, virus type A, type H3N2 virus type A(H1N1)v non-typeable viruses | 447 cases | Absence of circulation of seasonal A (H1N1) viruses and almost permanent circulation of the pandemic virus and an upsurge of type B viruses. |
| 23 | 2011 | Cholera and Shigellosis | Investigation of an outbreak of cholera Attecoubé | gastroenteritis | Vibrio cholera | 634 cases | ongoing monitoring for drug resistance can help choose a standardized treatment regimen. Further genotypic characterization of Vibrio choleraeO1 isolates will be needed [15]. |
| 24 | 2011 | Diarrhea virus | epidemiological and virological monitoring of pediatric rotavirus diarrhea in five (5) sentinel sites (CHU Yopougon, CHU Cocody, HGYOPAT, HGAN, HGPB). | diarrhea monitoring | rotavirus diarrhea; enterovirulent viruses | 200 cases | (Report 2011; Unpublished data). |
| 25 | 2012 | Influenza and respiratory viruses | surveillance of cases of flu-like illnesses and surveillance of severe acute respiratory infections | flu syndromes and surveillance of severe acute respiratory infections | virus type A and B A(H1N1) pdm09 virus co-infections between types and subtypes of influenza viruses. | 111 | Cases of co-infections between types and subtypes of influenza viruses have been observed (Report 2012; Unpublished data). |
| 26 | 2012 | ORMICI | Monitoring Multi-Resistant Bacteria abidjan and CHR | | ESBL-producing Enterobacteriaceae *Staphylococcus Meti R* | Hurt 24.6% SAMR 29.4 | The monitoring of the evolution of BMR (Multi-Resistant Bacteria) shows a catastrophic situation in our hospitals but also in the city of Abidjan. These figures challenge us. It is time to react. Infections will become increasingly untreatable (Report 2012; Unpublished data). |
| 27 | 2012 | Cholera and shigellosis | Regional cholera epidemic (south comoé) | gastroenteritis | V. cholerae were serogroup O1. | 67 cases | In different African epidemiological settings, substantial variation has occurred in cholera incidence, age distribution, clinical presentation, culture confirmation, and testing frequency. These results can help guide prevention activities, including the use of vaccines (Sauvageot *et al.* 2016). |

**Continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 28 | 2012 | Bacterial meningitis | National epidemic | Meningeal syndrome | Neisseria meningitdis serogroup W135 | 163 cases | travelers to the meningitis belt of sub-Saharan Africa may be at risk of infection with N. meningitidis serogroup W135 (Taha *et al*. 2013). |
| 29 | 2012 | Tuberculosis | Animal pathology laboratory | Tuberculosis syndrome in cattle | Mr bovis | 1 case | (Report 2012; Unpublished data). |
| 30 | 2012 | RIISIN | -Public structures 5 Services of the CHU of Cocody -SAMU -3 Private medical structures | monitoring the circulation of pathogenic bacteria in the hospital environment | *Enterobacteriaceae No Enterobacteriaceae Staphylococcus spp Streptococcus species Pseudomonas* multi-resistant | 249 samples | *Pseudomonas* multi-resistant and resistant to Imipenem was observed for the first time in the intensive care unit of the University Hospital of Cocody. An alert was given to the Ministry of Health and the Fight against AIDS on February 7, 2012. |
| 31 | 2013 | Yellow fever | Epidemic | Hemorrhagic fever | yellow fever virus | 7 | (Report 2012; Unpublished data). |
| 32 | 2013 | Bacterial meningitis | Laboratory network monitoring | Meningeal syndrome | *-S. pneumonia -NmA -NmC -NmW135 -Hib -S agalactiae* | 28 cases | The majority of the samples came from the health region of Abidjan 2. The main germs were S. pneumoniae followed by N. m W135. Northern regions included in the meningitis belt sent fewer samples. Several hypotheses can be mentioned: difficulties in transporting CSF to the CNRm, reduction in cases of meningitis following the vaccination campaign (tetravalent vaccine ACYW135). |
| 33 | 2013 | Influenza and respiratory virus | Surveillance | ARI in children | other non-influenza respiratory viruses | 1509 ca | Multiplex RT-PCR assays targeting 10 severe acute respiratory infection (SARI) respiratory viruses were tested [16]. |
| 34 | 2015 | Rage | Diagnosis of rabies in suspected persons on biopsy of skin, saliva and urine | Rabies suspect | rabies virus | 10 cases | All samples processed by molecular techniques were found to be positive. (Tiembre *et al*. 2010). |
| 35 | 2015 | Hemorrhagic fever | the threat of the Ebola virus fever epidemic, | Ebola suspect | Hemorrhagic fever virus | 5 sera of suspected cases | negative results in Ebola gene amplification test but vigilance must remain. |
| 36 | 2017 | Hemorrhagic fevers | National epidemic | Hemorrhagic fever | Dengue virus | 2849 samples | DENV-2 dominated this outbreak even though all three serotypes were detected by RT-PCR. The increasing trend of co-circulation of dengue virus serotypes suggests that Abidjan is transitioning from an endemic to a hyperendemic state [17]. |
| 37 | 2018 | Hemorrhagic fevers | dengue fever outbreak | Hemorrhagic syndrome | dengue virus, lassa virus | 1 case | fatal human case of Lassa fever in Bangolo district in western Côte d'Ivoire in 2015 [18]. |

**Continued**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 38 | 2019 | Hemorrhagic fevers | District Abobo | Hemorrhagic syndrome | Crimea Congo Virus | 1 case | Cirulation of crimean congo virus in Ivory Coast [19] [20]. |
| 39 | 2020 | Influenza and respiratory virus | pandemic | corona virus | corona virus | More than 1 million direct debits | This pandemic has put all the economic and health systems of the countries of the world to the test. Several works have been carried out [21] [22]. |
| 40 | 2020 | Bacterial meningitis | national | Diagnostic test | *Neisseria meningitidis* | 1 trial | Validation of a new immunochromatographic test (MeningoSpeed, BioSpeedia, France) for the detection and clustering of Neisseria meningitidis [23]. |

respiratory diseases; vector-borne and parasitic diseases; and nosocomial infections.

The program has four stages of development [3]: investigation of epidemics, initial targeted studies, axis or line of complete research and research program carried out.

Outbreak investigations provided a concrete first stage of activity between NRC and collaborative partners in the field, such as health services and laboratory scientists. In addition, outbreak investigations have revealed health issues that require further planned epidemiological investigation. These surveys have forged collaborations between the laboratories (LNR), the University laboratories (Cocody, Nangui Abrogoua), the veterinary health department (VHD), the laboratories of the regional hospital centers (RHC). A technical laboratory working group (TWG-Laboratory) was formed in the one health approach to develop a future research and surveillance program for communicable diseases.

The second stage of the program was to initiate targeted studies involving unique research projects to address specific health issues. Seventeen (17) short-term research projects were initiated. These included a study of hepatitis B and C, risk factors for the development of quinolone resistant diseases in one hospital, prevalence and risk factors of Staphylococcus aureus methicillin resistance in hospitals, three studies on the influenza vaccination coverage (**Table 5**).

The third stage, Axis of applied research carried out over a period of several years in each in several fields, is developed sequentially because it requires considerable human resources, financial commitment and experience. In June 2007, the Ministry of Higher Education and Research in collaboration with Switzerland began to fund the development of networks for applied research and surveillance of infectious diseases as part of the Strategic Support Program for Scientific Research (PASRES) [7]. The selection criteria and proposal review committee were chosen to ensure that funded projects had an appropriate mix of epidemiology and laboratory science. IPCI has received an average of 850,000 US$ per year for the President's Emergency Plan for AIDS Relief (better known as PEPFAR) for a decade and an average of 600,000 US$ per year for the global

**Table 5.** Projects and collaboration reported by the NRCs of the IPCI, 2006-2021.

| | Title | Units | Start date |
|---|---|---|---|
| **1** | Influenza virus surveillance program in Côte d'Ivoire (2007-2009)* | Virology<br>Molecular<br>Epidemiology | January 2007 |
| **2** | WHO measles control program | epidemic viruses | January 2000 |
| **3** | IDSR National Influenza Program | INHP<br>IPCI | January 2007 |
| **4** | Project Evaluation of the immunogenicity of the anti (meningococcal) conjugate vaccine (Men Vac A, C, Y, W135 DT) in healthy volunteers | NRC Meningitis<br>University Hospital<br>Bouake | 2007 |
| **5** | ACIP pneumo | Clinical Bacteriology | 2007 |
| **6** | Epidemiological and etiological study of diarrheal diseases in the village of Béago, commune of Yopougon Abidjan | Clinical Bacteriology | 2007 |
| **7** | Immunogenicity of Mycobacterium tuberculosis lipids in the non-replicating status of latency. EU project | LDR Immunology<br>molecular microbe<br>Epidemiology<br>Mycobacteria | 2007-2010 |
| **8** | Ozone therapy in the treatment of Buruli Ulcer. | Immunology<br>Molecular M<br>Epidemiology<br>Mycobacteria<br>Biochemistry | 2007 |
| **9** | QNR project: Molecular study of the resistance to quinolones of enterobacteriaceae responsible for human infections and from the hospital environment in Abidjan | ASSURMI | 2006 |
| **10** | Virulence factors of Streptococcus agalactiae strains isolated from vaginal carriage in pregnant women<br>*UNESCO project* | ASSURMI<br>Bacteriology | 2006 |
| **11** | ACTIV project (S pneumoniae, Hib) | ASSURED<br>Bacteriology | 2007 |
| **12** | Protocol SP-C-007-07: Phase III clinical study* | Malaria Unit<br>FSU Abobo | 2007 |
| **13** | Protocol SP-C-004-06: Phase III clinical study** | Malaria Unit<br>FSU Abobo | 2007 |
| **14** | Efficacy and Tolerance of the association Artesuante/mefloquine Pediatric formulation versus Artemether/lumefantrine in the treatment of uncomplicated P. falciparum malaria in Côte d'Ivoire | Malaria Unit<br>FSU Abobo | 2007 |
| **15** | Prevalence of viruses in chimpanzees (Pan troglodytes verus) and other primates from the Taï National Park (Côte d'Ivoire) among human populations in the region. | DVE<br>RKI | 2006 |
| **16** | Hepatitis C virus heterogeneity in Côte d'Ivoire | IPCI<br>RIIP | 2006 |
| **17** | ORA Project/Malaria | IPCI<br>RIIP | 2007 |

**Continued**

| | | | |
|---|---|---|---|
| **18** | Role of aquatic bugs in the transmission of M ulcerans: Bioecological study | IPCI<br>INSP<br>INHP | 2007 |

health security program better known as the Global Health Security Agenda (abbreviated as GHSA) to develop a research network on foodborne, vector-borne, and environmental infections.

The final stage, a fully realized research program with field epidemiologists specializing in each of the research areas and with integrated surveillance, laboratory and prevention components, is a long-term goal. The program would have a steady stream of research funding for short- and long-term projects, with priority determined by IPCI and its collaborating partners based on immediate and long-term public health needs.

### 3.2.4. Strengthening Surveillance Systems

The current International Health Regulations (IHR) use case definitions, and many pathogens are newly identified. There are provisions for laboratory reports. Since 2006, the NRCs for surveillance of communicable diseases have been set up by interministerial decree and the data obtained by the system are published in an annual report to the Ministry of Health.

A 2017 order from the Ministry of Health on infectious diseases classifies pathogens into 4 categories came into force in January 2017 and the 2020 orders from the prime minister's office organizing the response to public health events: Order of 20 March 2020 from the prime minister setting the organizational framework for the fight against the Coronavirus pandemic (COVID-19), decree of April 30, 2020 of the prime minister on the creation, organization and functioning of the operational monitoring committee for the response plan against the Coronavirus pandemic. In addition to authorizing single case notifications using case definitions and specifying both laboratory and healthcare provider-based notification, these new orders also give a clear mandate for laboratories and the IPCI to be the central authority for the organization and conduct of surveillance and applied laboratory research on infectious diseases.

The time it took to draft and pass these infectious disease orders allowed the IPCI and new surveillance programs to develop. Thus, NRL staff members have already undergone training, which will facilitate the implementation of the new monitoring system in the field. In addition, IPCI management has initiated studies to assess existing surveillance systems or initiate sentinel surveillance.

### 3.2.5. Improved Communication

Because the impact of emerging and re-emerging infectious diseases on public health has been vastly underestimated, a deliberate communication strategy was needed to raise public awareness [3]. It was also important to involve health service personnel in implementing new surveillance initiatives and conducting outbreak investigations using analytical epidemiology. Finally, the collaboration

of other scientific authorities, such as university research departments and professional associations, was necessary. IPCI participates in meetings of the public health emergency operations center (COUSP) located at the national institute of public hygiene (INHP)

Five communication strategies were used and the main target groups were identified (Figure 2). Outbreak investigations were initially a high priority, in part to get the public to recognize infectious disease threats and the role of public health authorities in responding to those threats. Subsequent public health guidelines also highlighted the roles of IPCI and health services in promoting science-based public health. Guidelines on the diagnosis and management of sexually transmitted infections (STIs) (Table 6) a biosafety manual, a guide to the fight against Ebola and several other manuals have been developed (Table 6).

The Epidemiology Bulletin (le Vigile) reaches a wide audience, including the media, public health services and other researchers. It provides a weekly source of epidemiological findings and surveillance data, giving IPCI, INHP and participating health services a regular and visible central role in infectious disease epidemiology. Additionally, the bulletin publishes public health guidelines for one communicable infectious disease per month.

The journal Bioafrica (scientific journal with reading committee) receives scientific publications on communicable diseases at national and international level.

To give credibility and to support the NRCs fighting against communicable diseases, scientific conferences, congresses and symposiums are regularly organized at the IPCI.

Although the emphasis is on publication in national journals, publication in international medical journals is essential as it is more widely read by public health practitioners.

Several general public communication actions are undertaken. In 2009, participation in a television program on the second national channel enabled the head of the NRC to contribute to raising public awareness of rabies.

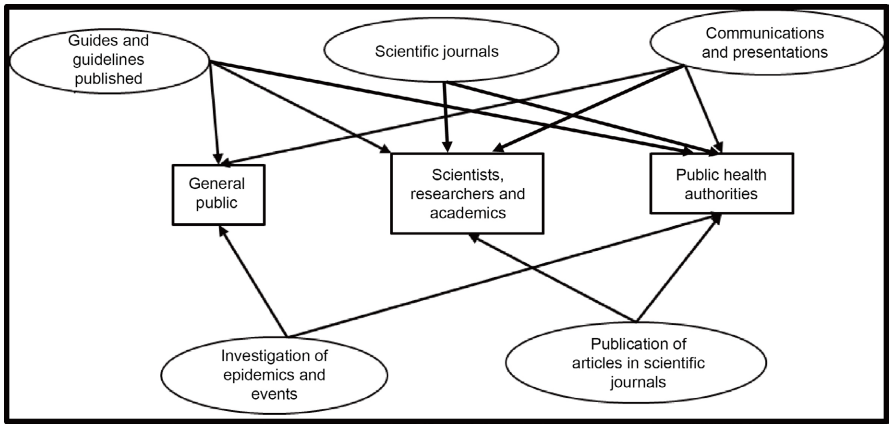


Figure 2. Communication strategies and main target groups for capacity development of the NRCs for infectious diseases at the Pasteur Institute of Côte d'Ivoire (Source: Petersen L. R. *et al.* 2000 [3]).

**Table 6.** Publications reported by the NRCs of the IPCI in the activity reports from 2006-2021.

| No. | NRC | First author *et al.* | Year of publication | securities | Journal (volume, number, page) | Commentary (publication reference) |
|---|---|---|---|---|---|---|
| 1 | Agents of sexually transmitted infections | | 2006 | National documents and management algorithms for patients with an STI. •the medical care program for PLHIV. •the HIV/AIDS Biology Technical Group in Côte d'Ivoire | | |
| 2 | Agents of sexually transmitted infections | | 2006 | prevalence of resistance of Neisseria gonorrhoeae strains to antibiotics | | 1 Strain (146/07) is resistant to ampicillin, to tetracyclines, it produces a beta-lactamase, it is sensitive to 3rd generation cephalosporins and to ciprofloxacin. The presence of strains producing betalactamase and having a high MIC to Penicillin G requires that monitoring of the resistance of *N gonorrheoae* to antibiotics be organized and that a collection network for strains or samples be initiated. |
| 3 | Agents of sexually transmitted infections | | 2006 | development of a national guide for the evaluation of HIV tests in Côte d'Ivoire. | | |
| 4 | Agents of sexually transmitted infections | | 2006 | Validation of the revision of the PMTCT policy and procedures manual | | |
| 5 | Tuberculosis | N'guessan K *et al.* | 2008 | Primary resistance to antituberculosis drugs: trends in Cote d'Ivoire from 1995 to 2006. | J.Med Mal Infect. 2008 Apr; 38(4): 231-2. doi: 10.1016/j.medmal.2007.11.004. Epub 2008 Feb 8. PMID: 18262379 | [24] |
| 7 | ORMICI | | 2011 | development of tools and guides: Technical data sheet for the popularization of the detection of the production of extended-spectrum beta-lactamases, Antibiogram procedures manual. | | |

**Continued**

| | | | | | | |
|---|---|---|---|---|---|---|
| 8 | Tuberculosis | | 2011 | drafting of the training kit for biotechnologists in tuberculosis microscopy. | | |
| 9 | Hemorrhagic fever | Akoua-Koffi C *et al.* | 2011 | Febrile states and Dengue3 in the Abidjan conurbation (Côte d'Ivoire) in 2008 | Bio-Africa Review, 9: 54-61 | The availability of dengue and West Nile virus diagnostic reagents made it possible to carry out a definitive diagnosis for the active surveillance of Yellow Fever before confirmation at the regional laboratory [11]. |
| 10 | Viral liverworts | Doumbia M *et al.* | 2013 | Molecular characterization of hepatitis B virus isolated from two groups of patients at risk in Cote d'Ivoire | Journal of Microbiology Research and Review vol 1(5): 61-66; October, 2013 ISSN: 2350-1510 pp 61-66; | [25] |
| 11 | RIISIN | | 2013 | Development of the national biosafety guide: medical biology laboratory in Côte d'Ivoire | | |
| 12 | Poliomyelitis | Koffi Affoué Carole *et al.* | 2015 | Cytotoxic and Antiviral Activity of Methanolic, Ethanolic and Acetate Extracts of Six Varieties of Capsicum | Int.j.Curr.Microbiol.Ap.Sci,2015;4(10):76-88 | [26] |
| 13 | Yellow fever | | 2015 | Development of national guides for the fight against Ebola fever | | |
| 14 | Yellow fever | CG Akoua-Koffi, *et al.* | 2014 | Yellow Fever and Dengue Fever Serotype 3 Viruses Co-circulation in Côte D'Ivoire in 2008 | African Journal of Pathology and Microbiology, 2014 Vol. 3, 5 pages | [27] |
| 15 | Yellow fever | Ngazoa ka Niedrig Mattias 2 *et al.* | 2014 | Evaluation of molecular detection for viral hemorrhagic infection cases of Yellow fever and Dengue fever in Côte d'Ivoire 2010-2012, | British journal of medicine and medical research, BJMMR, 2014, 3: 396-403 | [28] |
| 16 | Tuberculosis | N'guessan K, *et al.* | 2014 | Assessment of the genotype MTBDR plus assay for rifampin and isoniazid resistance detection on sputum samples in Cote d'Ivoire. | Eur J Microbiol Immunol (Bp). 2014 Sep;4(3):166-73. doi: 10.1556/EUJMI-D-14-00014. Epub 2014 Sep 11. PMID: 25215193 | [29] |
| 17 | Tuberculosis | N'guessan K, *et al.* | 2014 | Use of rapid molecular test for multidrug-resistant tuberculosis detection among relapse cases in Cote d'Ivoire. | .Int J Mycobacteriol. 2014 Mar;3(1):71-5. doi: 10.1016/j.ijmyco.2013.11.003. Epub 2013 Dec 23. PMID: 26786227 | [30] |

**Continued**

| | | | | | | |
|---|---|---|---|---|---|---|
| 18 | Tuberculosis | N'guessan K *et al.* | 2016 | Rapid detection of Mycobacterium tuberculosis complex in sputum specimens using the PURE TB-LAMP assay | Int J Mycobacteriol. 2016 Dec;5 Suppl 1:S164-S165. doi: 10.1016/j.ijmyco.2016.09.025. Epub 2016 Nov 9. PMID: 28043530 | [31] |
| 19 | Tuberculosis | Herve A Kadjo *et al.* | 2018 | Epidemiology of rubella infection and genotyping of rubella virus in Cote d'Ivoire, 2012-2016 | J Med Virol.2018 Nov;90(11):1687-1694. doi: 10.1002/jmv.25252. Published online July 25, 2018 | [32] |
| 20 | Tuberculosis | Yeo A, *et al.* | 2019 | Establishment of a Gonococcal Antimicrobial Surveillance Programme, in Accordance With World Health Organization Standards, in Côte d'Ivoire, Western Africa, 2014-2017. | Sex Transm Dis. 2019 Mar;46(3):179-184. doi: 10.1097/OLQ.0000000000000943.PMID: 30461598 | [33] |
| 21 | ORMICI | Goualié BG *et al.* | 2019 | Antimicrobial resistance and virulence associated genes in Campylobacter jejuni isolated from chicken in Côte d'Ivoire. | MJ Infect Dev Ctries. 2019 Aug 31;13(8):671-677. doi:10.3855/jidc.11355.PMID:32069250 | [34] |
| 22 | Viral liverworts | Sévédé D *et al.* | 2019 | Increased liver injury in patients with chronic hepatitis and IgG directed against hepatitis E virus. | EXCLI J. 2019 Oct 25;18:955-961. doi: 10.17179/excli2019-1827. eCollection 2019.PMID: 31762722 | [35] |
| 23 | Viral liverworts | Moussa Doumbia *et al.* | 2021 | Viral and bacterial factors of mother-to-child transmission of hepatitis B virus | PMID: 34467609/ DOI: 10.1111/jvh.13607 | [36] |

In 2012, the positive consequences of the awareness of the previous cholera epidemic of 2010 to 2011 were still vivid in the population.

In 2012, the NRC Ivorian Network for the Investigation and Surveillance of Nosocomial Infections (RIISIN) organized assistance to professionals for clinical services through the microbiological control of the effectiveness of disinfection of sensitive sites at the university hospital of cocody (resuscitation neonatology pediatric surgery). And for the general public, a TV program on the second channel of national television (TV2) on the occasion of Global Hand washing Day.

In 2014 the NRC haemorrhagic fever participated in the development of public awareness spots in the written and audio-visual press, conferences and train-

ing on how to behave were carried out by the department and the management of IPCI on behalf of Ebola virus fever

#### 3.2.6. Building National and International Collaborations

Although the primary focus of the infectious disease NRCs is national, the integration ofCote d'Ivoire into WHO, ECOWAS, and european and american networks required that the NRCs have an international presence. Some measles and polio NRCs are Africa-wide regional surveillance laboratories, through networks, requiring many member states to play an active role in managing one or more multinational surveillance systems. To help build this capacity, heads or staff of the NRCs of the IPCI took part in sub-regional missions to support the establishment of national reference laboratories in certain southern countries.

#### 3.2.7. Establishment of Technical and Technological Platforms

The management of biological risks linked to certain events requires that a policy concerning the management of biological risks in the laboratory (biosafety and biosafety) be put in place in accordance with international regulations resulting in the issuance of a Ministerial Order on pathogens at risk [8]. The level of lab security varies from lab to lab. Respectively laboratories are of level P1, P2 and P3. Most laboratories have only certified level 2 biosafety cabinets (PSM type II).

With regard to samples, samplings and packagings of samples from all NRCs are processed according to international standards.

In view of the high costs of laboratory equipment, technical and technological platforms have been set up. To meet the requirements of containment and conservation of biological resources [9] of the NRCs, a biological resource center was set up in 2010 with a variety of conservation methods: by freeze-drying, encapsulation of nucleic acids by IMAGENE®, conservation in liquid nitrogen in straws and in microtubes [10]. A high-level security laboratory has been under construction since 2019.

A molecular biology platform was set up with a view to pooling molecular biology diagnostic equipment in 2010 for the molecular characterization of infectious pathogens [11] [12] [13].

The IPCI has set up a genomic sequencing pole, a microbial genomics and metagenomics laboratory. One of these activities was to determine the variants of the corona virus that circulated in Abidjan during the pandemic. This genomics and meta genomics platform has been in service since 2021 to support the genetic characterization of infectious pathogens

#### 3.2.8. Funding of NRCs

The financing of the various NRCs as part of their activities is mainly carried out by the IPCI. In particular, there is no funding from other national institutions.

The development partners, in particular the united nations system, through the WHO, provide considerable financial support, in particular to the NRC Poliovirus and to the NRC Measles and NRC yellow fever, NRC Influenza.

Every year:

- Through the IPCI's annual budg*et al*located by the ministry of higher education and ecientific research (staff salaries, small equipment, reagents and consumables, maintenance, subscriptions, etc.).
- Through an annual allocation from the WHO for certain NRCs: Polio, Measles.

By projects and/or on an ad hoc basis, particularly in the event of epidemics:

- By the ministry of health and public hygiene as part of the plans (Flu Action Plan, Global AIDS and Tuberculosis Fund).
- Through occasional support from development partners (donations of equipment, reagents and consumables, etc.).
- By WHO funds for certain NRC activities (Polio, Measles, Influenza, Buruli, Meningitis, Gonococcus).
- Through research projects funded outside Côte d'Ivoire.
- Through the international network of the Pasteur Institute (support for strengthening expertise (study grants) and quality control and improving capacities such as the biosafety of premises and equipment).

The financial balance sheet for the IPCI's NRC activities is proving difficult, and is directed towards development partners. Additional funds are needed to improve the microbiological surveillance network (for nosocomial infections and to develop the network for food-borne and vector-borne diseases), but also to give greater visibility to the IPCI's support for national health programs in Côte d'Ivoire and the West African region.

## 4. Analysis

### 4.1. Strengths: "Success Stories"

Several factors have contributed to the success of NRCs of IPCI. The first was to achieve a broad consensus on the scope and objectives of the program among future NRC participants and partners. In Cote d'Ivoire this included the ministry of health, ministry of scientific research, state health services. The second ingredient of the program's success was the initial emphasis on training, particularly for the development of a national epidemiological program. The short-term training program quickly produced a growing network of collaborators in the health services. Long-term (European) training programs have produced technically competent biologists,

A final key to the program's success has been a gradual and deliberate plan to develop a network of partners in the field and in the lab and to market the program to information consumers.

### 4.2. Weakness and Challenges

Beyond the improvement of their internal functioning, several indices nevertheless show the difficulties of the CNRs in giving visibility to their activity of scientific contribution and in articulating it with the actors of research: few collec-

tions declared in connection with networks themes, accumulation of stored cryo samples, difficulty of exhaustive inventory of biological resources and low percentage of samples used, contributions to publications that are difficult to assert.

In the future, the consolidation of NRC structuring investments should focus on infrastructure, improving the interface with surveillance, research, conservation and biomedical industry teams. This interface is not reduced to establishing a "preformatted" technical service according to "quality" standards, but must take into account many elements established between partners. It involves the management of the establishment to define a real strategy and governance of activities.

## 5. Conclusions and Perspectives

Since 2000, the policy led by the IPCI, the INHP has enabled the overall and national structuring of the CNRs in support of the surveillance and research teams for communicable diseases. Structuring investments have made it possible to improve the organization and operation of these technical platforms, in particular through the diversification of diagnostic confirmation and response preparation services and through the implementation of operating information systems and management of associated data, through the implementation of a national quality approach.

There is great heterogeneity in the volumes of activity according to the NRCs, linked to the size and volume of activity of the health establishments which are in their network and to the event of national scope. On the other hand, there is an organizational distinction according to the network of the reference laboratory. The scientific contribution activity results from local investments, to improve the quality of the service and contribute to research projects.

The objective, undertaken by the IPCI for several years, of optimizing the confirmation of cases, surveillance in the NRCs and their use for research, has been pursued and reinforced.

The actions and recommendations of the IPCI aim to optimize the organization of NRCs with a view to the surveillance of communicable diseases, according to a local strategy and within the framework of multicentre networks.

The need to set up an information system whose objective is to stimulate the federation of different actors to constitute, around the transmissible diseases under surveillance, clinical epidemiological and biological databases associated with biological samples. This surveillance database is a tool for collecting and managing data relating to individuals, patients and/or subjects suspected of communicable diseases. The data combines clinical information, scientific and medical analyzes carried out on biological samples taken from samples, surveys or questionnaires, administrative and demographic information.

The database must make it possible to optimize, on a national scale and for a defined pathology, the collection of all this information, its integration and its transversal exploitation by different research disciplines (epidemiological, fundamental, translational, clinical). It must make it possible to study relations for a

large number of cases.

The multicentric and multidisciplinary organization aims to standardize the collection of data and associated biological resources, their pooling and their sharing with the scientific and medical communities.

This evaluation is also necessary for the supervisory bodies, in order to measure the impact of investments in indirect support for research and to justify their renewal.

Today the measurement of the scientific contribution of the NRCs is all the more difficult to achieve as the measurement of the scientific impact of a research project is already complex and sometimes shifted in time.

The IPCI to propose a model for access to state subsidies in support of NRC contributions. This would involve an evaluation of the NRCs, according to specifications and according to developments in recent years. The subject is important, and raises questions about the objectives, the eligibility criteria, the evaluation methods. An in-depth reflection will be carried out, in conjunction with the professionals, in order to define, communicate and organize this evaluation in complete transparency, on the basis of our achievements and in order to consolidate them.

## Lessons Learned

Our experiences during the first 10 years of the program have shown that a NRC program applied to communicable diseases organized with a high degree of technical expertise at the national level is necessary to respond effectively to emerging infections.

For example, by taking into account the 21 epidemic events studied to date, 4 were traditional epidemics of vector origin originating from the same mosquito. Most of the others concerned multinational or sub-regional COVID 19 and Ebola epidemics, disease threats or community epidemics of rare agents or bacterial strains, difficult to detect or resistant to several drugs or new viruses: crimea congo or lassa. The traditional approach to outbreak investigation that emphasizes the collection by a single health service of case samples for microbiological analysis would not have been adequate to determine the extent of the almost-all of these events nor to identify their modes or vehicles of transmission.

IPCI's activities to date have formed the basis for the continued development of a national reference laboratory program with integrated surveillance, research and prevention components for most transmissible pathogens. Further development is essential, as experiences to date suggest that biologists, epidemiologists, public health officials and laboratory scientists are likely to become involved in increasingly complex scientific endeavors as they respond to emerging infections in Côte d'Ivoire.

## Acknowledgements

The director of the IPCI and the heads of the NRCs should be congratulated for

their constant support of this effort. Laboratories were invited to contribute to this original article, which undergone peer-review. We are indebted to the large number of reviewers who supported this article with their work and expertise.

## Statement

The results and conclusions of this article are those of the authors and do not necessarily represent the official views of the ministries or the IPCI.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

[1] Ahmed, S.S., Alp, E., Ulu-Kilic, A. and Doganay, M. (2015) Establishing Molecular Microbiology Facilities in Developing Countries. *Journal of Infection and Public Health*, **8**, 513-525. https://doi.org/10.1016/j.jiph.2015.04.029

[2] Oaks Jr, S.C., Shope, R.E. and Lederberg, J. (1992) Emerging Infections: Microbial Threats to Health in the United States. National Academies Press, Washington DC.

[3] Petersen, L.R., *et al*. (2000) Developing National Epidemiologic Capacity to Meet the Challenges of Emerging Infections in Germany. *Emerging Infectious Diseases*, **6**, 576-584.

[4] Binder, S., Levitt, A.M. and Aguilar, J.R. (1998) Preventing Emerging Infectious Diseases: A Strategy for the 21st Century. US Department of Health and Human Services, Centers for Disease Control and Prevention (CDC).

[5] MSHP and MESRS (2006) Arreté interministeriel designant la liste des centres nationaux de reference (CNR) de l'institut pasteur de Côte D'ivoire dans le domaine des maladies transmissibles.

[6] (2023) Cote D'ivoire. https://www.google.com/search?gs_ssp=eJzj4tDP1TdIKzMpM2D04k3OL0lVSFHPLMvPLEoFAGCpCAA&q=cote+d%27ivoire&rlz=1C1CHZN_frCI1055CI1055&oq=cote+&gs_lcrp=EgZjaHJvbWUqBggBEC4YAzIGCAAQRRg5MgYIARAuGAMyBggCEAAYAzINCAMQLhiDARixAxiABDINCAQQABiDARixAxiABDIGCAUQRRhAMg0IBhAAGIMBGLEDGIoFMg0IBxAuGK8BGMcBGIAE0gEJMTUzMDFqMGo3qAIAsAIA&sourceid=chrome&ie=UTF-8

[7] Cervical Spine Research Society (CSRS) (2007) Programme d'Appui Stratégique Recherche Scientifique. https://www.csrs.ch/pasres/presentation-pasres.php

[8] MSHP (2019) Arreté n° 0022 MSHP/CAB du 11 mars 2019 portant classification des pathogenes en Côte D'Ivoire.

[9] Bouagnon, R., *et al*. (2022) Design and Implementation of Nasopharyngeal Specimen Storage in Straws during the COVID19 Pandemic in Côte D'Ivoire. *Journal of Biosecurity and One Health*, **1**, 43-52. https://doi.org/10.36108/GJOBOH/2202.10.0250

[10] Bouagnon, R., *et al*. (2023) Resin Straws: A System to Safely Store Nasopharyngeal Specimens Collected during the COVID-19 Pandemic in Ivory Coast. *Scholars Academic Journal of Biosciences*, **2**, 69-73. https://doi.org/10.36347/sajb.2023.v11i02.005

[11] Akoua-Koffi, C., *et al*. (2011) Etats fébriles et dengue3 dans l'agglomération Abidjanaise (Côte D'Ivoire) en 2008. *Revue Bio-Africa*, **9**, 54-61.

[12] Dagnogo, O. (2018) Polymorphisme des gènes Chloroquine Resistance Transporter (crt), dihydrofolate reductase (dhfr) et Kelch13 propeller (K13 propeller) de Plasmodium falciparum dans la salive et les urines chez le sujet atteint de paludisme. Ph.D. Thesis, Université Félix Houphouët-Boigny, Abidjan. https://theses.hal.science/tel-02358468

[13] Ehui, B.K., Alain, Y., Abdoulaye, O., Daniel, S., Faye-ketté, H. and Dosso, M. (2018) Diagnostic par Polymerase Chain Reaction en temps réel des infections à Mycoplasma genitalium dans les syndromes d'écoulement génitaux chez les hommes à Abidjan. Real-time Polymerase Chain Reaction diagnosis of Mycoplasma genitalium infections in genital discharge syndromes in men in Abidjan. *Revue International des Sciences Médicales*, **20**, 288-292.

[14] Akoua-Koffi, C., *et al.* (2007)Aspects épidémiologiques et virologiques des diarrhées dues aux Rotavirus à Abidjan, Côte D'Ivoire (1997-2000). *Bulletin de la Société de pathologie exotique*, **100**, 246-249.

[15] Kacou-N'douba, A., Blessa Anné, J.C. and Okpo, L.S. (2012) Antimicrobial Resistance of Vibrio Cholerae O1 Isolated during a Cholera Epidemic in 2011 in Dry Season in Cote D'Ivoire. *The Journal of Infection in Developing Countries*, **6**, 595-597. https://doi.org/10.3855/jidc.2001

[16] Kadjo, H.A., *et al.* (2018) Detection of Non-Influenza Viruses in Acute Respiratory Infections in Children under Five-Year-Old in Cote D'Ivoire (January-December 2013). *African Journal of Infectious Diseases*, **12**, 78-88. https://doi.org/10.21010/ajid.v12i2.13

[17] Sylla, Y., Diane, M.K., Adjogoua, V.E., Kadjo, H. and Dosso, M. (2021) Dengue Outbreaks in Abidjan: Seroprevalence and Cocirculating of Three Serotypes in 2017. *Outbreak*, *Surveillance*, *Investigation & Response* (*OSIR*) *Journal*, **14**, 94-103. https://doi.org/10.59096/osir.v14i3.262527

[18] Mateo, M., *et al.* (2019) Fatal Case of Lassa Fever, Bangolo District, Côte D'Ivoire, 2015. *Emerging Infectious Disease*, **25**, 1753-1756. https://doi.org/10.3201/eid2509.190239

[19] Adjogoua, E.V., *et al.* (2021) Geographical Distribution of Ticks Ixodidae in Côte D'Ivoire: Potential Reservoir of the Crimean-Congo Hemorrhagic Fever Virus. *Vector-Borne and Zoonotic Diseases*, **21**, 628-634. https://doi.org/10.1089/vbz.2020.2745

[20] Adjogoua, E.V., Diaha-Kouame, C.A., Guindo-Coulibaly, N., Diane, M.K., Konan, K. and Dosso, M. (2021) Première détection du virus de la fièvre hémorragique Crimée Congo dans les tiques circulant à Bouaflé, région de la Marahoue, Côte D'Ivoire. *Revue Bio-Africa*, **25**, 51-60.

[21] Odegue, D.K., *et al.* (2021) Nasopharyngeal Samples Management Strategy during the COVID-19 Pandemic: Experience of the Pasteur Institute of Côte D'Ivoire (2020). *Journal of Scientific Research and Reports*, **27**, 72-79. https://doi.org/10.9734/jsrr/2021/v27i430380

[22] Kouao, M.D. and Diaha-Kouame, C.A. (2021) Improvement of the Pre-Analytical Phase of Nasopharyngeal Samples during the COVID 19 Pandemic: Experience of the Institute Pasteur De Côte D'Ivoire in 2020. *International Journal of Infectious Diseases*, **2**, 1-6.

[23] Haddar, C.H., *et al.* (2020) Validation of a New Rapid Detection Test for Detection of *Neisseria meningitidis* A/C/W/X/Y Antigens in Cerebrospinal Fluid. *Journal of Clinical Microbiolog*, **58**, e01699-19. https://doi.org/10.1128/JCM.01699-19

[24] N'guessan, K., Dosso, M., Nahoua, I., Koffi, M.S. and Kouakou, J. (2008) Primary

Resistance to Antituberculosis Drugs: Trends in Cote D'Ivoire from 1995 to 2006. *Médecine et Maladies Infectieuses*, **38**, 231-232. https://doi.org/10.1016/j.medmal.2007.11.004

[25] Doumbia, M., Kouassi, M.A., Kakou, N.S. and Sevede, D. (2013) Molecular Characterization of Hepatitis B Virus Isolated from Two Groups of Patients at Risk in Côte D'Ivoire. *Journal of Microbiology Research and Reviews*, **1**, 61-66.

[26] Koffi Affoué, C., *et al*. (2015) Cytotoxic and Antiviral Activity of Methanolic, Ethanolic and Acetate Extracts of Six Varieties of Capsicum. *International Journal of Current Microbiology and Applied Sciences*, **4**, 76-88.

[27] Akoua-Koffi, C.G., *et al*. (2014) Yellow Fever and Dengue Fever Serotype 3 Viruses Cocirculation in Côte D'Ivoire in 2008. *African Journal of Pathology and Microbiology*, **3**, 1-5.

[28] Solange, N.K.E., *et al*. (2015) Evaluation of Molecular Detection for Viral Hemorrhagic Infection Cases of Yellow Fever and Dengue Fever in Côte D'Ivoire 2010-2012, West Africa. *British Journal of Medicine and Medical Research*, **5**, 396-403. https://doi.org/10.9734/BJMMR/2015/12582

[29] N'guessan, K., *et al*. (2014) Assessment of the Geno Type MTBDRplus Assay for Rifampin and Isoniazid Resistance Detection on Sputum Samples in Cote D'Ivoire. *European Journal of Microbiology and Immunology*, **4**, 166-173. https://doi.org/10.1556/EUJMI-D-14-00014

[30] N'guessan, K., *et al*. (2014) Use of Rapid Molecular Test for Multidrug-Resistant Tuberculosis Detection among Relapse Cases in Cote D'Ivoire. *The International Journal of Mycobacteriology*, **3**, 71-75. https://doi.org/10.1016/j.ijmyco.2013.11.003

[31] N'guessan, K., *et al*. (2016) Rapid Detection of Mycobacterium Tuberculosis Complex in Sputum Samples Using PURE TB-LAMP Assay. *The International Journal of Mycobacteriology*, **5**, S164-S165. https://doi.org/10.1016/j.ijmyco.2016.09.025

[32] Kadjo, H.A., *et al*. (2018) Epidemiology of Rubella Infection and Genotyping of Rubella Virus in Cote D'Ivoire, 2012-2016. *Journal of Medical Virology*, **90**, 1687-1694. https://doi.org/10.1002/jmv.25252

[33] Yéo, A., *et al*. (2019) Establishment of a Gonococcal Antimicrobial Surveillance Programme, in Accordance with World Health Organization Standards, in Côte D'Ivoire, Western Africa, 2014-2017. *Sexually Transmitted Diseases*, **46**, 179-184. https://doi.org/10.1097/OLQ.0000000000000943

[34] Goualié, B.G., Akpa, E.E., Kakou-N'Gazoa, S.E., Ouattara, H.G., Niamke, S.L. and Dosso, M. (2019) Antimicrobial Resistance and Virulence Associated Genes in Campylobacter Jejuni Isolated from Chicken in Côte D'Ivoire. *The Journal of Infection in Developing Countries*, **13**, 671-677. https://doi.org/10.3855/jidc.11355

[35] Sévédé, D., Doumbia, M., Kouakou, V., Djehiffe, V., Pineau, P. and Dosso, M. (2019) Increased Liver Injury in Patients with Chronic Hepatitis and IgG Directed against Hepatitis E Virus. *EXCLI Journal*, **18**, 955-961.

[36] Doumbia, M., *et al*. (2021) Viral and Bacterial Factors of Mother-to-Child Transmission of Hepatitis B Virus. *Journal of Viral Hepatitis*, **28**, 1683-1689. https://doi.org/10.1111/jvh.13607

## Abreviations' List

| | |
|---|---|
| ASSURMI | Unit for Antibiotics, Natural Substances and Surveillance of Resistance of Microorganisms to Anti-infectives |
| CHU | University hospital center |
| COUSP | Public health emergency operations center |
| VH | Veterinary health department |
| DVE | Epidemic Virus Department |
| ECOWAS | Economic Community of West African States |
| FSU | Urban health facility |
| GHSA | Global Health Security Agenda |
| INHP | National Institute of Public Hygiene |
| IHR | International Health Regulations |
| INSP | National Institute of Public Health |
| IPCI | Institute Pasteur deCôte d'Ivoire |
| KRI | Robert Koch Institute |
| LDR | Light Dependent Resistor |
| NRL | National Reference Laboratory |
| NRC | National Reference Center |
| PASRES | Strategic Support Program for Scientific Research |
| PSM | Microbiological safety cabinet |
| RIIP | International Network of Pastoral Institutes |
| RHC | Regional hospital centers |
| RIISIN | Ivorian network for the investigation and surveillance of nosocomial infections |
| STI | Sexually transmitted infections |
| TWG | Technical working group |
| WHO | World Health Organization |